Recent synthetic applications of the dealkoxycarbonylation reaction. Part 2. Dealkoxycarbonylations of β-keto esters, α-cyanoesters and related analogues

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Abstract
In Part 2, the synthetic applications of dealkoxycarbonylations of β-keto esters, α- cyano esters and related activated esters will be reviewed for the period 1981 to the middle of 2006. In Part 1, the dealkoxycarbonylations of malonate esters were reviewed for this same period.

Keywords: Dealkoxycarbonylations, decarbalkoxylations, Krapcho, β-keto esters, α-cyano esters, activated esters

Contents

1. Introduction

In Part 1, the synthetic applications of the dealkoxycarbonylations of malonate esters were presented. In Part 2, the synthetic applications of the dealkoxycarbonylations of β-keto esters, α-cyano esters and related activated ester derivatives will be illustrated with selected examples. The literature search covers the period 1981 throught mid 2006 and complements our prior review.[1]

2. Ketones

### 2.1. From monosubstituted β-keto esters
2.1.1. Water alone

As noted in our previous review,[1] dealkoxycarbonylations of mono substituted β-keto esters (or the corresponding enols) can be effected on heating in DMSO and water without the addition of salts. Additional examples of this methodology have been reported.

Treatment of cis-**1a** (n = 1) with DMSO and water (150°C, 15 h) led to cis-**2a** (68%, n = 1), the product from the decarbomethoxylation of the β-keto ester moiety. Analogue cis-**1b** (n = 2) in DMSO and water (140°C, 2 h) afforded cis-**2b** (80%).[2]

1   a, n = 1; b, n = 2   2
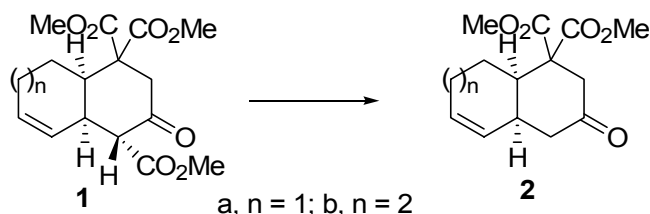
In routes to several sex pheromones of the peach fruit moth and the Douglas fir tussock moth, decarbomethoxylations of several long chain β-keto esters were investigated. Treatment of **3a,b,c**   with DMSO and water (150°C, 3.5 h) led to the products **4a,b,c** in yields of 80%.[3]

a, x = 7, y = 5 ; b, x = 8, y = 5; c, x = 9, y = 4
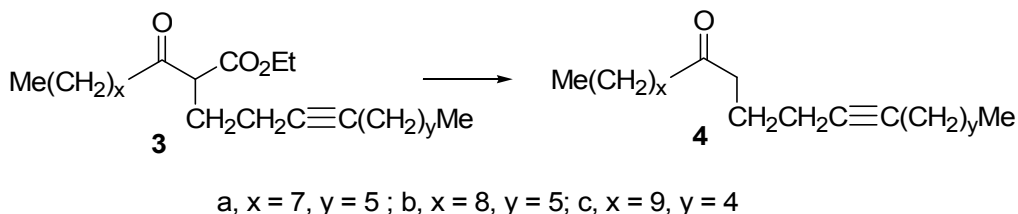
Brief microwave irradiation of mono-alkylated β-ketoesters at 160-200 °C in wet DMF induced smooth and selective decarboalkoxylations. For example, treatment of **5** with DMSO and water (160°C, 3 min) under microwave irradiation led to **6** (89%).[4]

OPG = Si(-Pr)$_2$(CH$_2$CH$_2$C$_8$H$_{17}$)
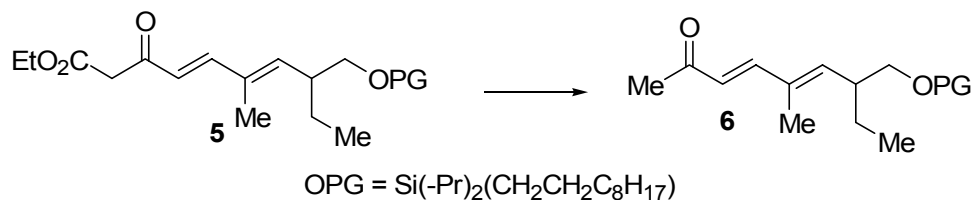
The deethoxycarbonylation of **7a,b** in wet DMSO (reflux, 4 h) afforded **8a** (44%) or **8b** (66%), respectively.[5]

a, R = CH$_3$ (44%)
b, R = C$_6$H$_5$ (66%)
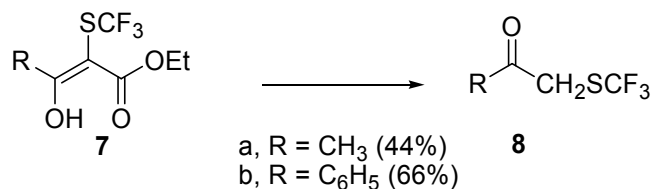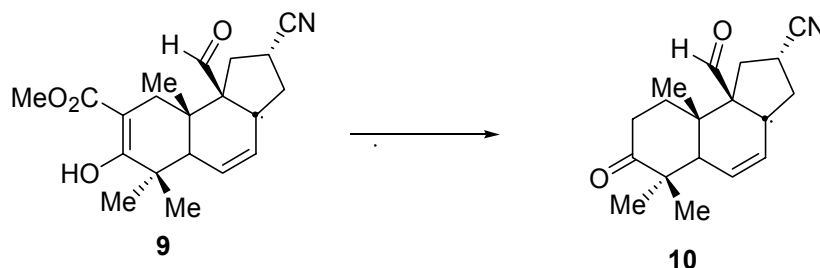
The demethoxycarbonylation of enantiomer **9** in DMSO and water (155°C, 2.5 h) led to the enantiomeric tricycle **10** (92%).[6]


2.1.2. Water-salts
2.1.2.1. From alkyl, aryl, heterocyclic and heteroaryl substituted open chain substrates. A number of optically active acetoacetates were alkylated on a solid support (Al$_2$O$_3$, t-BuOH) with alkyl bromides and the products subjected to dealkoxycarbonylations using LiCl in DMSO. For example, derivative **11** led to **12** with an optical purity of 13% (S-configuration).[7]
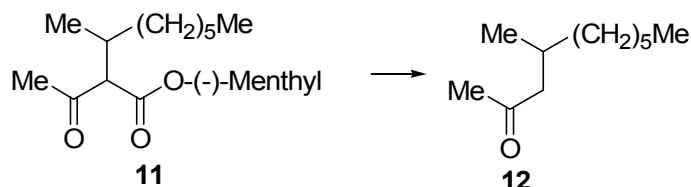
Keto ester **13** on treatment with DMSO, NaCl and water (70°C, 12 h) led to (+)-**14** in good yield. This intermediate was easily converted into the alkaloid (+)-pinidine. [8]
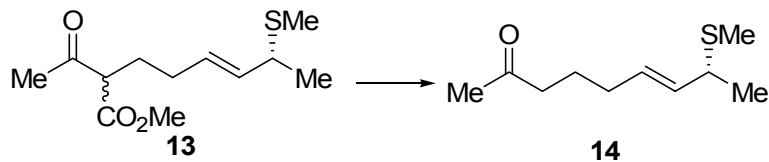
The β-keto ester **15** on heating in DMF, NaCl and water (reflux, 72 h) led to **16** (88%), which was converted into a octahydropyridopyrrolizine-2-(1H)-one.[9]
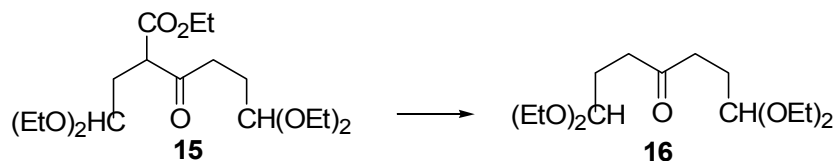
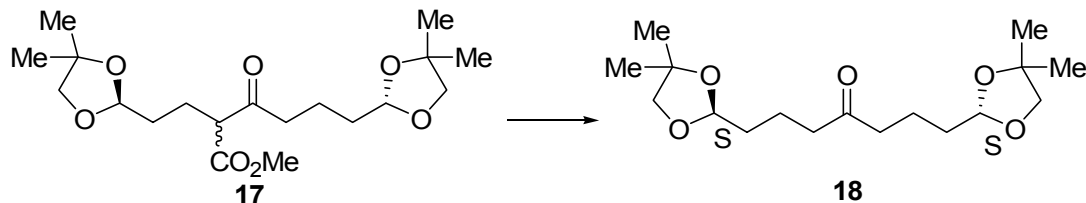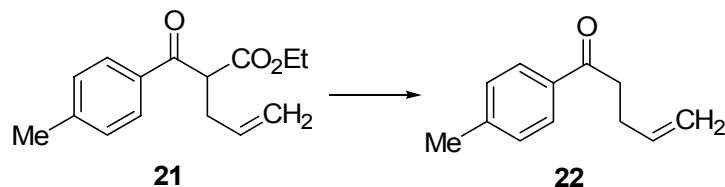The decarbomethoxylation of **17** using DMSO, LiCl and water (reflux, 10 min) led to the C-2 symmetrical ketone **18** (94%).   This intermediate could be readily transformed into the corresponding enantiomeric spiroketal on treatment with aqueous acetic acid.[10]

The decarbomethoxylation of **19** with DMSO, LiCl, and water (190°C, 40 min) provided the C_2-symmetric ketone **20** (3*E*,5*S*,9*S*,10*E*) (96%). This ketone on asymmetric syn- dihydroxylation and acid catalysis led to a mixture of dioxaspiro[5,5]undecane and dioaxospiro[4,5]decane.[11]
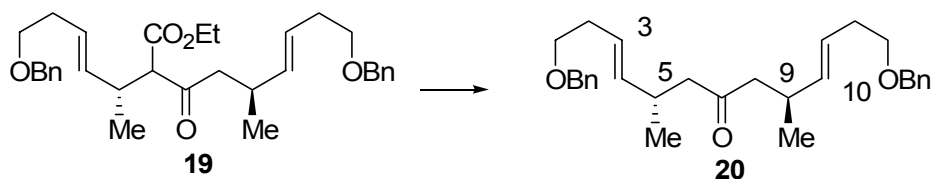
A number of ω-alkenyl ketones have been prepared by deethoxycarbonylation of the appropriate β-keto esters. For example, treatment of **21** with DMF and LiBr (195-200°C, 3 d) led to **22** (67%).[12]

Treatment of **23** (isomeric mixture) with DMSO, NaCN (90°C, 22 h) led to **24** (70%) as an isomeric mixture. This intermediate was used in the synthesis of estrone derivatives.[13]
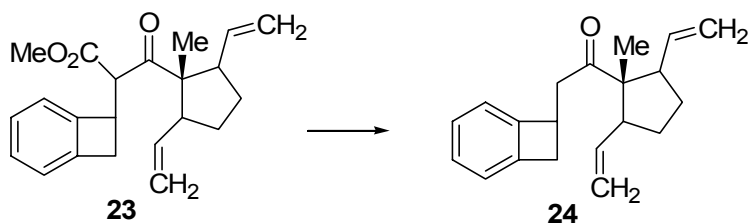
The deethoxycarbonylation of **25** was accomplished using DMSO, LiCl and water (160°C, 24 h) to yield **26** (83%). This was converted into an acerogenin-type diaryl heptanoid holding an endocyclic biaryl ether bond.[14]

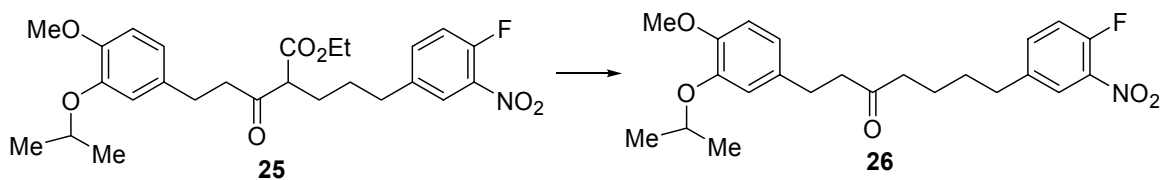The chemoselective demethoxycarbonylation of the β-keto ester **27** was accomplished by treatment with DMSO, NaCl and water (125°C, 24 h) to afford optically active **28** (78%), which in a subsequent series of steps could be converted into (-)-virantmycin.[15]
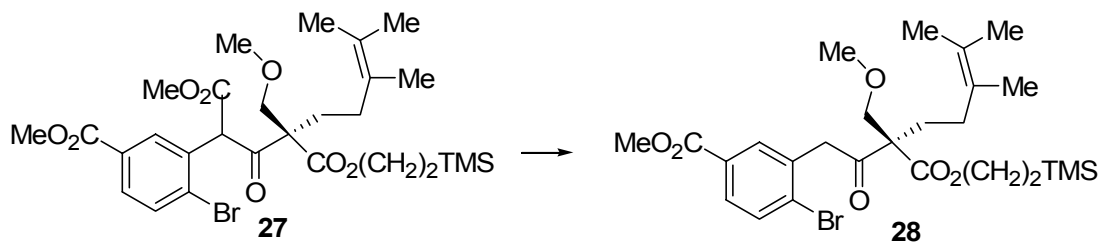
In a pathway to racemic chrysolic acid, the deethoxycarbonylation of **29** with DMSO, NaCN and water (140-150°C, 10 h) led to intermediate **30** (60%).[16]
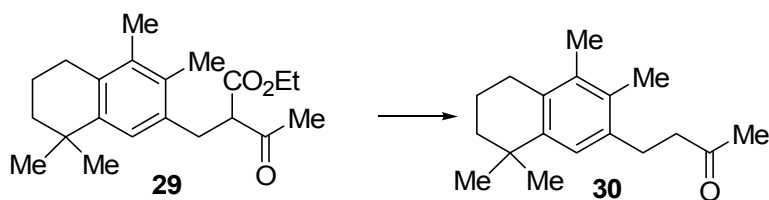
Treatment of **31** with DMSO, NaCl and water (135°C, 8 h) led to **32** (82%), isolated as the HCl salt.[17]
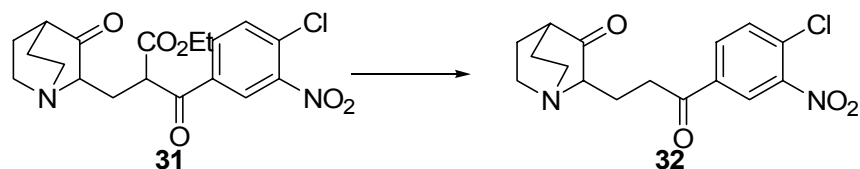
Treatment of keto ester **33** with DMSO, NaCl and water (150°C, 2 h) led to ketone **34**(70%).[18]

The enantiomeric β-keto ester **35** on treatment with DMF, NaCl and water (reflux, 9 h) led to the de-t-butoxycarbonylated pyrrolidine **36-**(3R) (92%). The stability of the BOC group under the reaction conditions is of particular note.[19]

Treatment of β-keto ester **37** with DMSO, NaCl and water (135°C, 2 h) led to **38** (80%). This intermediate was converted into 1,6-dideoxynojirimycin (a polyhydroxy piperidine) in a series of subsequent steps.[20]
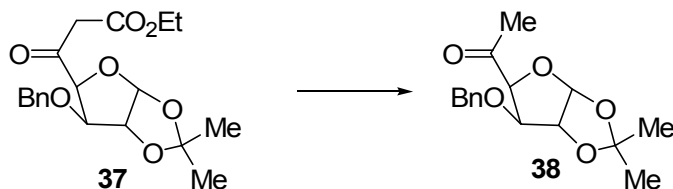
A mixture of enol **39** and the corresponding β-keto ester in DMSO, NaCl and water (150-160°C, 5 h) afforded the flavanoid **40** (89%).[21]
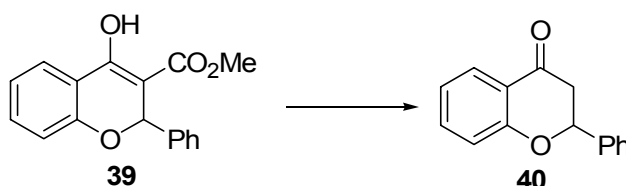
The deethoxycarbonylation of **41** was accomplished by heating in DMSO, NaCl and water (150-160°C, 8 h) to afford **42** (42%).[22]
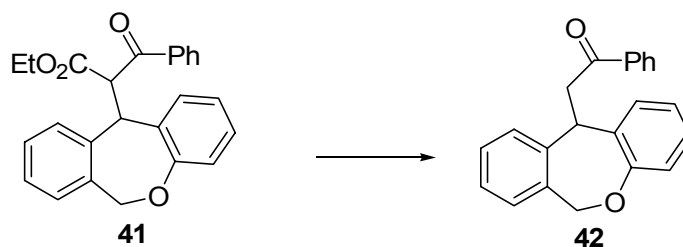
The synthesis of (-)-secodaphniphylline (**44**) (44%, 99.6% ee) has been accomplished by heating β-keto ester **43** with NaCN in DMSO containing a few drops of water (150°C, 2 h).[23]
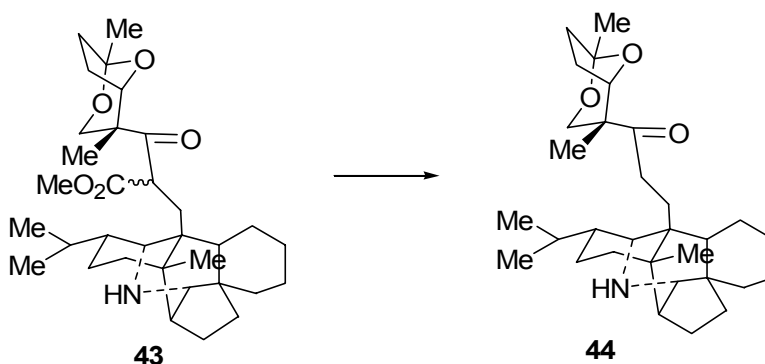
Treatment of **45** (and the enol tautomer) with DMSO, NaCl and water (150°C, 5 h) led to the ethyl thiazole-5-carboxylate **46** (47%).[24]
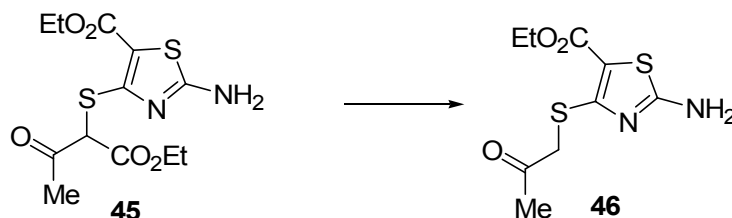
2.1.2.2. From fluoro substituted substrates. In a general method for the preparation of trifluoromethyl ketones, derivatives **47** on treatment with DMF, LiCl and water (reflux, 2 h) led to the ketones **48** (38-90%).[25a,b]

R = *n*-octyl, benzyl, CH₂CH₂Ph, C₆H₅CH=CHCH₂
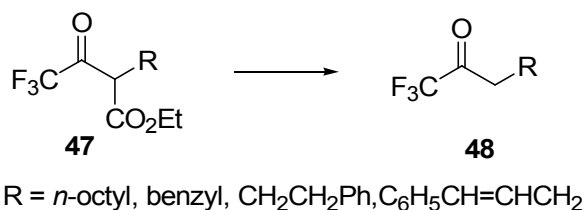
Treatment of **49** with DMSO, NaCl and water (150-160°C, 15 min) led to the loss of a methoxycarbonyl group to afford the fluoro keto ester **50** (32%).[26]
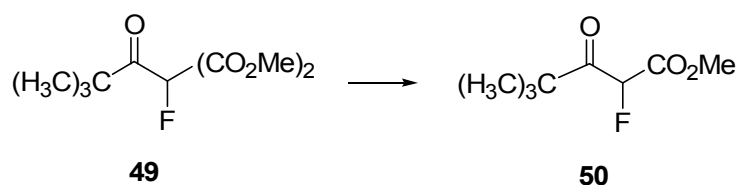
2.1.2.3. From carbocylic β-keto esters. The β-keto ester **51** on treatment in DMF with LiI (reflux, 2 h) led to **52** (76%), an intermediate used in an attempted approach to the sesquiterpene quadrone.[27]
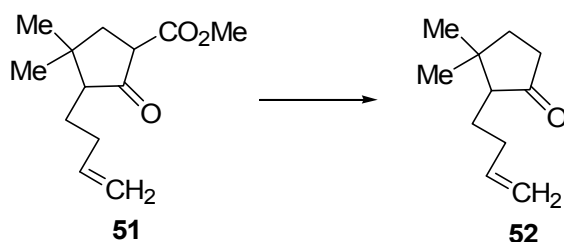
A mixture of **53a** and **53b** was treated with DMSO, LiCl and water (120-130°C, 3 h) to afford a mixture of optically active **54a** and **54b** (64%, ratio 2.45:1).[28]
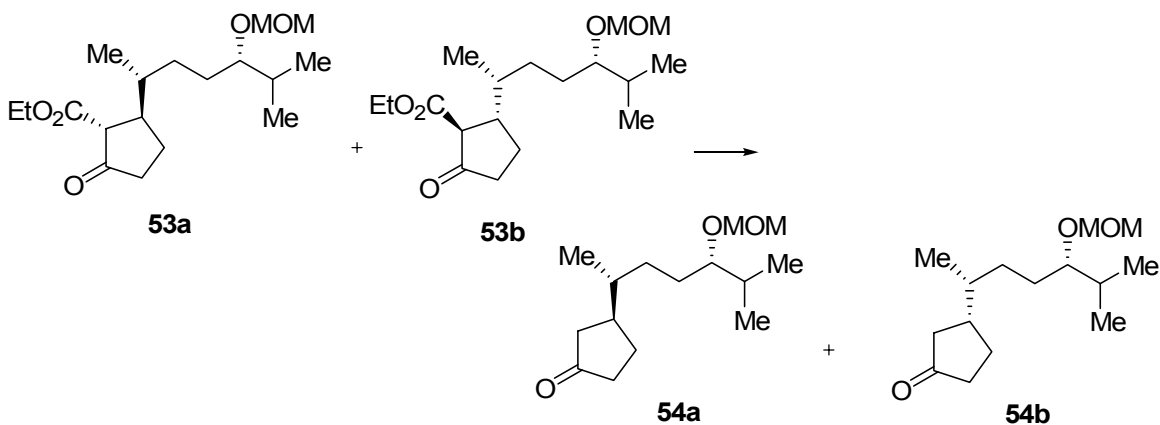
Treatment of chiral **55** with DMSO and NaI (100°C, 3 h) led to the (-)-**56** (3S, 4S) (89%). This intermediate was subsequented converted into cuparene, laurene, (-)-α- and (+)-β-cuparenones.[29]
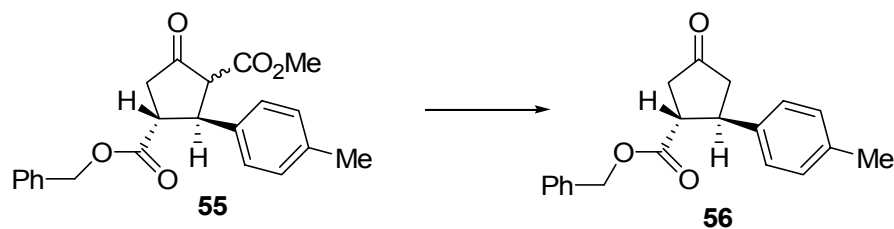
The synthesis of (+)-**58** (69%) was accomplished by heating **57** in DMSO, NaCl and water (165°C, 45 min). This intermediate was converted into (+)-estrone methyl ether.[30]
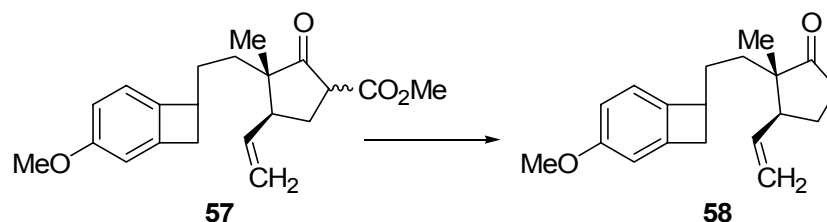
Upon heating β-keto ester **59** in DMSO, LiCl and water (190°C, 2 h), the α,β-unsaturated ketone **60** (73%) was obtained. This intermediate was subsequently transformed into cis-jasmone.[31]
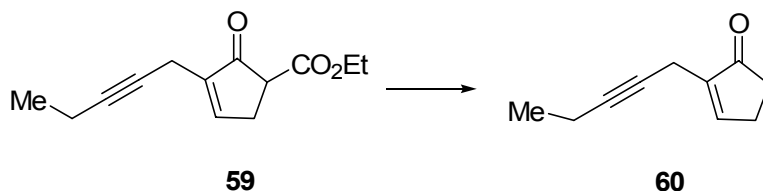
The bis-silylated keto ester **61** on treatment with DMSO, NaCl and water (130-150°, 3 h) led to the decarbomethoxylated product **62** (86%).[32]

Tol = 4-MePh
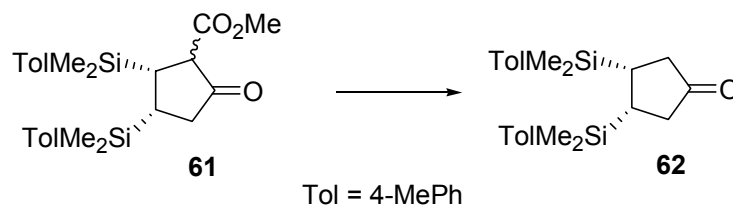
Treatment of rac-**63** with DMSO, LiCl and water (reflux, 5 h) led to rac-**64** (40%) which was used in a synthesis of (-)-norgestrel.[33]
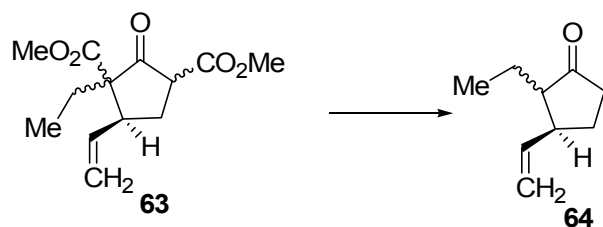
Treatment of **65** with DMSO, NaCl and water (reflux, 5 h) led to a mixture of **66a**:**66b** (69%).[34]
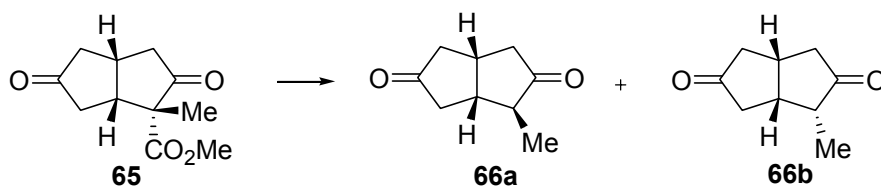
Treatment of **67** with DMSO, LiCl and water (145°C, quickly to room temperature) led to racemic **68** (96%) which was used in a synthesis of racemic silphinene.[35]
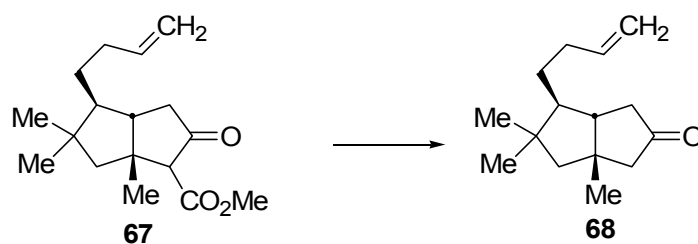
Treatment of **69** with DMSO, NaCl and water (150°C, 6 h) afforded (-)-**70** (86%) which in a series of steps could be converted into (+)-capnellene.[36]
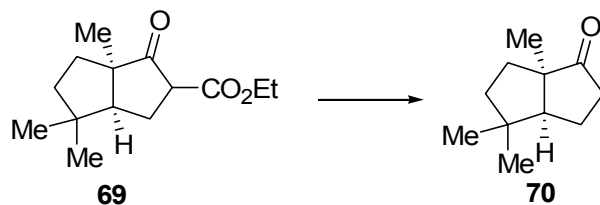
Treatment of enolic triester **71** with DMSO, NaCl and water (140°C, 2 h) led to keto diester **72** (92%). This was used as an intermediate in the synthesis of tricyclo octane structure.[37]
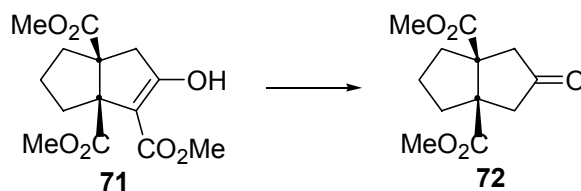
The demethoxycarbonylation of **73** was accomplished by heating in DMSO, NaCl and water (85°C, 19 h) to afford racemic **74** (62%). This was subsequently converted into the cedrenoid sesquiterpenes racemic α-biotol and β-biotol. [37a] Other similar conversions have also been reported.[38b,c]
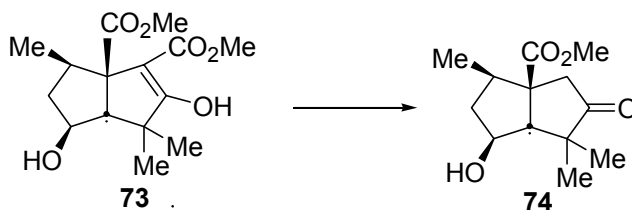
Enantiomerically pure **75** on treatment with DMSO and water (155°C, 2.5 h) led to the deethoxycarbonylated ketone **76** (1*R*,6*R*) (92%). Attempts to convert this ketone into (+)-papuamine, a pentacyclic alkaloid isolated from a sponge, were not successful.[39]
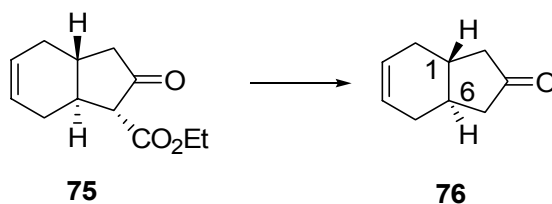
Treatment of **77** with DMSO, LiCl and water (120-140°C, 2 h) led to (3aR,7*a*R)-**78** (91%). This ketone was subsequently converted into (+)-grindelic acid in a 10-step sequence.[40]
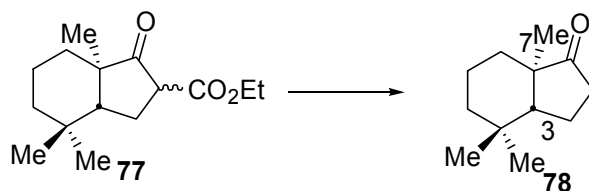
The dealkoxycarbonylation of **79** using DMSO, LiCl and water (reflux, 30 min) led to the removal of the protective group with formation of the keto diol **80** (78%).[41]
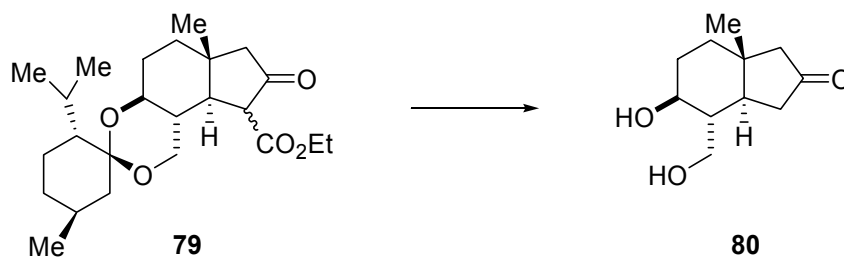
Treatment of **81** with N-methylpyrrolidone, LiCl and water (120-125°C, 6 h) led to **82** (70%), used in a synthesis of racemic strigol, a seed germination stimulant.[42]
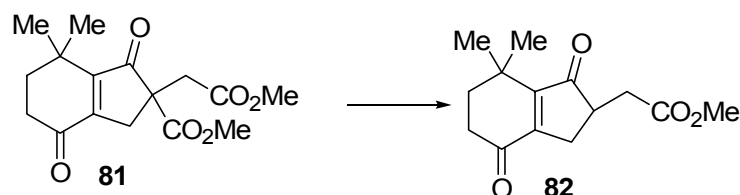
Treatment of **83** (THF = 2-tetrahydrofuranyl) with DMSO-LiCl, sodium bicarbonate and water (150°C, 3 h) led to racemic product **84** (92%), which was converted into a intermediate for the synthesis of racemic perhydrohistrionicotoxin.[43]
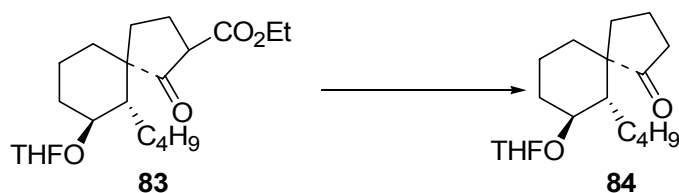
The demethoxycarbonylation of **85** (and the enol tautomer) with DMSO, LiCl and water (165-170°C, 8 h) led to **86** (67%) in which the tertiary ester was also hydrolyzed to the carboxylic acid.[44]
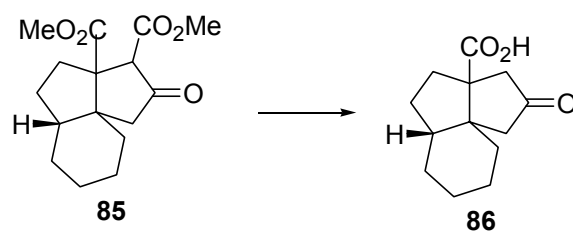
The demethoxycarbonylation of β-keto ester **87** with DMSO, NaCl and water (150°C, 8 h) led to **88** (88%) which was used in a synthetic pathway to several natural tricyclic sequiterpenes.[45]
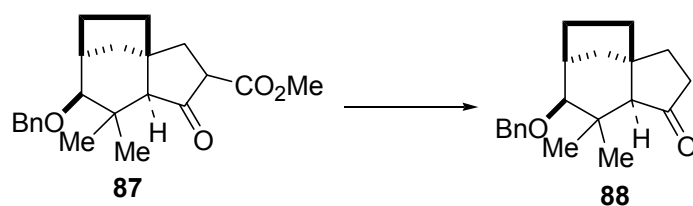
The β-keto ester **89** and DMSO, NaCl and water (110°C, 16 h) yielded **90** (72%), which could be converted into other functionalized tricycloundecanes.[46]
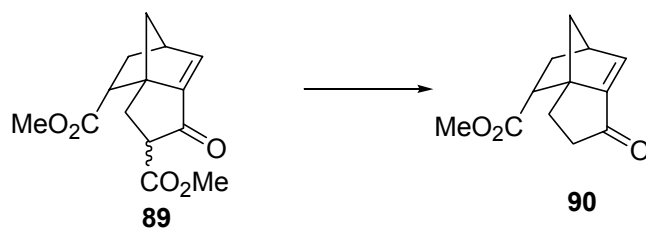
The deethoxycarbonylation of **91** with DMSO, NaCl (70°C, 3 h) led to (-)-**92** (73%, for 2 steps with prior CrO$_3$ oxidation of alcohol to the ketone), a common intermediate utilized in the synthesis of the indole diterpenes (+)-paspalicine and (+)-paspalinine.[47]
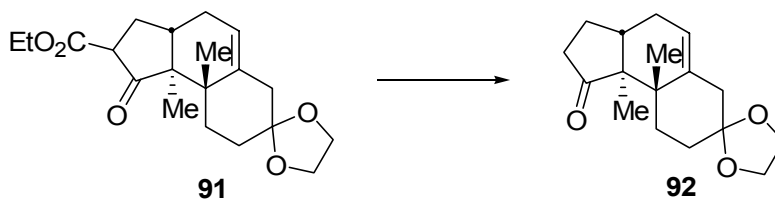
Treatment of racemic **93** with DMSO, LiCl and water (170°, 1.25 h) led to racemic **94** (92%).[48]
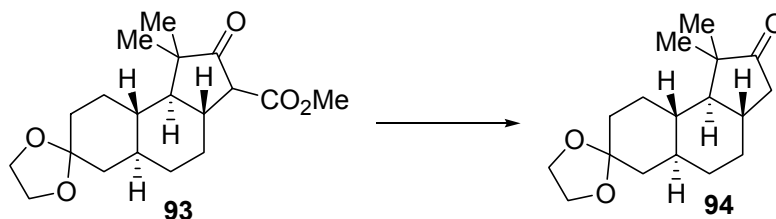
Treatment of **95** with DMSO, NaCl and water (150°C) led to **96**, used in a synthesis of a racemic capnellene.[49]
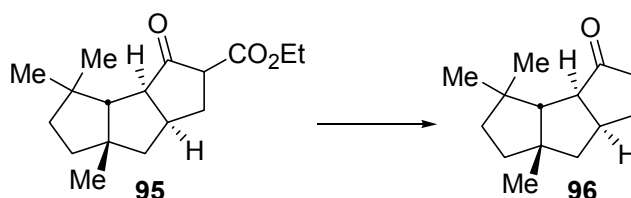
The deethoxycarbonylation of **97** with DMSO, MgCl$_2$ hexahydrate (140°C, 28 h) led to racemic **98** (74%) with the α-trisubstituted ester intact. Ester **98** was utilized in a synthesis of the sequiterpenes cedranediol and cedranoxide.[50]
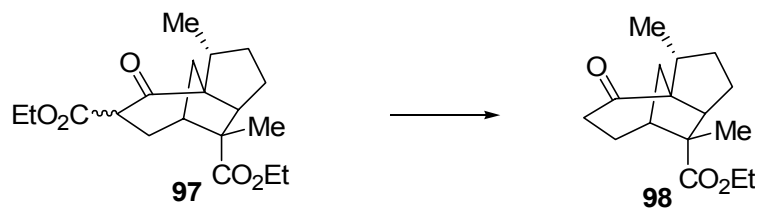
A 12:1 mixture of **99a** and **99b** on treatment with DMSO, NaCl and water (reflux, 24 h) led to **100** (*S*) (83%ee) (59%).[51]

R = (-)-phenylmenthyl
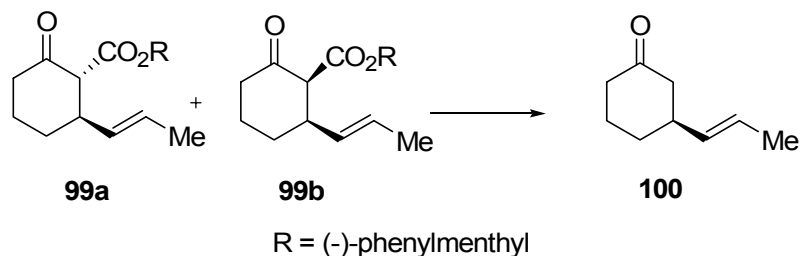
Treatment of **101** with DMSO and water (130°C, 24 h) led to the demethoxycarbonylation product **102** (2*S*, 1*R*) (99%) which in a number of steps could be converted into (-)-epibatidine, an alkaloid isolated from the skin of a Ecuadorian frog and exhibiting potent activity as a nonopiate analgesic.[52]
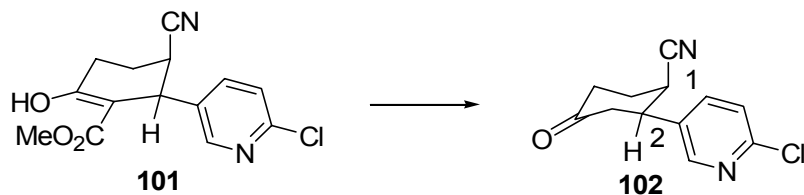
Treatment of optically active **103** with DMSO, NaCl and water (180-185°C, 3.5 h) led to (3*S*)-**104** (79%).[53]
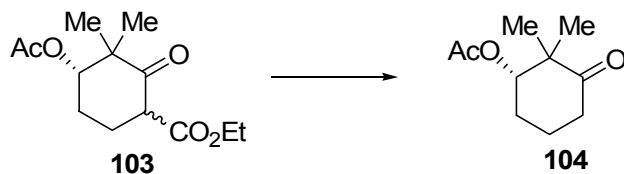
The β-keto ester **105** underwent decarbomethoxylation when treated with DMSO, NaCl and water (150°C, 4.5 h) to yield racemic β-vetivone **106** and racemic epi β-vetivone (1.7:1 ratio) (77%), which could be separated by column chromatography[54].

105   **106**

The spiro β-keto ester **107** on treatment with DMSO, NaCl and water (130°C, 2 h) led to the (1*R*,5*R*) spiro[4,5]decan-7-one (**108**, 70%).[55]

107   **108**
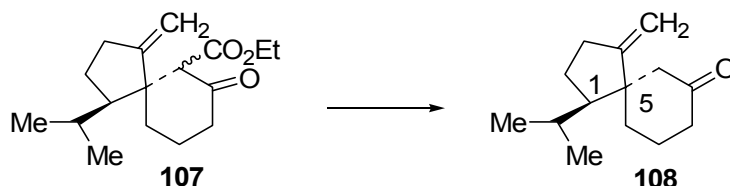
Treatment of **109** with DMSO and water (115-120°C, 3 h) gave **110** (73%).[56]

109   **110**
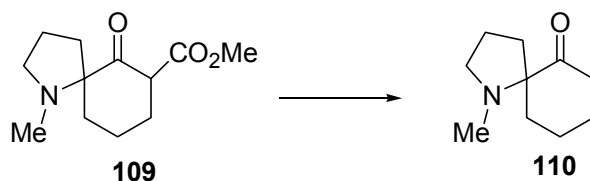
Treatment of **111** (and the enolic tautomer) with DMSO, NaCl and water (140°C, 4 h) led to homothujone **112** (as a mixture of α- and β-diastereoisomers in a 10:1 ratio).[57]

111   **112**
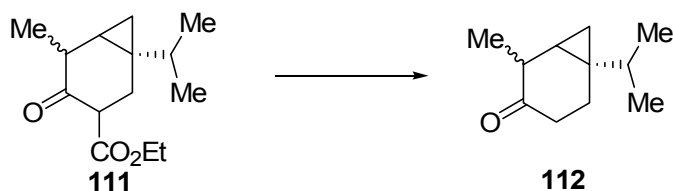
Treatment of enol **113** with DMSO, LiCl and water (150°C, 4 h) led to **114** in a quantitative yield, which was utilized in a synthesis of a benzindene prostacyclin analogue.[58]

113   **114**
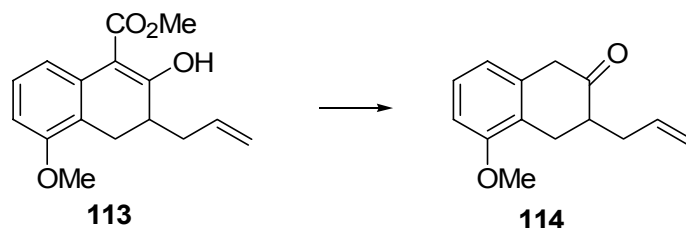
Treatment of **115** with DMSO, NaCl and water (heat) led to **116** (47%).[59]

115   **116**
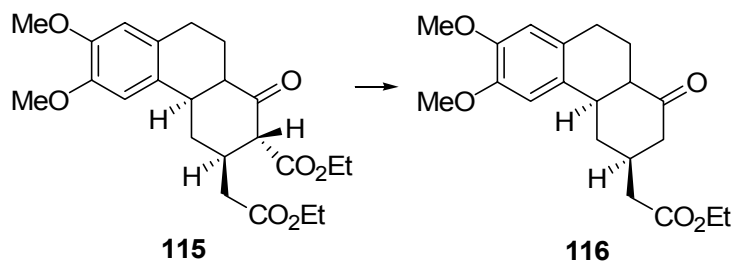
In a study dealing with thromboxane A_2 analogues, it was reported that treatment of crude **117** (obtained as two regioisomers via a ring expansion of a prostaglandin intermediate with ethyl diazoacetate) with DMSO, NaCl and water (150°C, 2 h) led to optially active **118** (52%).[60]

117   **118**
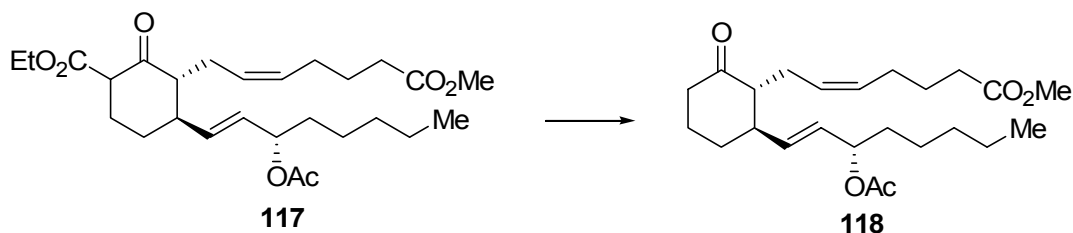
In the total synthesis of tetracyclic Lycopodium alkaloids, the intermediate **120** was prepared by treatment of **119** with NaCl in DMF (no conditions or yield).[61]

119   **120**
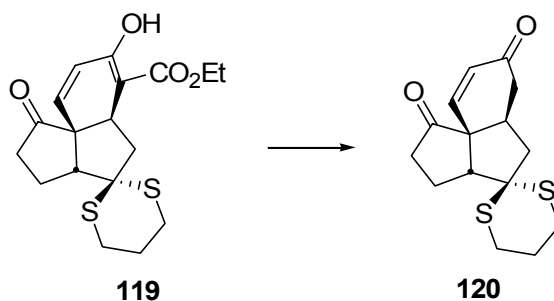
Treatment of β-keto ester **121** with DMSO, NaCl and water (160°C, 6 h) led to **122** (85%) which was used in a synthesis of racemic isoclovene, a tricyclic ketonic sesquiterpene.[62]

121   **122**
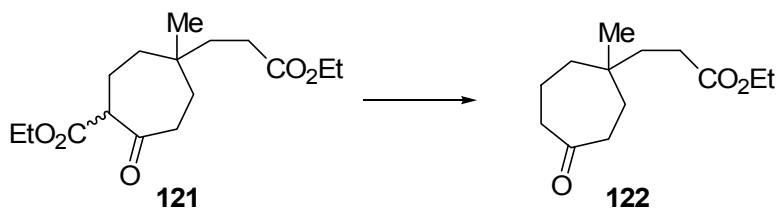
Treatment of a number of bicyclic β-keto esters with DMSO, NaCl and water led to the corresponding deethoxycarbonylated products. As an illustration, **123** on treatment with DMSO, NaCl and water (reflux, 2 h) led to chiral **124** (1*S*, 6*S*, 7S, 9*R*, 10*R*) (86%), used in a route leading to an enantiospecific synthesis of clavukerin A, a trinorguaiane sesquiterpene.[63]
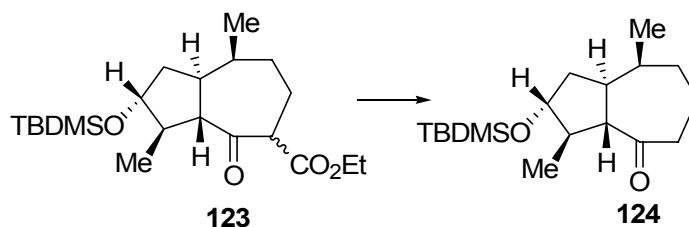
Treatment of **125** with DMSO, NaCl and water (140°C, 0.5 h) led to **126** (82%).[64]
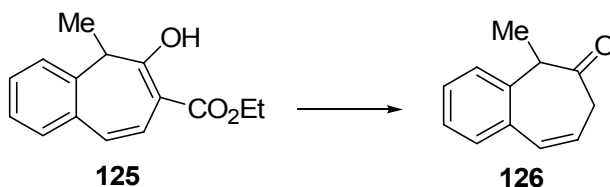
Treatment of **127** with DMSO, LiCl and water (175°C, 3 h) led to racemic **128** (86%) which in a subsequent series of steps was converted into the furano sesquiterpene dihydropallescensin.[65]
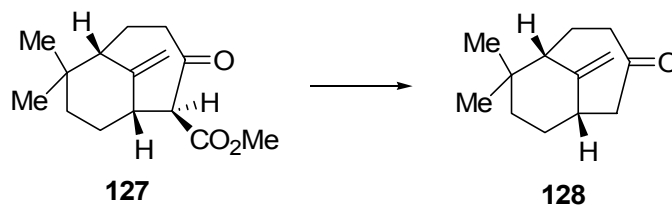
The deethoxycarbonylation of **129** with DMSO, NaCl and water (160°C, 3 h) led to **130** (quantitatively). This key intermediate, in a series of steps, was converted into the sesquiterpene, racemic isoclovene.[66a,b]
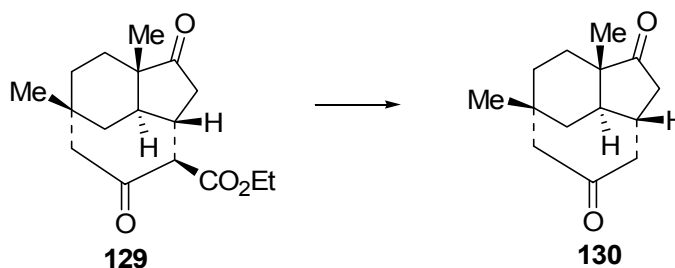
The deethoxycarbonylation of **131** with DMSO, NaCl and water (150-160°C, 6 h) led to the hexacyclic dione **132** (56%).[67]

131   **132**
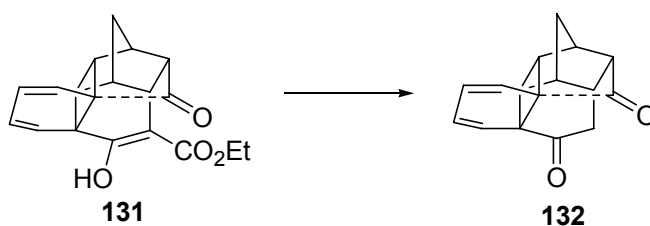
The deethoxycarbonylation of **133** with DMSO, NaCl and water (150°C, 4 h) led to **134** (91%).[68]

133   **134**
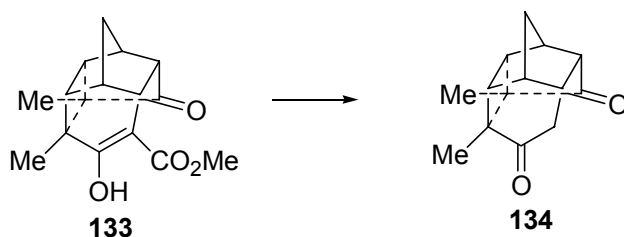
The deethoxycarbonylations of a mixture of chiral **135a** and **135b** with DMSO and water (165°C, 4 h) led to (*R*)-(-)-muscone (**136,** 59%).[69]

135a   **135b**   **136**
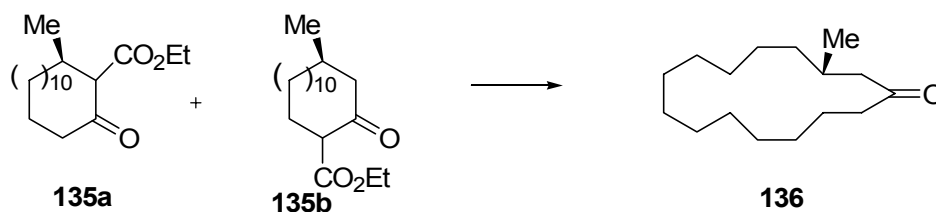
In synthetic routes to m-pyrrolophanes, the β-keto ester **137** on treatment with DMSO, NaCl and water (180-190°C, 1.5 h) led to ketopyrrole **138** (91%).[70]

137   **138**
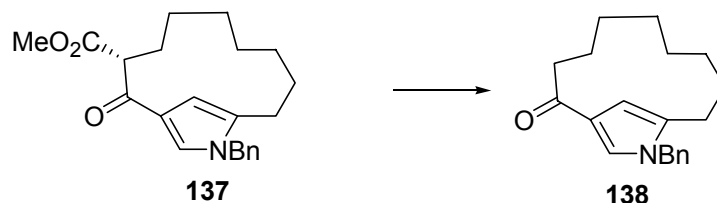
2.1.2.4. From heterocyclic β-keto esters. Treatment of macrocycle **139** with DMSO, LiCl and water (reflux, 1 h) led to **140** (78%), which was used in a synthesis of glucosporone, an autoinhibitor of spore germination.[71]

139   **140**
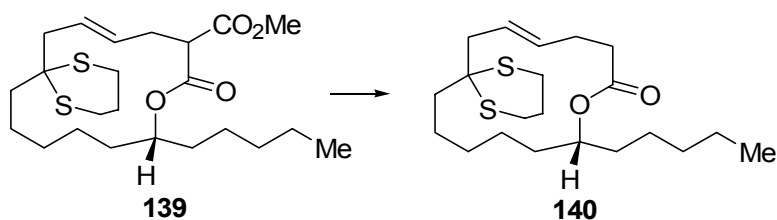
The lactone **141** on treatment in DMF with LiBr (reflux, 8 h) led to racemic **142** (90%) used in a synthesis of the male sex pheromones of Carribean and Mexican fruit flies.[72]

141   **142**
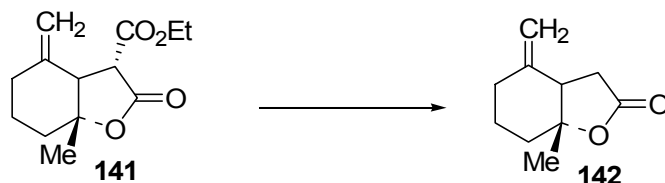
Treatment of lactone **143** with DMSO, NaCl and water (110°C) led to **144** (83%), which in a subsequent series of steps could be converted into racemic Corey's lactone.[73]

143   **144**
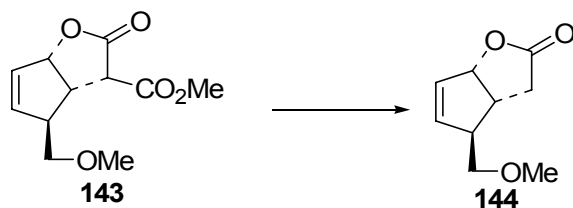
Treatment of (R)-**145** with refluxing aqueous DMF for 12 h led to lactone (R)-**146** (99%ee) in good yield.[74]

145   **146**
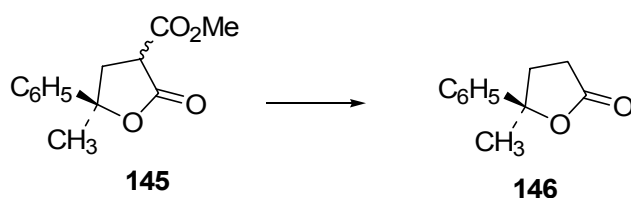
Treatment of **147** with DMSO, LiCl and water (100°C, 24 h) led to racemic **148** (85%) which was used in the synthesis of the partial ring skeleton of the ginkolides.[75]

147   **148**
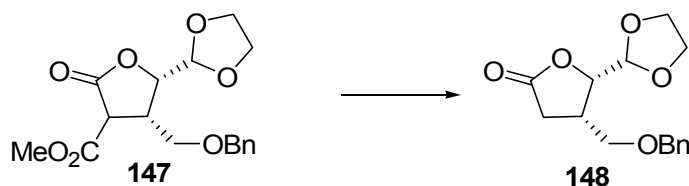
Treatment of **149** with DMSO, NaCl and water (180°C, 50 min) afforded **150** (95%) which were used in a synthesis of guaianolides and related derivatives.[76]
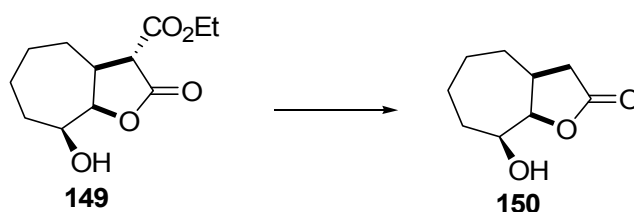
Lactam **151** on treatment with DMF, NaCl and water (heat, 12 h) led to **152** (40%) and ring opened product **153** (29%).[77]
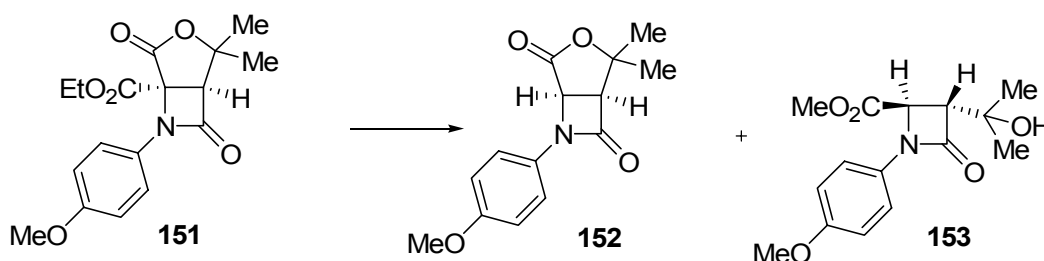
The dealkoxycarbonylation of **154** (where R* is a chiral appendage) with DMSO, NaCl and water at reflux led to (S)-**155** (84%).[78]
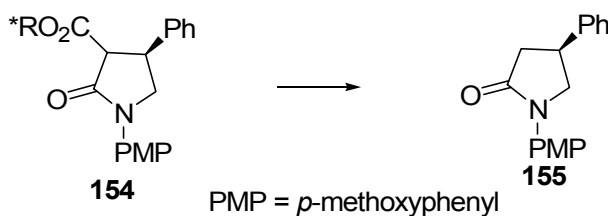
The deethoxycarbonylation of the β-keto ester **156** in DMSO, NaCl and water (130-135°C, 20 h) led to a crude product which on chromatography gave enantiomer **157** (36%).[79]
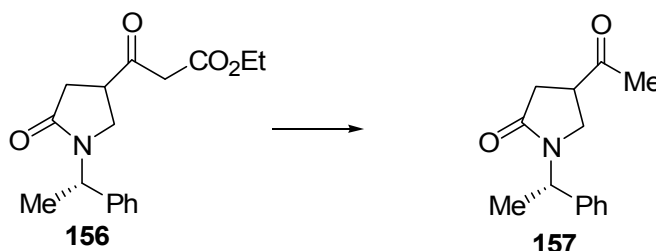
The optically active ester lactams **158a** and **158b** on treatment with DMSO, NaCl and water (150°C, 28 h) led to **159a** and **159b** in good yields. In **158c,** a similar procedure led to the desired product **159c** along with some mono-desilylated product in a 1:4.3 ratio.[80]

a, R = Ph; b, R = CH₂Ph; c, R = 4-MeOPh
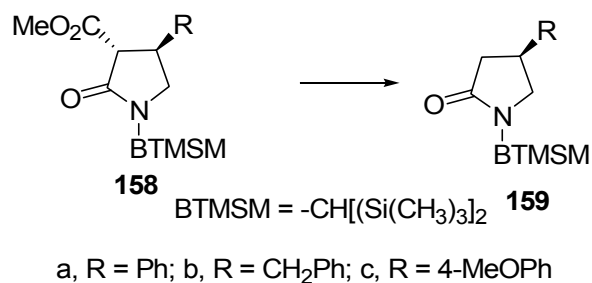
Treatment of a number of 4-ethoxycarbonyl-N-substituted pyrrolidin-3-ones with DMSO, NaCl and water led to the corresponding decarbethoxylation products. For example treatment of **160a** or **160b** with DMSO, NaCl and water (130°C) led to **161a** (81%) or **161b** (83%), respectively.[81]

a, R = H; b, R = *n*-C₅H₁₁
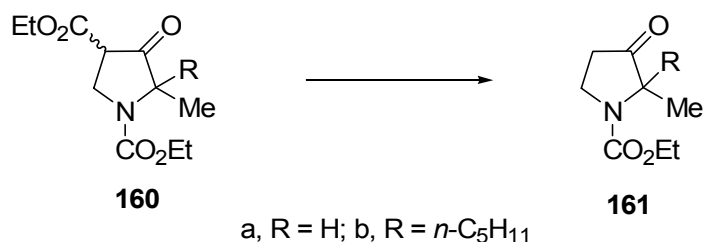
A key 4-substituted 2-pyrrolidone intermediate **163** (97%, which after crystallization led to an optically pure sample (71%), was prepared by decarbomethoxylation of **162** (88%ee) on treatment with DMSO, NaCl and water (160°C, 2 h). This intermediate was converted into a phoshodiesterase type IV inhibitor (*R*)-(-)-rolipram.[82]
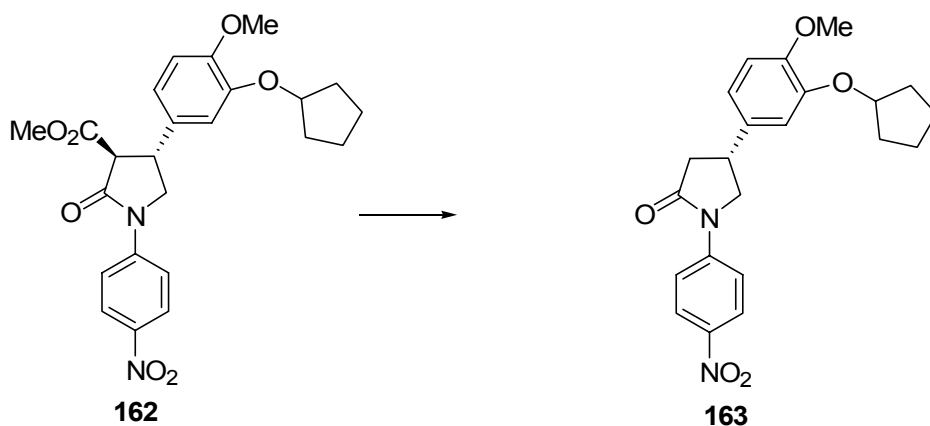
Treatment of the enol ester **164** with DMSO, NaCl and water (155-160°C, 3 h) led to the 3-oxo-2-piperidine-propionic acid **165** (78%). The intramolecular acylation of this analogue into the corresponding enol lactone was accomplished.[83]

164   **165**
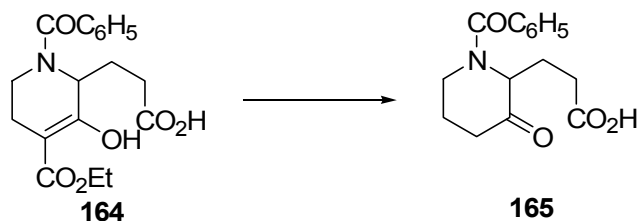
Enantiomer **166** with DMSO, NaCl and water (160-170°C, 1 h) led to enantiomer **167** (63%), an intermediate used in the study of the synthesis of (+)-sesbanimide.[84] In this case, perhaps the addition of salt might not be necessary.

166   **167**
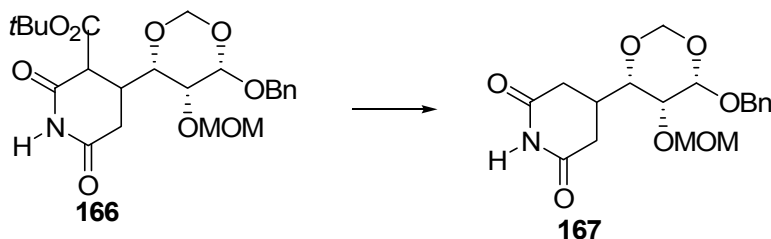
The deallyloxycarbonylation of substrate **168** with DMF, MgCl$_2$ hexahydrate and water (reflux, 20 h) yielded **169** (91%).[85]

168   **169**
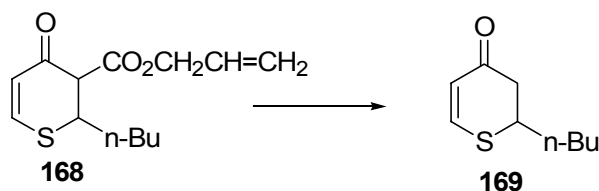
The decarbomethoxylation of **170** in DMSO, NaCl and water (155°C, 10 h) led to **171** (99%) which was converted into racemic pyrrolizidine alkaloid isoretronecanol.[86]

170   **171**
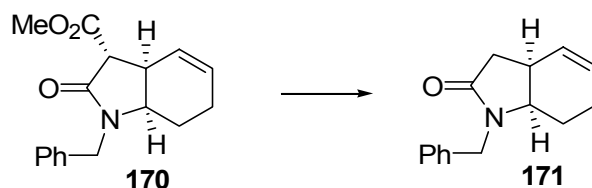
The decarbomethoxylation of a mixture of the enol esters **172** and **173** in DMSO, NaCl and water (130°C, 4 min) led to the indolizinone **174** (92%). Intermediate **174** was subsequently transformed in a series of steps into natural (+)-lentiginosine.[87]
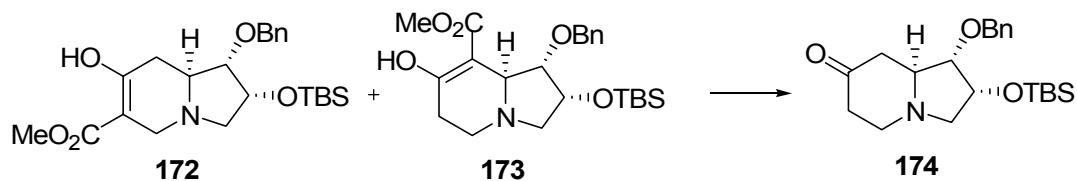
Treatment of **175** with DMSO, NaCl and water (155-160°C, 3 h) gave **176** (74%).[88]
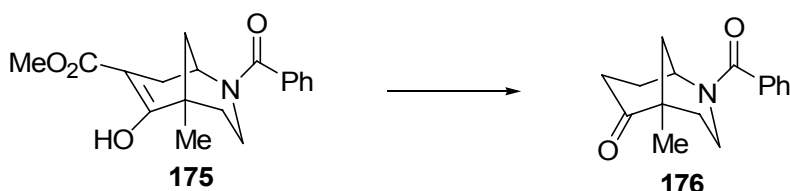
Treatment of (*R*)-**177** with DMSO, NaCl and water (140°C, 3 h) led to (*R*)-**178** (60%). However, the ee of (R)-**178** was only 0.5% which appeared to indicate that racemization had occurred in the demethoxycarbonylation step.[89]
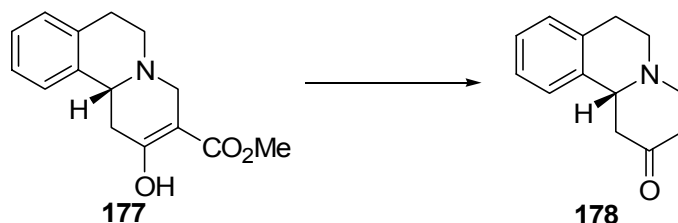
The decarbomethoxylation of (-)-**179** (and the enol form) with DMF, NaCl and water (130°C, 6 h) led to (-)-**180** (73%, >95%ee). A similar procedure on the enantiomer led to (+)-**180** These intermediates could then be converted into several indole alkaloids such as (-)-ajmaline.[90]
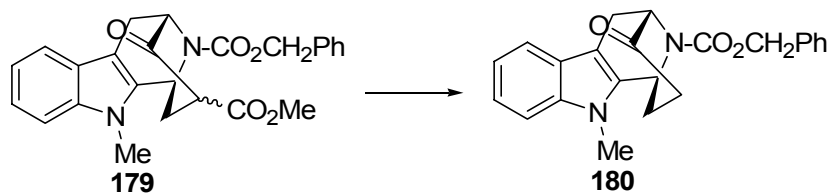
The demethoxycarbonylation of derivative **181** proved to be quite difficult. The best result was obtained by treatment of **181** with dry DMSO and LiI dihydrate (132°C, 36 h) to afford **182** (56%). The use of DMSO, NaCl and water at 180°C did not lead to demethoxycarbonylation.[91]
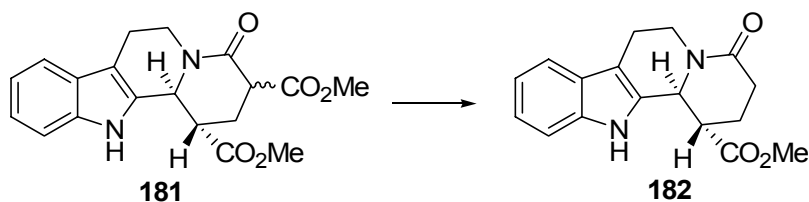
Treatment of ester **183** with DMSO, LiCl and water (160°C, 3.5 h) led to **184** (99%ee). This intermediate was converted into (+)-geissoschizine.[92]
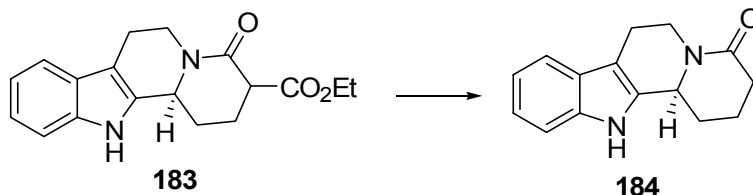
The decarbomethoxylation of of **185** with DMSO, LiCl and water (150°C, 25 min) led to **186** (98% ee), a known degradation product of vindoline.[93]
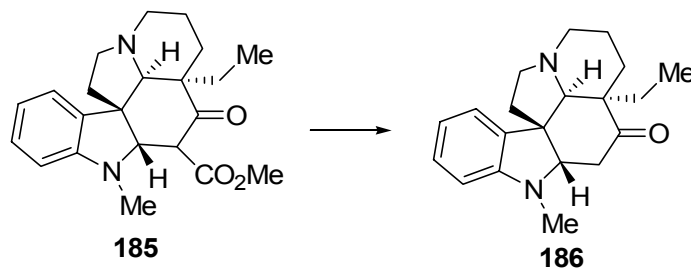
Keto ester **187** on treatment with DMSO, LiCl and water (reflux, 2.5 h) led to **188** (78%). A subsequent series of steps led to the racemic sesquiterpene davanone.[94]
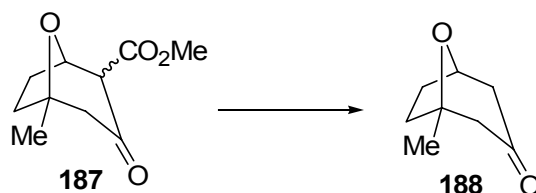
In approaches to the cladiellin skeleton, the intermediate **189** on treatment with LiCl, DMSO (130°C, 3 h) and water led to enantiomer **190** (86%).[95]

189   **190**
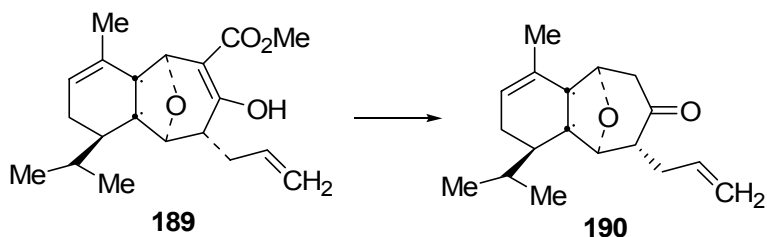
The preparation of enantiomer **192** (41%) was perfomed by heating **191** in dry DMF and LiI dihydrate (130°C, 2.5 h).[96]

191   **192**
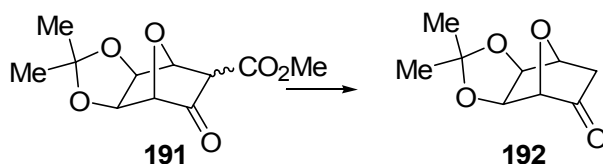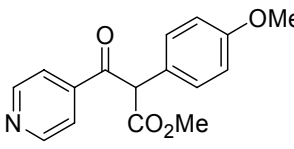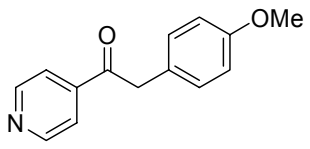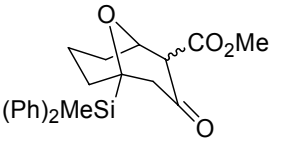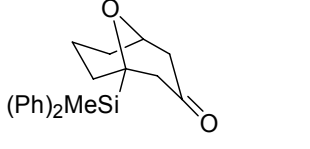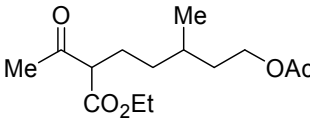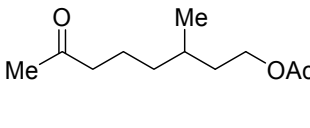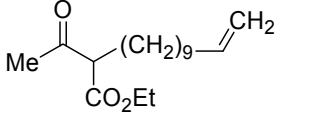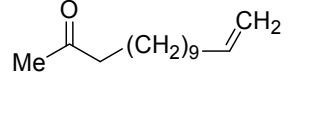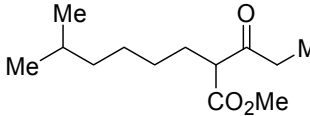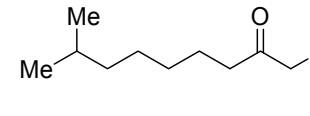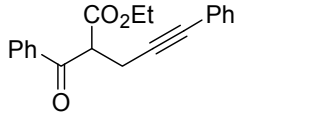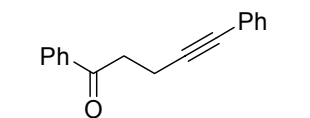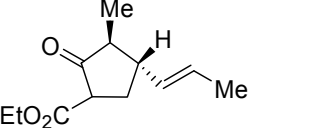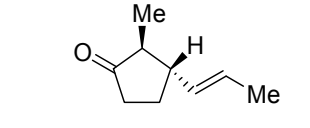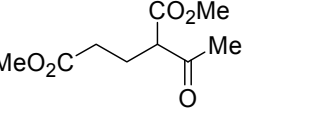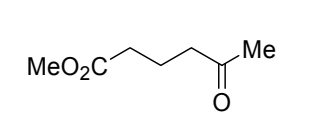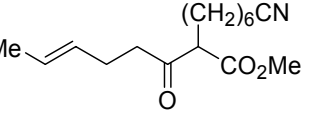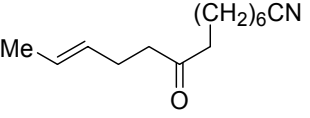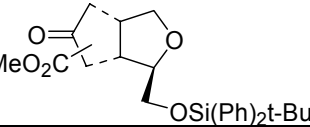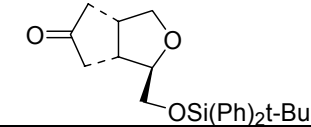
The demethoxycarbonylation of **193** (and the tautomeric enolic ester) was easily accomplished in DMSO and water (150°C, 1 h) to yield the thienoazepine dione **194** (82%).[97] A related pyrimidine analogue underwent deethoxycarbonylation in DMSO and anhydrous NaCl.[98]

193   **194**
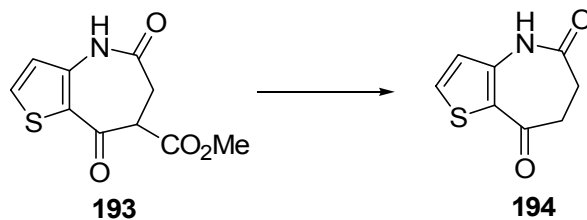
Additonal examples are tabulated in Table 1.

Table 1. Dealkoxycarbonylations of monosubstituted β-keto esters

Starting Material	Conditions	Product	Yield (%)	Reference
	DMSO,NaCl, H$_2$O 150°C		47	99
	DMSO, LiCl, H$_2$O 130°C, 2 h		91	100
	DMF, LiI reflux, 12 h		81	101
	DMSO, LiCl, H$_2$O reflux, 10 h		40	102
	DMSO, LiCl, H$_2$O reflux, 24 h		88	103
	DMSO, LiCl, H$_2$O reflux, 10 h		74	104
	DMSO, NaCl, H$_2$O 130°C, 3 h		quant	105
	DMSO, LiCl, H$_2$O 160°C, 4 h		73	106
	DMSO, LiCl, H$_2$O reflux, 3.5 h		76	107
	DMSO, NaCl, H$_2$O 100°C, 5.5 h		83	108

2.1.2.5. From an α,α-diethoxycarbonyl ketone. Treatment of **195** with DMSO, NaCl and water (160-170°C, 6 h) afforded **196** (90%) the bis-deethoxycarbonylation product **196** (90%).[109]

195   **196**
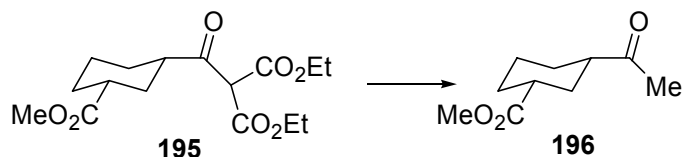
2.2. Disubstituted β-keto esters
2.2.1. Water alone
The de-t-butoxycarbonylation of the bis-(thiomethyl) substrate **197** with DMSO and water (160°C, 4 h) led to 1,1-bis-(methylthio)-2-propanone **198** (85%).[110]

197   **198**
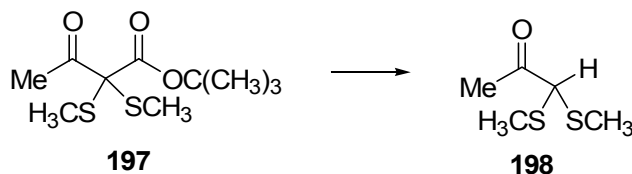
2.2.2. Water-salts
2.2.2.1. Open chain substitutents. The racemic β-keto ester **199** on heating in DMSO with LiCl and water (170°C, 1.5 h) led to a key intermediate **200** (89%), which was converted in 2 steps to racemic stigmalone.[111]

199   **200**
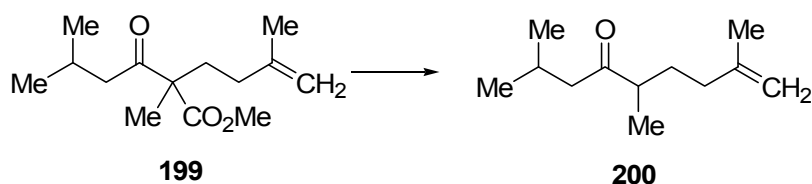
A number of 3-acyloxymethyl ketones were synthesized by the chemoselective dealkoxycarbonylation of the tert-butoxycarbonyl group using DMSO, LiCl and water (160°C, 5 h). A typical illustrative example is the conversion of **201** to **202** (64%).[112] In this case the presence of the salt might not be necessary.

201   **202**
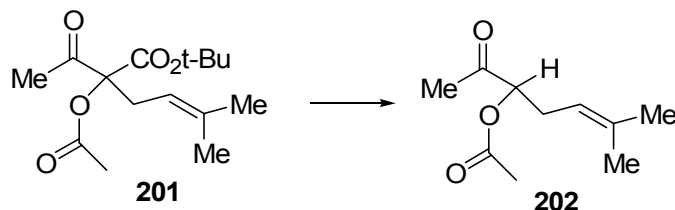
The preparation of a number of 1-alkyl-1,3-dimethoxyacetones has been accomplished by treatment of the appropriate β-keto ester with DMSO, LiCl and water (120-140°C, 10 h). For example, under these reaction conditions the demethoxycarbonylation of **203** led to **204** (72%).[113]
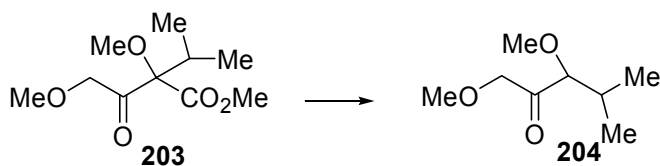
2.2.2.2. From carbocyclic β-keto esters
2.2.2.3. Water-salts. Treatment of **205** with DMSO, NaCN and water (140°C, 1 h) led to **206** (53%).[114]
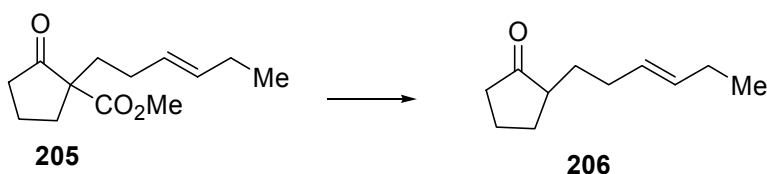
Upon treatment of **207** with DMSO and NaCN (135-140°C, 2 h) the de-ethoxycarbonylation and displacement of the bromide occurred to afforded nitrile **208** (75%).[115]
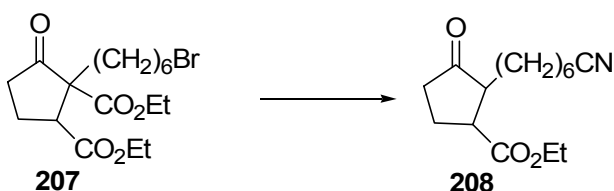
Treatment of enantiomer **209** with DMF and LiI (reflux, 2 h) led to enantiomer **210** (76%), which was used in a synthesis of a triquinane portion of retigeranic acid.[116]
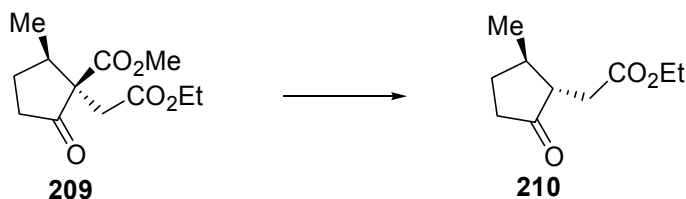
Treatment of **211** with DMSO, NaCl, water (155-160°C, 5 h) led to **212** (53%), along with some ring-opened product. This intermediate was to be used in a synthetic approach to 11-deoxyprostaglandins.[117]

211   **212**
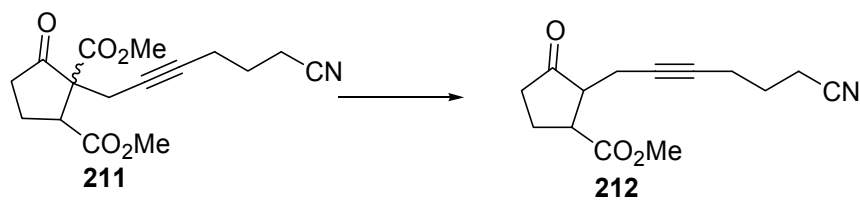
In studies dealing with the synthesis of protaglandins, the treatment of **213** with HMPA and NaCN (75-80°C, 1.5 h) led to racemic **214**.[118]

213   **214**
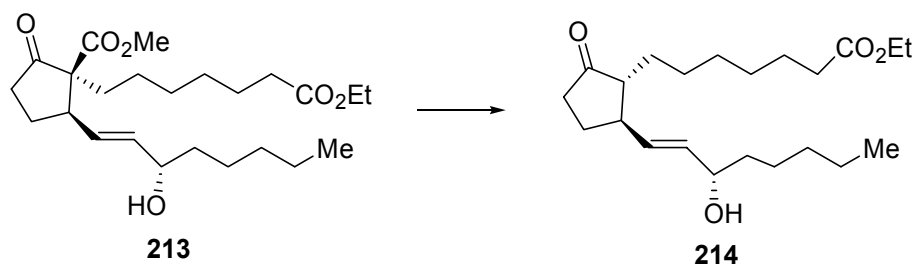
The β-keto ester **215** on treatment with DMF and LiI (reflux, 8 h) led to **216** (85%), a prostaglandin synthon.[119]

215   **216**
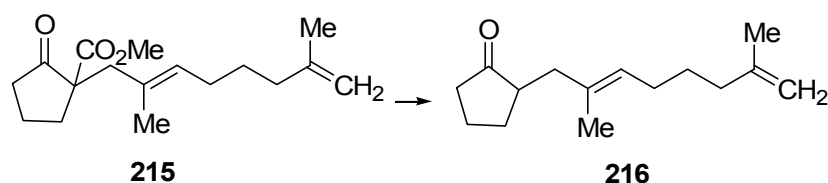
The synthesis of racemic jasmonate **218** (78%) was accomplished by heating β-keto ester **217** in DMSO, NaCl and water (180°C, 4 h, sealed tube).[120]

217   **218**
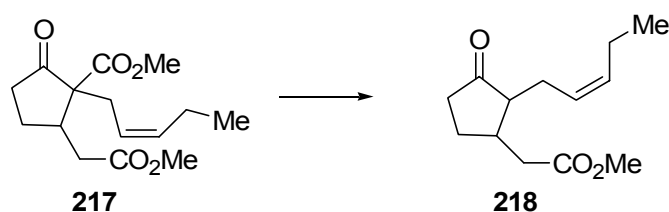
Racemic **219** on treatment with DMSO, NaCl and water (170°C, 18 h) led to methyl dihydrojasmonate **220** (83%). Under these conditions the demethoxycarbonylation of only the β-keto ester moiety occurred.[121]

219   **220**
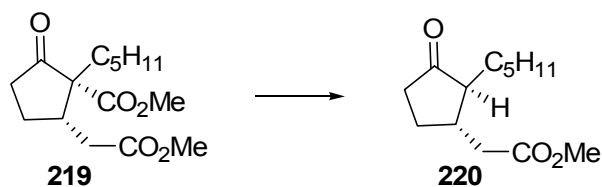
Treatment of **221** with HMPA and NaCN (75°C, 5 h) led to chiral **(2R,3R,1R)-222** (72%).[122]

Treatment of (+)-**223** with DMSO, NaCN and water (140°C, 36 h) led to ketone (*S*)-**224** (89%) with a *trans*:*cis* ratio of 9:1. The mixture of ketones was converted into the sesquiterpenic alcohol (+)-conocephalenol in several subsequent steps.[123]

223   **224**
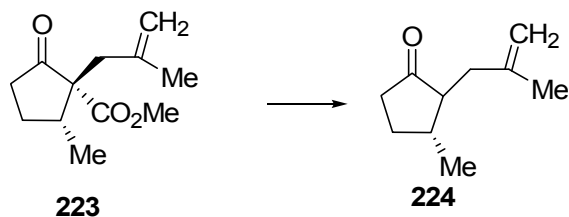
The decarbomethoxylation of **225** in DMSO and NaCN (160°C, 2 h) yielded **226** (92%) used in a synthesis of chiral phenylalanine analogues isolated from *Praxelis clematidea*.[124]

225   **226**
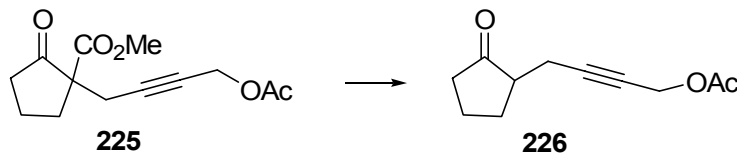
On treatment of (-)-**227** (a vinylogous β-keto ester) with DMF and LiI trihydrate (reflux, 1 h) the demethoxylated products (+)-**228a** and (-)-**228b** (90%, 5:4 ratio) were isolated and could be separated by chromatography. Compound **228a** was subsequently converted into the chiral sequiterpene alcohol (-)-silphiperfol-5-en-3-ol.[125]

227   **228a**   **228b**
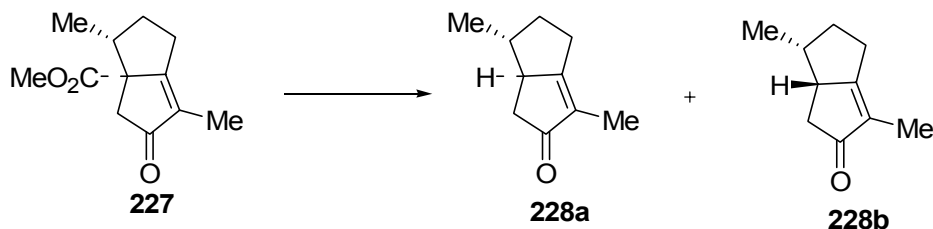
In the preparation of 16-(bromoalkyl)-estradiols, the intermediate **230** (71%, as a 16α,16β mixture 15:85) was obtained by treatment of **229** with DMF, LiCl and water (reflux). Other side chains at C-16 were also prepared by this route.[126]

229   **230**
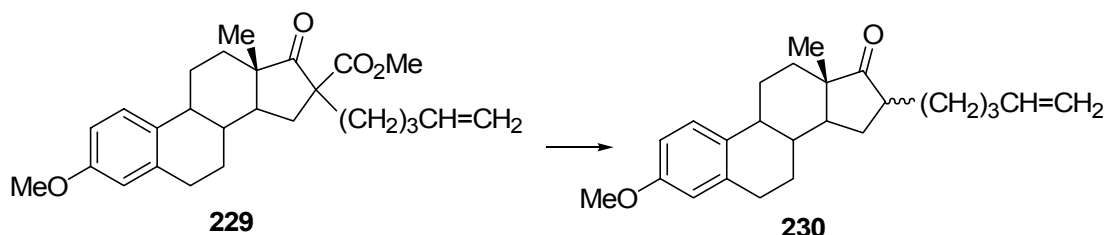
Treatment of **231a** or **231b** with DMSO, LiCl and water (180°C, 1.5 h) led to **232a** (64%) or **232** (78%), respectively.[127]

231   **232**

a, R = C$_5$H$_{11}$, n = 1; R = C$_5$H$_{11}$, n = 2
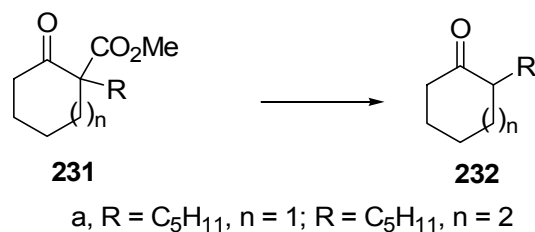
The decarbomethoxylation of **233** with DMSO, NaCl and water (160°C) led to a mixture of cis- and trans isomers **234** which could be separated by chromatography. These isomers were used in the synthesis of the sesquiterpene racemic vetiselinene. [128]

233   **234**
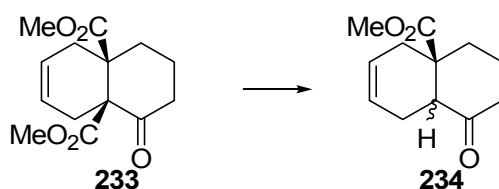
The Krapcho dealkoxycarbonylations of substituted cyclic β-keto esters using LiBr, Bu$_4$NBr and water under microwave irradiation have been reported. For example, under these conditions the conversion of **235** to **236** (87%) was accomplished in 20 min at 186°C.[129a,b,c]

235   **236**
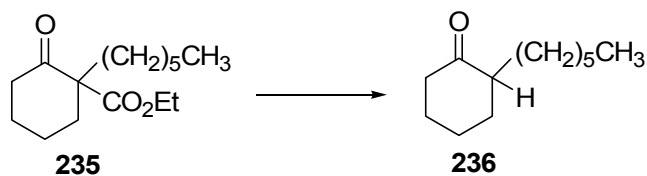
The β-keto ester **237** on treatment with DMPU (dimethylpyrimidinone) and LiCl (130°C, 48 h) gave cyclohexenone **238** (45%).[130]

237   **238**
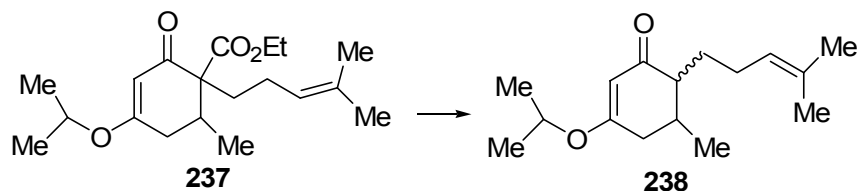
Treatment of **239** with HMPA and LiCl (130°C) led to the demethoxycarbonylated product **240** (72%) which was converted into (+)-dysideapalaunic acid, a sesquiterpene aldose reductase inhibitor.[131]
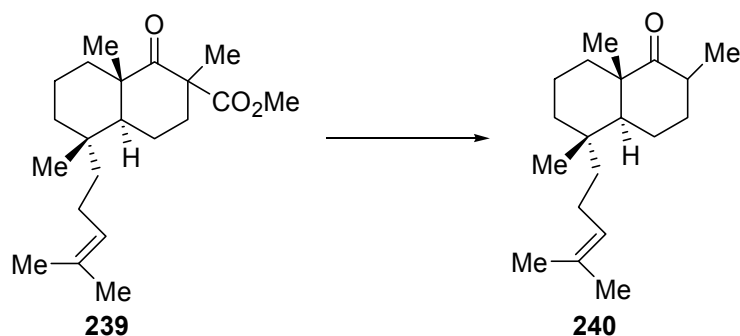
Treatment of **241** with LiCl in HMPA (130°C) afforded **242** (92%) which was used in at synthesis of (+)-perrottetianal A, sacculatane diterpene.[132]
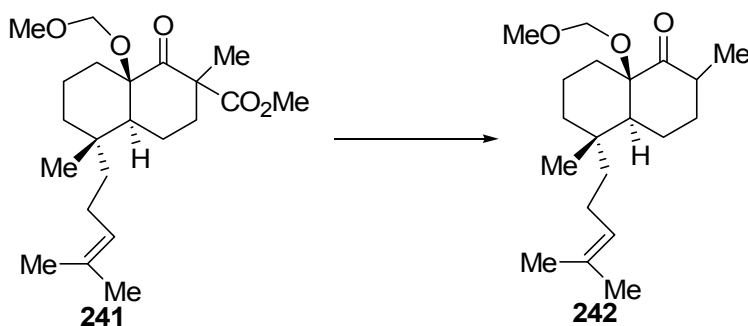
The crystalline and oily stereoisomers **243** were treated with HMPA and LiCl (120-140°C, 8 h) to afford the dione **244** (84%), which was subsequently converted into (+)-pisiferol, an abietane-type diterpene alcohol. [133]
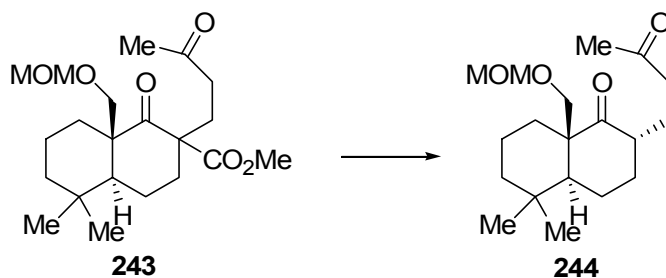
The demethoxycarbonylation of **245** with HMPA and LiCl (anhydrous conditions, 100°C, 20 h) led to a epimeric mixture of tricyclic ketones **246** (82%) which were subsequently converted into racemic sterpurene, a sesquiterpene hydrocarbon metabolite of Chondrostereum purpureum.[134]

245   **246**
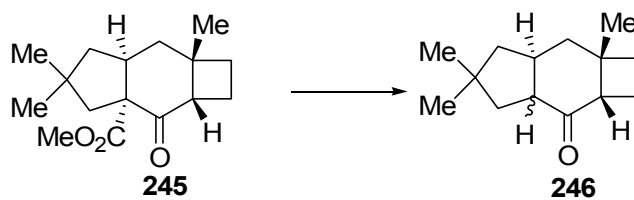
Treatment of **247a** (1-β-H) or **247b** (1-α-H) with DMSO, NaCl and water at reflux led to **248a** or **248b** (90%), which were used in the synthesis of a defense substance of a termite soldier.[135]

R = CO$_2$Me

247   **248**
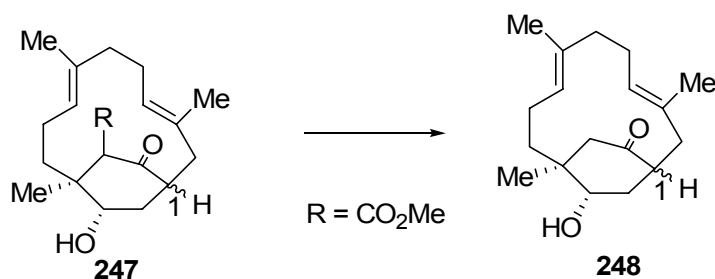
Treatment of **249** with DMSO, NaCl and water (150°C, 6 h) led to the decarbomethoxylation to afford racemic **250** (36%), an intermediate in approaches to a group of sesquiterpenes called tremulanes.[136]

E = CO$_2$Me

249   **250**
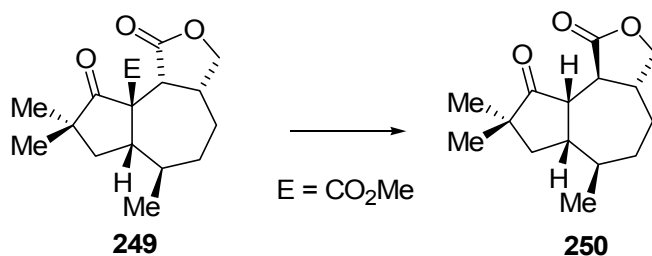
The decarbomethoxylation of **251** in aqueous DMSO (no conditions) led to ketone **252** (99%).[137]

251   **252**
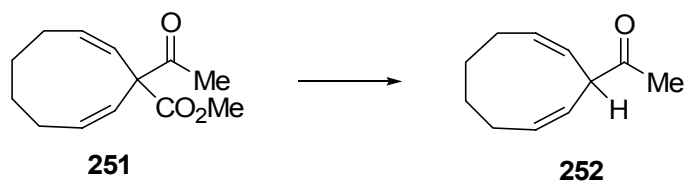
2.3. Heterocyclic substrates

2.3.1. From β-carbethoxy substituted lactones

The demethoxycarbonylation of the methoxycarbonyl substituted furanone **253** to γ-lactone **254** (72%) was accomplished on treatment with DMSO, NaCl and water (160°C, 12 h).[138]
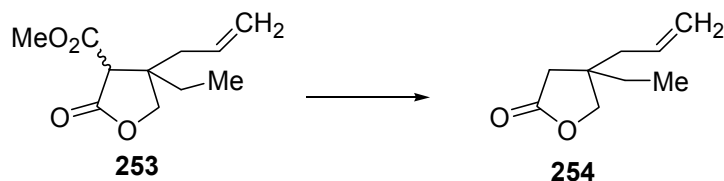
Decarbomethoxylation of γ-lactone **255** with DMSO, NaCl and water (110°C, 12 h) yielded chiral (4S) 2-butyrolactone **256** (84%) which in a series of subsequent transformations was transformed into the pentacyclic alkaloids (-)-eburnamonine and (+)-*epi*-eburnamonine.[139a,b]
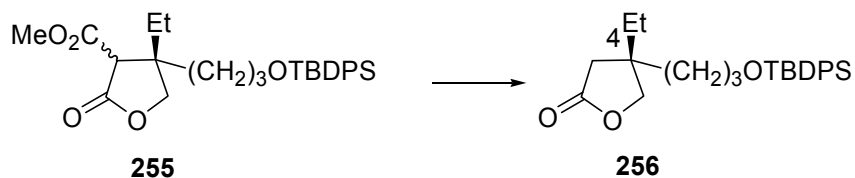
The demethoxycarbonylation of **257** in DMSO (or DMF), NaCl and water (150°C, 3-5 h) yielded the lactone **258** (75%).[140]
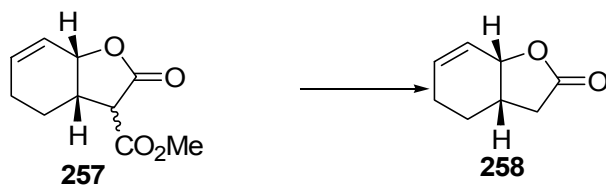
The silylated butenyl lactone **260** (77%) was obtained by treatment of **259** with DMSO and LiCl (reflux, 3 h). Further elaborations of the lactone and terminal silyl group were performed.[141]
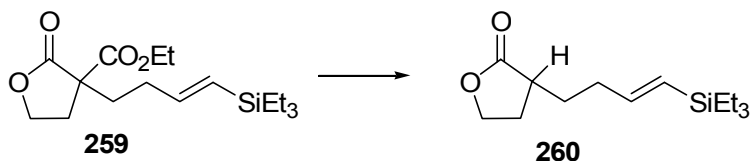
The deethoxycarbonylation of the fluorinated lactone **262** with DMSO, NaCl and water (reflux, 2.5 h) led to a diastereoisomeric mixture of lactones **263** (73%) which in a few steps could be converted in 5-amino-2-fluorolevulinic acid.[142]
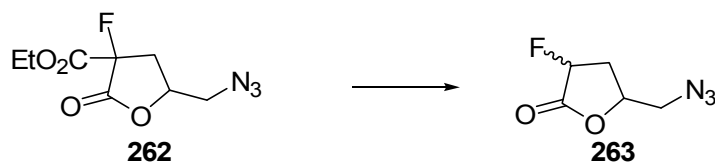
Of particular interest is the conversion of **264** to the naturally occurring racemic spirolactone andirolactone (**265**). Treatment of **264** with DMSO, NaCl and water (160°, 2 h) afforded **265** (90%).[143]
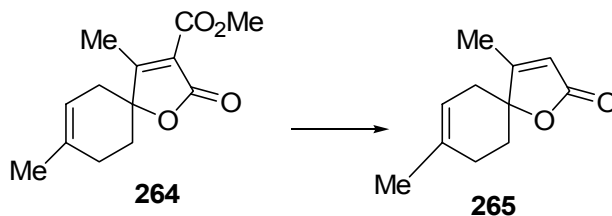
The lactone **266** on heating in DMSO, LiCl and water (125°C, 12 h) led to *(S)*-sotolon (**267**) (80%, 92%ee), a volatile compound isolated from raw cane sugar.[144]
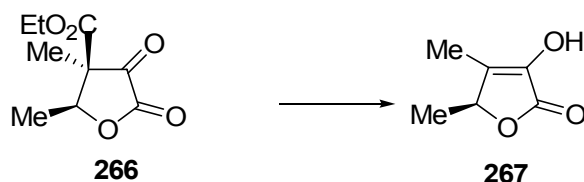
Treatment of lactone **268** with DMSO and water (110-120°C, 1 h) led to **269** (99%), which was used in the synthesis of potential phenolic antioxidants.[145]
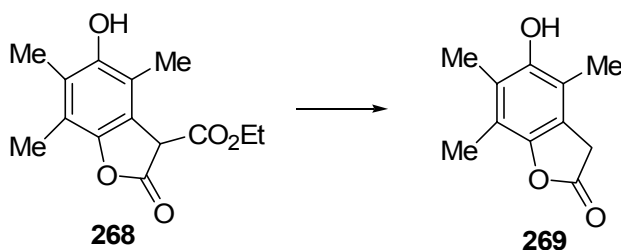
The synthesis of (3*S*, 4*S*) **271** (60%, 99.9%ee) was accomplished by treatment of **270** with DMSO, LiCl and water (reflux, 3.5 h). This intermediate was used in a synthesis of the sex pheromones of pine sawflies.[146]
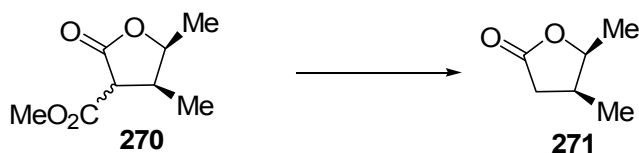
The bicyclic lactone **272** on treatment with DMSO, LiCl and water (195°C, 3 h) led to the bicyclic lactone **273** (64%).[147]
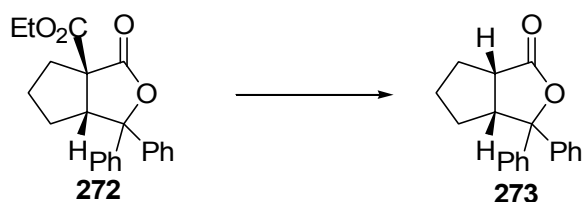
The α-carbomethoxy-α-hydroxy-γ-lactone **274** on treatment with DMF, NaCl and water (150°C, 3 h) led to **275a** and **275b** (84%, 68:32 ratio) which could be separated by chromatography.[148]
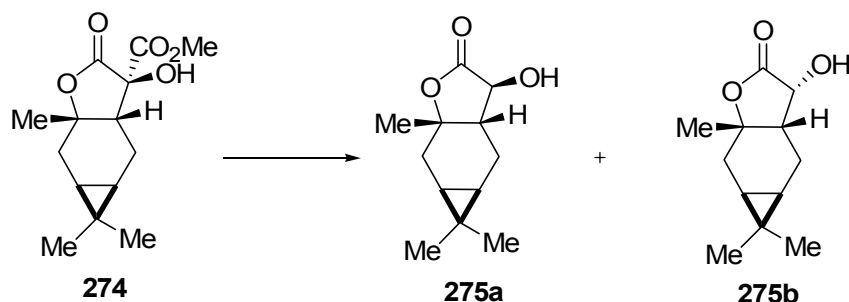
The demethoxycarbonylation of **276** (a 3:1 mixture of diastereoisomers) with DMF and LiI (reflux) led to **277** (86%) which in a subsequent series of reactions was used in an enantioselective total synthesis of (+)-methyl pederate.[149]
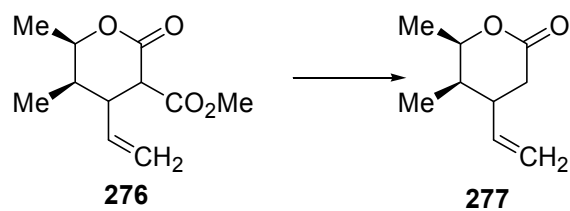
The lactone **278** with DMSO, NaCl and water (150-160°C, 2 h) led to **279** (75%). In a similar manner the β-methyl analogue was converted into the corresponding deethoxycarbonylated product. Other substituted analogues were also deethoxy-carbonylated. These derivatives were used in a synthesis of perhydrofuro[2,3-b]furan ring systems.[150]
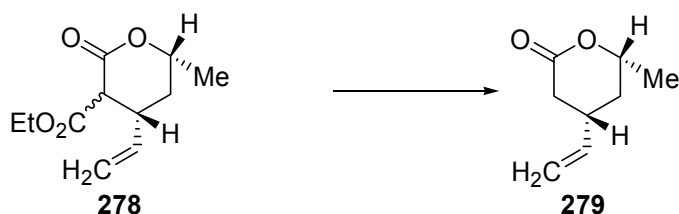
Treatment of lactone **280** with HMPA, NaCl and water (190°C, 2.5 h) gave **281** (65%).[151]

280   **281**
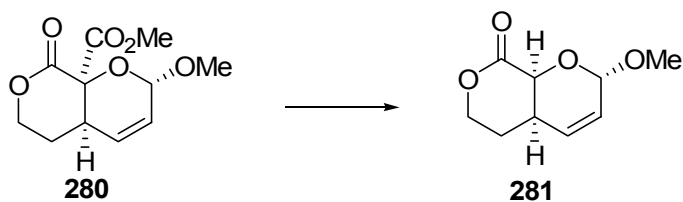
Treatment of 11-carbomethoxy-18-norestrane **282** with DMSO and NaCN (100°C, 19 h) led to racemic **283** (no yield given).[152]

282   **283**
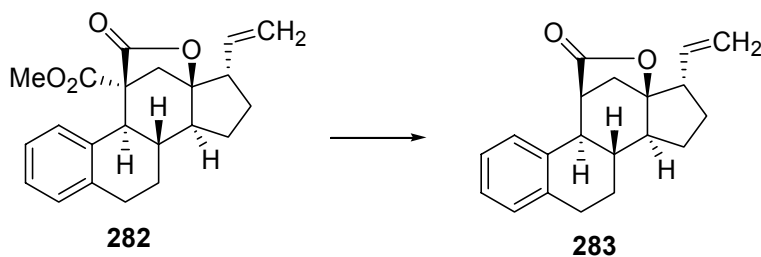
The decarbomethoxylation of **284** on treatment with DMSO, and NaCN (90°C, 24 h) led to isomeric mixtures of **285a** and **285b** (78%), which were used in a steroid analogue synthesis.[153] A similar strategy was used for the incorporation of fluoro substitutent[153] and a 3-hydroxy steroidal group.[154]

284   **285a**   **285b**
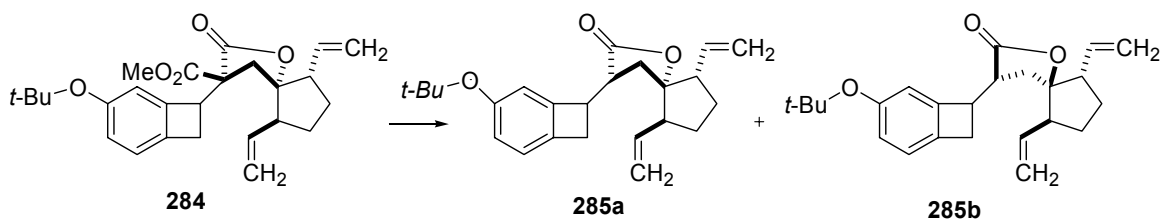
Treatment of **286a** and **286b** (diastereoisomeric mixture) with DMSO and NaCN (90°C, 24 h) led to an inseparable mixture of 4-azabenzocyclobutane diastereoisomers **287a** and **287b** (91%) which were subsequently converted into the aza steroidal analogues.[155]
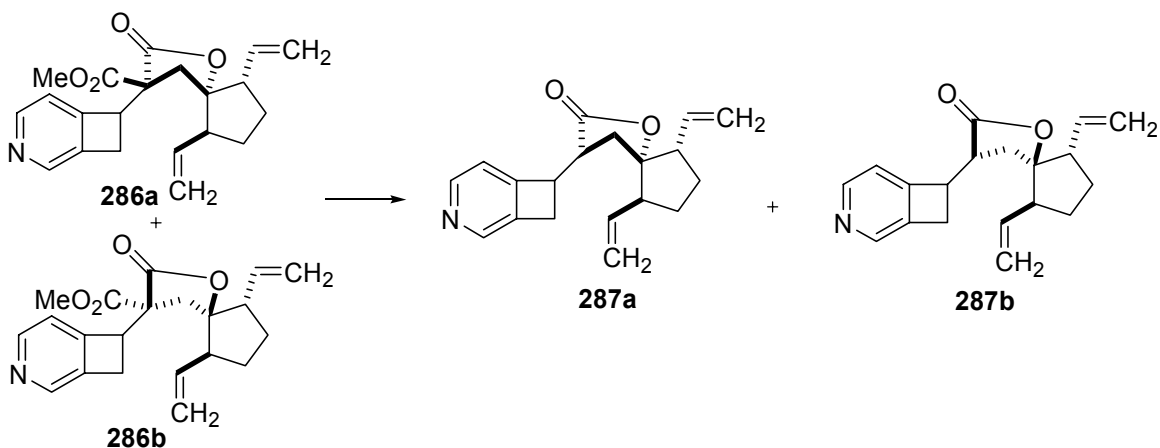
In the preparation of dihydroisoquinolines, the intermediate **289** was prepared by treatment of **288** (44%) with DMSO, NaCl and water (145-150°C, 6 h).[156]
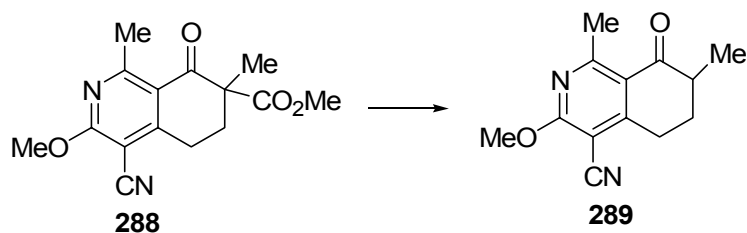
The ester **290** on treatment with DMF, LiCl and water (92°C, 16 h) led to compound **291** (78%) as an epimeric mixture which could not be separated.[157]
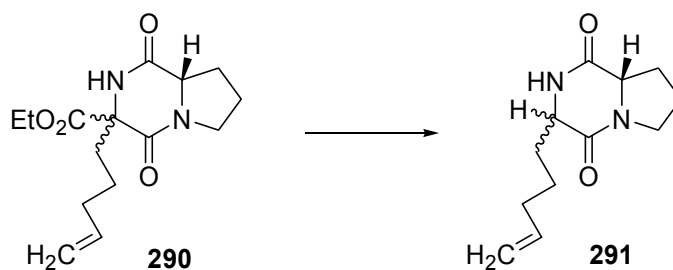
The thieno[2,3-d]pyrimidin-4-one (**292**) on treatment with DMSO, LiCl (150°C) led to the pyrimidinone **293**(no experimental conditions).[158]
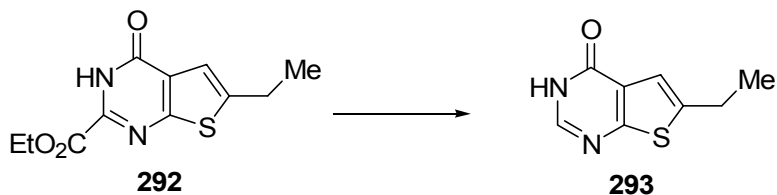
The use of MgCl₂ hexahydrate (in place of NaCl) in DMSO (130-140°C, 2.5 h) for the demethocycarbonylation of **294** led to deoxybrevianamide **295** (59%) along with the corresponding epimer (38%).[159]

294   **295**
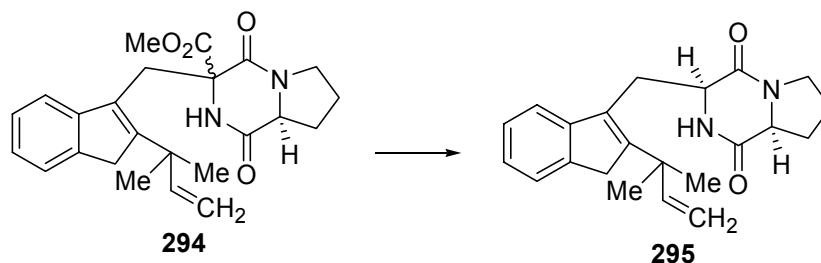
The dealkoxycarbonylations of β-keto esters using halides of group IIa metals have been studied. For example, treatment of **296** with MgCl₂ hexahydrate or CaCl₂ dihydrate in DMSO (in the presence of PhSH, at 150-160°C) led to **297** (50-60%).[160]

296   **297**
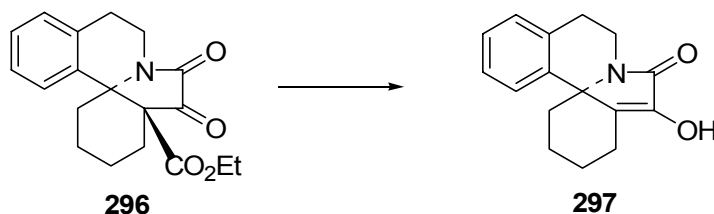
The deethoxycarbonylation of substituted derivatives such as **298** have been accomplished using MgCl₂ hexahydrate in DMSO (or HMPA) in the presence of PhSH (150-155°C, 2 h) to yield **299** (73%). These derivatives were used in a synthesis of erythrina and related alkaloids.[161]

298   **299**
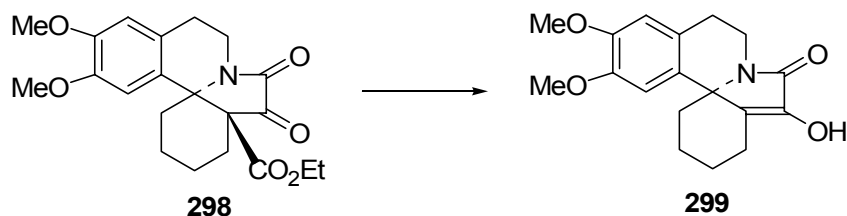
The decarbomethoxylation of **300** with DMSO, NaCl and water (135-140°C, 5-8 h) led to the ketones **301** (49-90%). Intermediate **301c** was converted into racemic α-lipoic acid.[162]

300   **301**
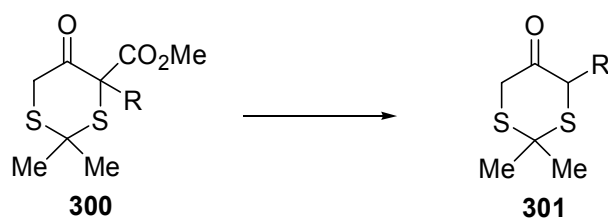
a, R = *n*-butyl; b, R = benzyl: c, R = (CH₂)₄CO₂Me; d, R = allyl; e, R = Et

Treatment of **302** with HMPA and LiCl (65-75°C, 20 h) led to **303** (65%), which was used in a synthesis of 2-alkyl-3-cyclopentenones.[163]

302   **303**
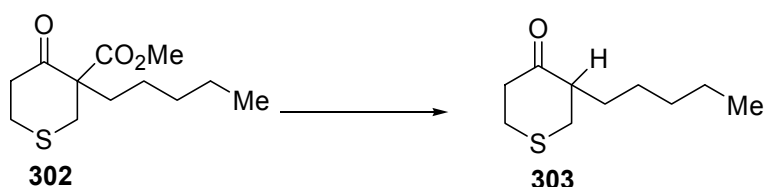
In a study of routes to thiathromboxane analogues, the dealkoxycarbonylations of a number of 3-methyoxycarbonyl- 3-substituted thiin-4-ones were evaluated. Treatment of **304** with DMF, anhydrous MgCl₂ and a phosphate buffer (160°C, 21 h) led to enone **305** (69%) as an inseparable mixture of the 2,3-*trans* and 2,3-*cis* isomers along with 16% of the corresponding desilylated products, namely the 2,3-*trans* and 2,3-*cis* alcohols.[164]

304   **305**
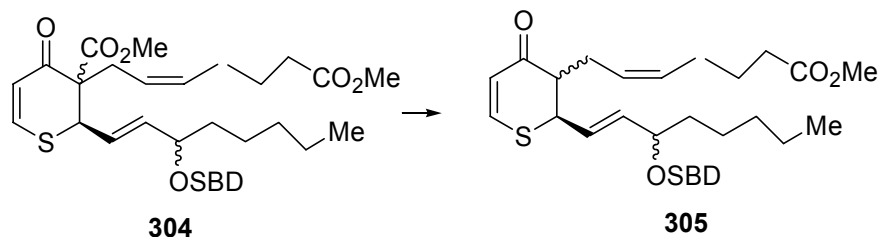
Treatment of **306** with DMF and LiBr (137°C, 5 h) in the presence of *p*-aminothiophenol (a trap for MeBr formed during the reaction) gave the demethoxycarbonylated product **307** (96%) with less than 3% of the corresponding *trans*-isomer. Initial attempts to use only DMF and LiI led to **307** along with 30% of the corresponding N-methyl analogues. Intermediate **307** was utilized in the preparation of analogues related to diltiazem used in the treatment of hypertension.[165]

306   **307**
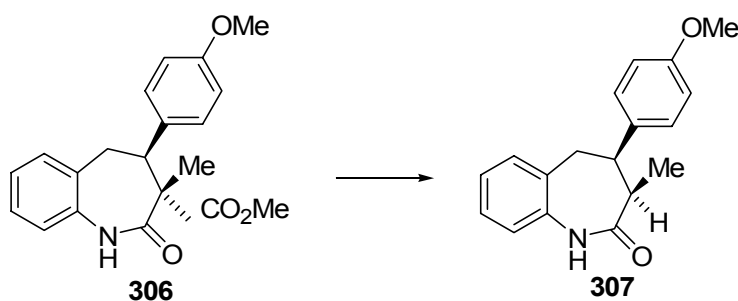
Upon heating **308** in dry HMPA and LiCl (120°C, 10 min) the demethoxycarbonylation led to the intramolecular cyclization product **309** (61%).[166]

308   **309**
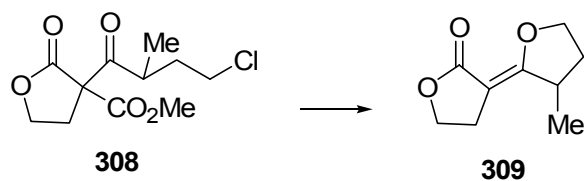
Table 2 lists some additional examples.

Table 2. Dealkoxycarbonylations of disubstituted β-keto esters

Starting Material	Conditions	Product	Yield (%)	Reference
	DMF, LiCl, H$_2$O reflux, 18 h		80	167
	DMSO, LiCl, H$_2$O 149°C, 20 h		54	168
	DMF, LiCl, H$_2$O reflux, 1h		64	169
	DMF, LiCl, H$_2$O HOAc, reflux, 5h	exo:endo 55:45	84	170

2.4. 1,3-Diones
2.4.1. From substituted 2-carbalkoxy-1,3-diones
A wide variety of β-diketones (for identification of potential secretions from the paracloacal glands of alligator and caimans) have been prepared by treatment of substituted 2-carbalkoxy-1,3-diones with NaCl and water at reflux (12 h). The following reaction sequence for the preparation of 5-ethylnonane-2,4-dione (**311**) from the corresponding β-2-carethoxy-1,3-dione is illustrative **310** (62%).[171]

310   **311**
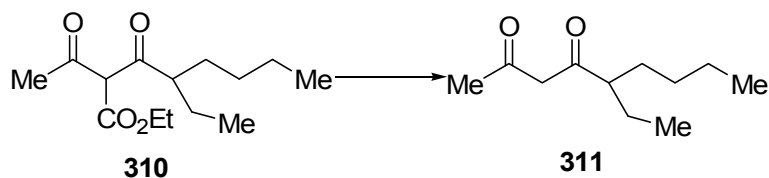
The synthesis of a wide variety of β-diketones found in sunflower pollen has been accomplished. For example, the conversion of **312** with DMSO, NaCl and water (reflux, 8 h) led to **313** (40-60%).[172]
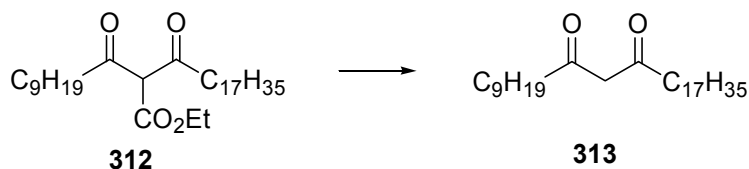
Treatment of enol **314** with DMSO, NaCl and water (reflux, 18 h) led to ketone **315** (62%).[173]
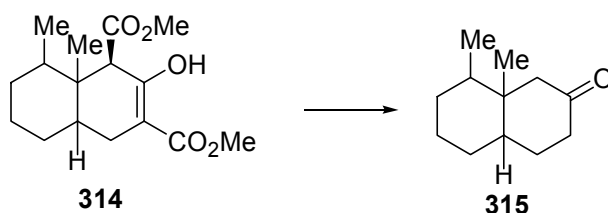
The facile demethoxycarbonylations of **316a** (n,m = 6) and **316b** (n = 6, m = 20) were accomplished by heating in DMSO and water to yield the corresponding long-chain 1,3-diones **317a** (82%) and **317b** (98%).[174]
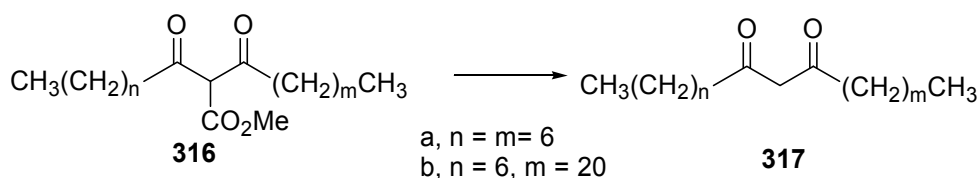
Treatment of **318** with DMSO, NaCl, water (reflux, 8 h) led to the 1,3-dione **319** in good yield.[175]

Treatment of the enolic tautomer **320** with DMSO, NaCl and H$_2$O (160-170°C, 4 h) led to the enolic form of the 1,3–dione **321** (54%).[176]

320   **321**
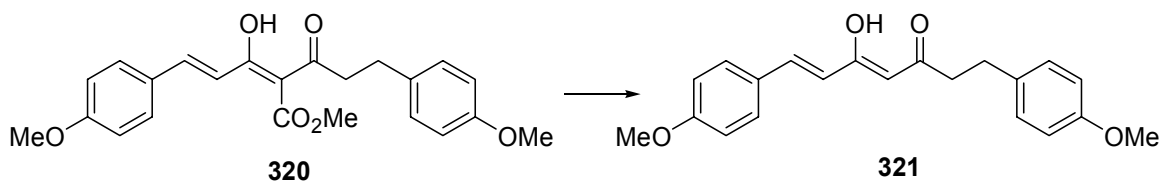
Treatment of **322** with DMSO, NaCl and water (reflux, 1 h) led to **323**.[177]

322   **323**
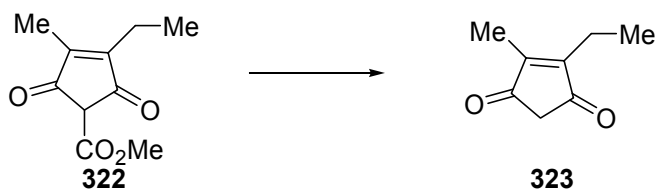
The ester **324** in acetonitrile and water was refluxed for 2.5 h to yield **325** (95%).[178]

324   **325**
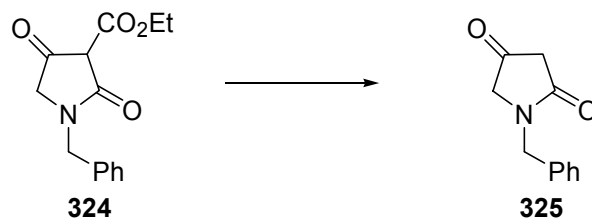
2.5. 1,4-Diones
2.5.1. From α-carbalkoxy-1,4-diones

The demethoxycarbonylation of **326** with DMSO, NaCl and water (160-170°C, 6 h) led to 1,4-dione **327** (40%).[179]

326   **327**
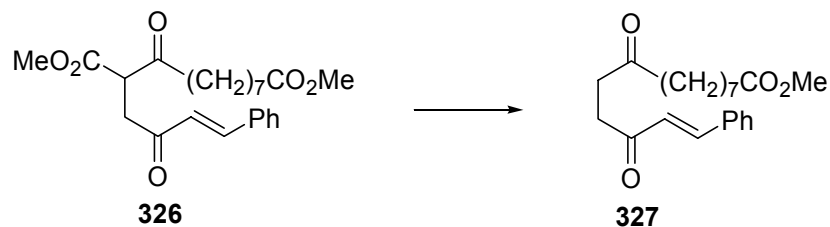
Treatment of the β-keto ester **328** with DMSO, NaCl and water (110°C, 2.5 h) led to 1,1,1-trifluoro-2,5-hexanedione **329** (73%).[180]

328   **329**
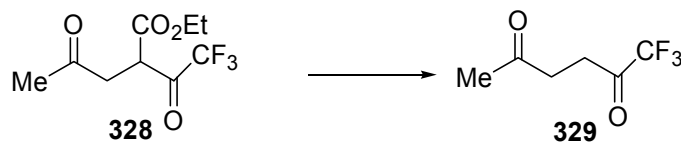
The deethoxycarbonylations of β-keto esters **330a-c** in DMSO, NaCl and water (180°C, 20 h) led to good yields of the corresponding 1,4-diones **331a-c** (48-75%).[181]

a, R = Me; b, R = Ph, c, R = C$_3$H$_7$
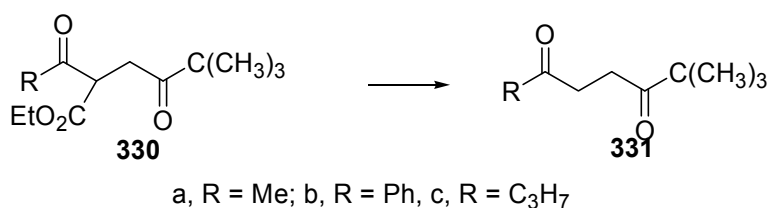
2.6. 1,5-Dione

2.6.1. From α-carbomethoxy substituted substrate

The decarbomethoxylation of β-keto ester **332** was accomplished using DMPU and LiCl (120°C, 7 h) to afford (*R*)-**333** (72%). It was noted that the use of HMPA or DMSO as solvents did not give satisfactory yields. The RCM macrocyclization of this keto diene led to the 15-membered carbocyclic substrate which was converted into (*R*)–(+)-muscopyridine.[182]
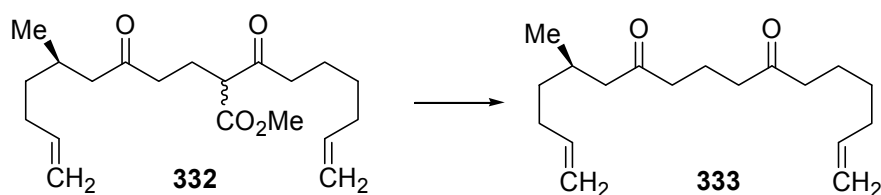
2.7. β-Keto ester and malonate ester polyfunctional substrates

Treatment of **334** with DMSO, NaCl and water (173°C, 45 min) led to **335**(65%), resulting from the decarbomethoxylation of the malonate ester group and the β-keto ester group.[183]
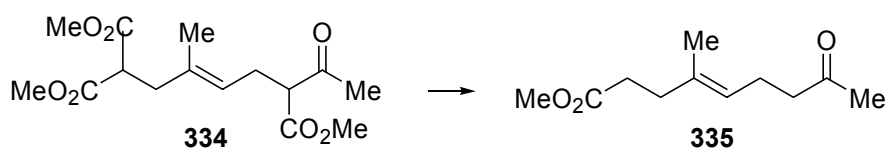
Compound **336** in DMF, LiCl and water (reflux, 18 h) led to **337a** (36%) and **337b** (25%).[184]

ax CO$_2$Et **337a**
eq CO$_2$Et **337b**
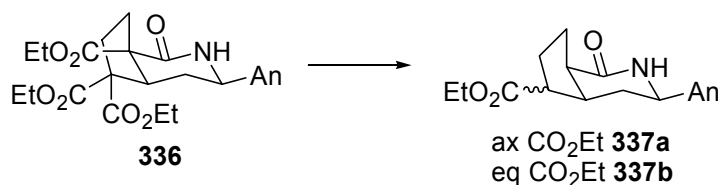
Treatment of **338** with DMSO, NaCl and water (155-160°C) led to **339** (61%).[185]
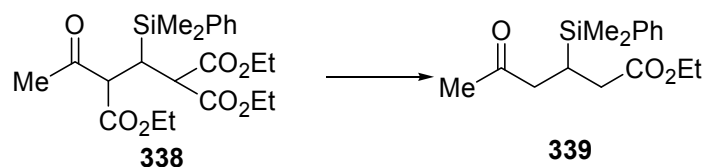
Upon heating **340** in DMSO, NaCl and water (150-160°C, 2 h) **341** was formed (83%), the product of a deethoxycarbonylation of the β-keto ester functionality. If diester **341** is heated with DMSO, LiCl and water with a small amount of pyridine (150-160°C, 14 h), **342** (72%) was obtained. Heating diester **340** with DMSO, LiCl and water (150-160°C, 14 h) and a small amount of pyridine afforded **342** (70%).[186]
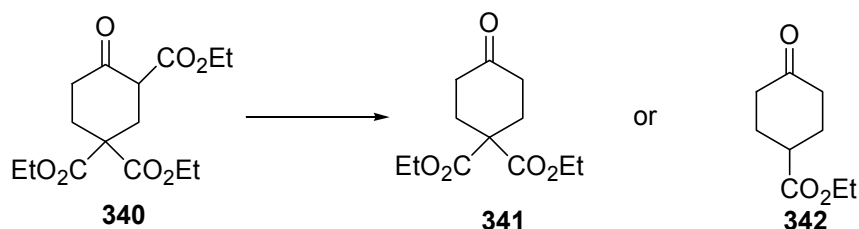
2.8. Aldehyde
2.8.1. From α-methoxycarbonyl aldehyde
Treatment of **343** with DMF and LiI hydrate (reflux, 1 h) led to racemic **344** (89%).[187]
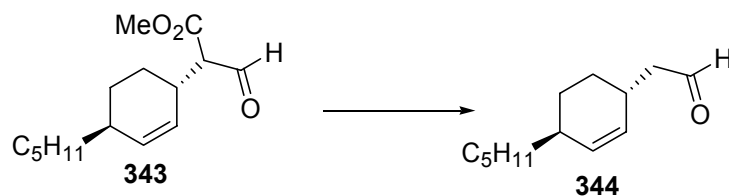
2.9. Nitriles

The dealkoxycarbonylation of an α-cyano ester is a useful preparative route leading to nitriles.

2.9.1. From α-cyano esters

2.9.2. From mono substituted substrates
The conjugate addition product obtained by addition of methyl cyanoacetate to 4-phenyl-3-buten-2-one using a chiral(salen)Al complex led to **345** which on treatment with DMSO and water (130°C) led to **346** (85% for two steps in 93% ee).[188]
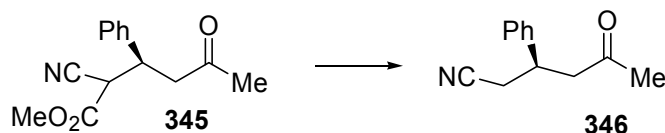
The chemoselective deethoxycarbonylation of α-cyano ester **347** was accomplished by treatment with DMSO, water and LiCl (140°C, 4 h) to yield **348** (75%).[189]
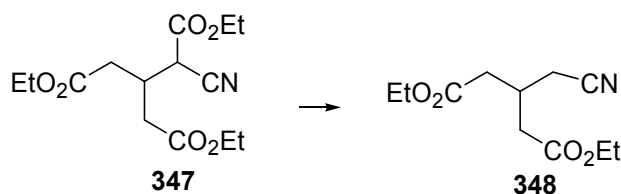
The deethoxycarbonylation of α-cyano ester **349** was accomplished by treatment with DMSO, water and NaCl (reflux, 20 h) to afford **350** (48%).[190]
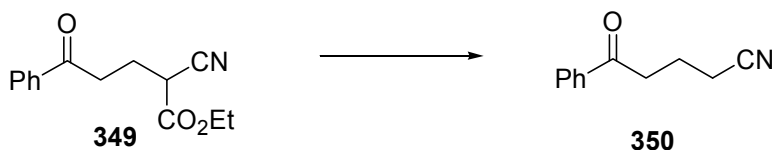
Treatment of **351** with DMSO, LiCl (130°C, 5 h) led to **352** (75%).[191]
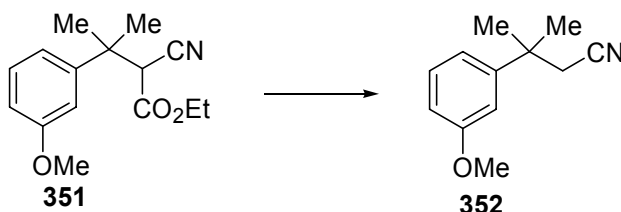
Treatment of the diester **353** with DMSO, NaCl and water (140°C, 2.5 h) led to the deethoxycarbonylation of the ester group attached to the carbon holding the cyanide group to afford **354** (77%). The ester was subsequently converted into the corresponding pyrrolidone.[192]
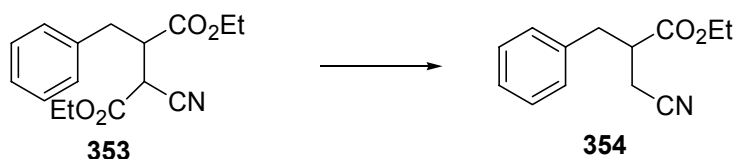
Treatment of **355** with DMSO, NaCl and water (160°C, 4 h) led to nitrile **356** (65%).[193]
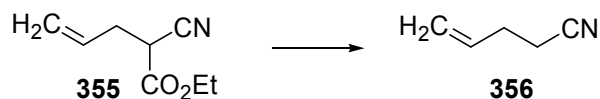
Treatment of cyano ester **357** with DMSO, NaCl and H$_2$O (160°C, 3 h) led to **358** (82%).[194]

The decarbomethoxylations of **359a** (64%ee) and **359b** (96%ee) with DMSO, water and NaCl (reflux, 4 h) led to the enantioselective synthesis of **360a** (74%) and **360b** (80%), respectively.[195]

Homo- and copolymers of CNEVE **361** were deethoxycarbonylated by heating in DMSO in the presence of NaCl to yield poly(vinyl ethers) with 2-cyanopropoxy side chains **362**.[196]

Treatment of α-cyano ester **363** (89%ee) with DMSO, water and NaCl (130°C, 24 h) led to chemoselective removal of the carbomethoxyl group α to the cyano group to afford **364** (89%ee) without loss of sterochemistry.[197]
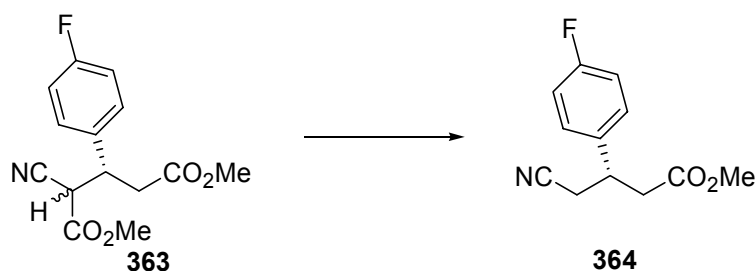
Analogue (2*S*, 4*R*)-**365** on heating with DMSO, NaCN and water (140°C, 1 h) led to **366** (67%).[198]

365 → **366**
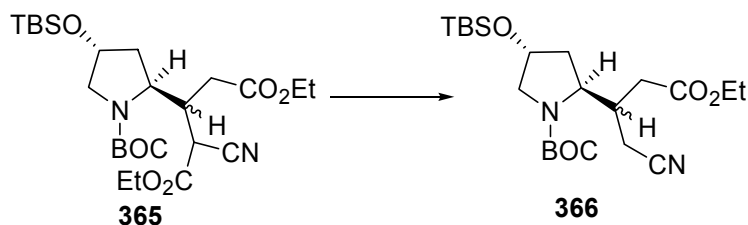
The deethoxycarbonylation of nitrile ester **367** was accomplished using DMSO, LiCl and water (150°C, 1 h) to yield nitrile **368** (84%).[199]

367 → **368**
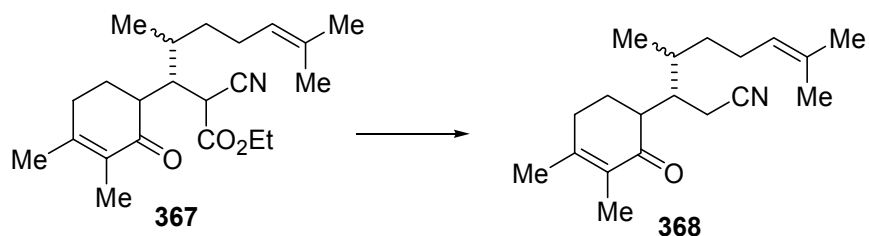
Treatment of the oxindole **369** with DMSO, NaCN and water (160°C, 2 h) led to **370** (80%) with decarbomethoxylation of the ester functionality and the N-CO$_2$Me group. This intermediate was converted into racemic physostigmine in a subsequent series of steps.[200]

369 → **370**
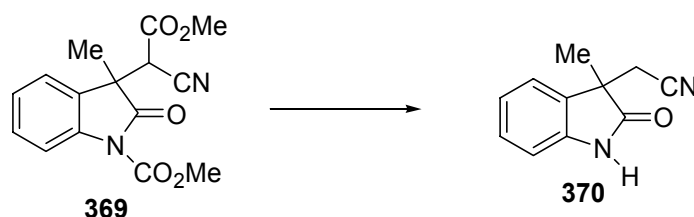
The lactonization of **371** to yield racemic **372** (70%, *cis-trans* fused ratio 4:1) was accomplished by heating in DMSO and water and additional NaCN (100°C, 0.5 h).[201] In this case, lactonization is faster then the expected Krapcho demethoxycarbonylation..

371 → **372**
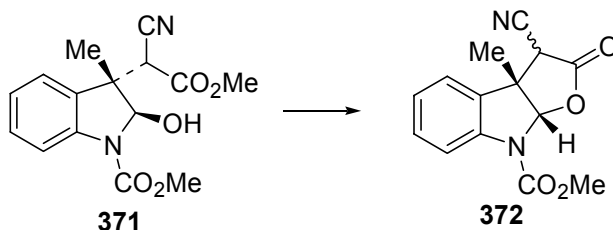
The N-benzyl protected analogue **373** on treatment in DMF, LiCl and water (no experimental conditions) led to **374**. This compound could readily be converted into the hexahydroazocino[4,5-b] indole on catalytic hydrogenation.[202]

373   **374**
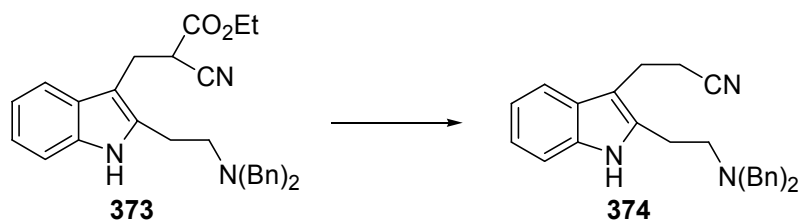
The α-cyano acid **375** on treatment with DMF and NaCl in water (125°C, 2.5 h) led to the decarboxylated product **376** (91%).[203]

375   **376**
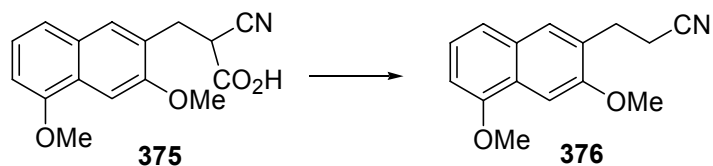
Treatment of the substituted cholesterol **377** with DMSO, LiCl and water (140°C, 20 h) led to the 7β-(2-cyanoethyl) analogue **378** (84%), the product of a de-t-butoxycarbonylation.[204]

377   **378**
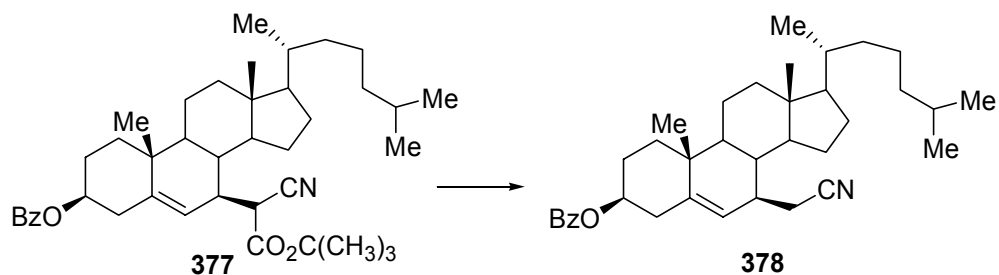
The deethoxycarbonylation of **379** with DMSO, NaCl and water (160°C, 2 h) led to nitrile **380** (91%).[205]

379   **380**
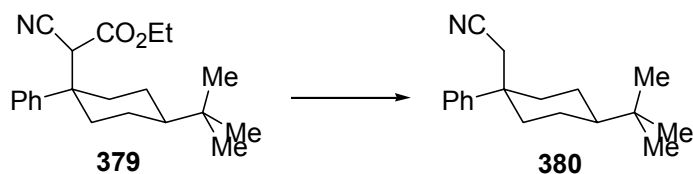
In the preparation of ^{13}C-labelled substrates, treatment of the phthalimido analogue **381** with DMSO, NaCl and water (no conditions or yield) led to **382**.[206]

381   **382**
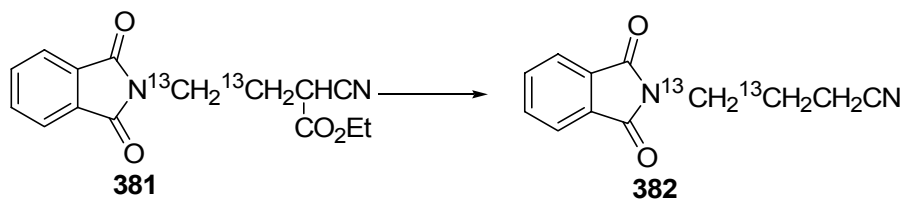
In a route to the antibiotic anticapsin, the intermediate **384** (73%) was prepared by deethoxycarbonylation of racemic **383** with DMSO, LiCl, water (reflux, 6 h).[207]
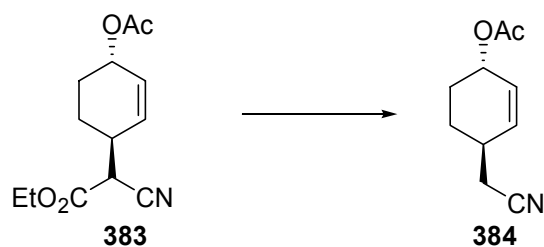
Treatment of **385** with DMSO, NaCl and water (165°C) led to cyano ester **386** and cyanolactone **387** (72- 78%, 1:1 ratio) with the removal of the *t*-butoxy group as well as deprotection of the MOM ether. This intermediate was converted into the AB ring system of sesbanamide.[208]
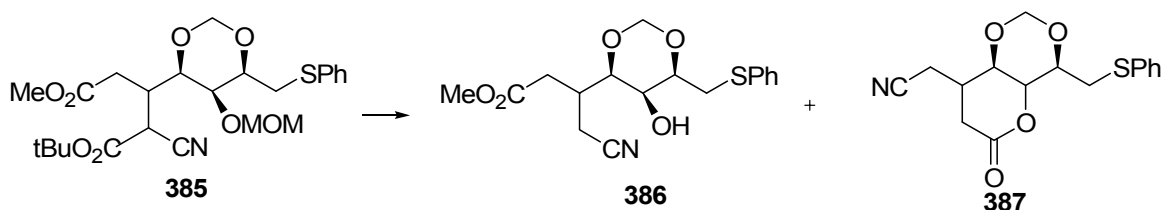
2.9.3. From disubstituted substrates

The pentafluoro α-cyano ester **388** on treatment with DMSO and water (160°C, 120 h, or for shorter times in aqueous DMSO containing NaCl) led to nitrile **389** (78%).[209]

Treatment of the cyano acid **390** with DMSO, LiCl and water (in the presence of NaHCO$_3$) at 165°C for 4.5 h led to the decarboxylation to give the cyclopropane nitriles **391** and **392** as a 55:45 mixture (60%). These derivatives were used in the synthesis of the acid component of insecticidal pyrethoids.[210]
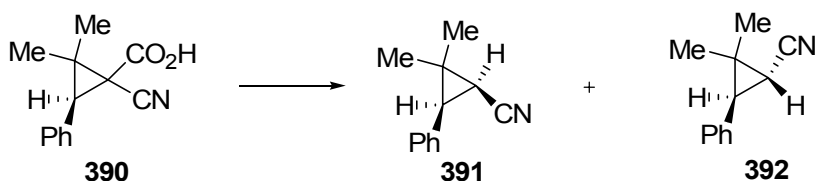
The demethoxycarbonylation of **393** with DMSO, LiCl (7 equivalents) and water (7 equivalents) in the presence of NaHCO$_3$ (2 equivalents) (165°C, 0.5 h) led to a 5:1 mixture of *cis-* and *trans* stereoisomers **394** and **395**. The product isomer ratio was dependent on the molar equivalents of the reagents.[211]
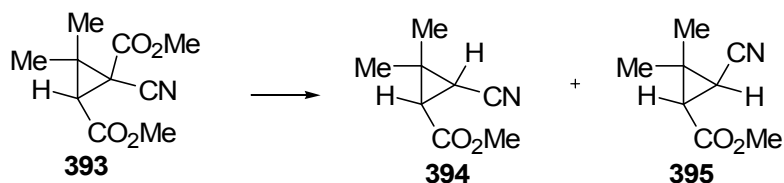
The decarbomethoxylation of the cyano cyclobutane **396** with DMSO, NaCl and water (150°C, 4 h) led to a mixture of *cis-* and *trans*-isomers **397** (77%).[212]
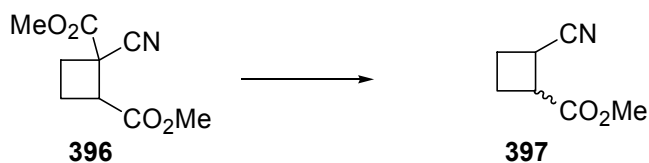
In the enantioselective synthesis of 11-keto steroids, treatment of a mixture of isomers **398** with DMF and LiI (140°C, 40 h) led to the demethoxycarbonylation product **399** (no yield recorded).[213]
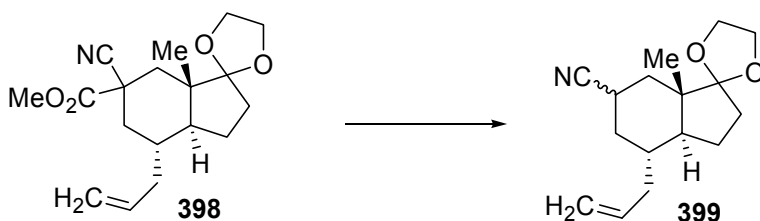
The transannular Diels-Alder reaction and demethoxycarbonylation of macrocycle **400** yielded **401** as a diastereoisomeric mixture (89%) was accomplished by treatment with NaCN and DMSO (160°C, 8 h) followed by an aqueous workup.[214] Treatment of **402** with NaCN and DMSO (160°C, 8 h) followed by water gave **403** (97%).[214]

402   **403**
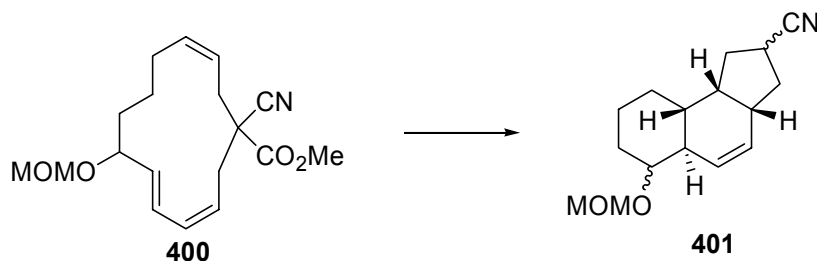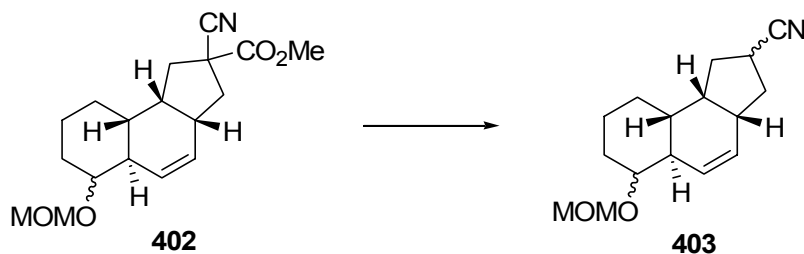
The deethoxycarbonylation and aromatization of dihydrocarbazole **404** with DMSO, LiCl and water (100°C, 26 h) led to **405** (45%).[215]

404   **405**
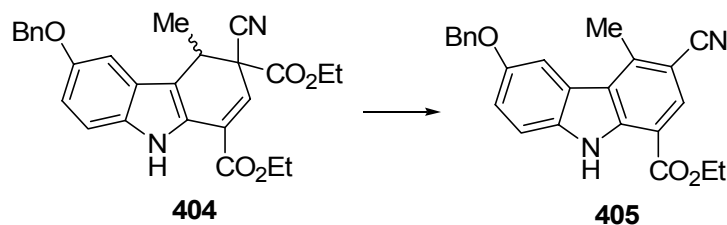
Treatment of α-cyano ester **406** with DMF, NaCN (160°C, 4 h) led to an epimeric racemic mixture of **407** and **408** (63%) in a 2:1 ratio.[216]

406   **407**   **408**
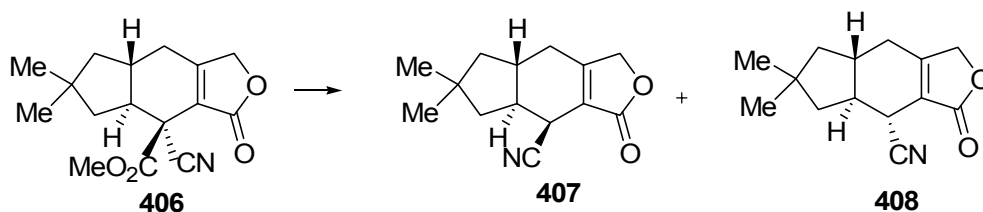
The deethoxycarbonylation of **409** with HMPA, LiCl (160°C, 3 h) yielded **410** (85%).[217]

409   **410**
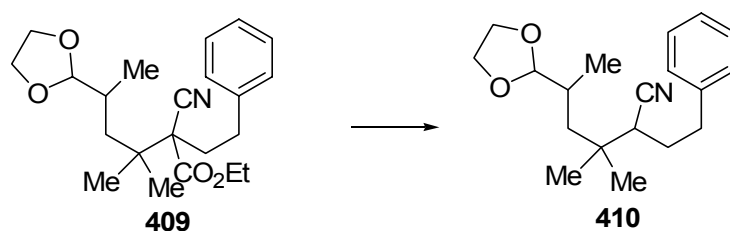
Treatment of **411** with DMF and CaCl$_2$ dihydrate (160°C, 2.5 h) led to mixture of exo/endo (1:1) epimers **412** (79%) which were used in a route leading to an azadicarbaprostaglandin.[218]

411   **412**
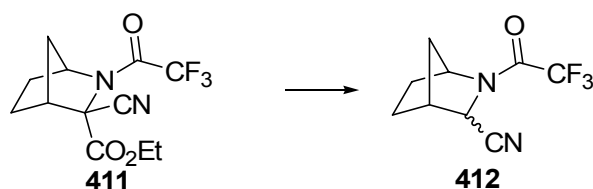
The deethoxycarbonylation of **413** (or the corresponding methyl ester) with DMSO, LiCl and H_2O ($173^{\circ}C$, 4 h) led to **414** (78%).[219]
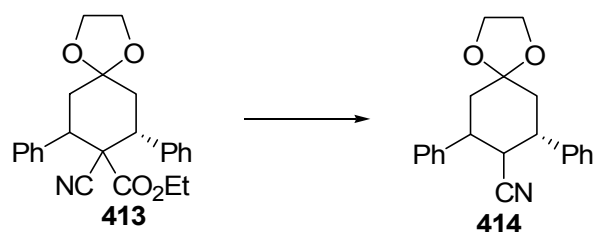
The demethoxycarbonylation of methyl ester **415** (or the corresponding ethyl ester) with DMSO, LiCl and NaHCO$_3$ ($165^{\circ}C$, 3 h) led to 1:1 mixture of the *E*- and *Z*-stereoisomeric nitriles **416** (75%), along with benzaldehyde (18%).[220]
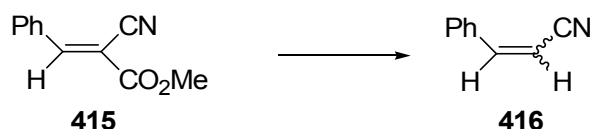
2.10. Sulfones

2.10.1. From α-sulfonyl esters

Treatment of sulfone **417** with DMSO, NaCl and water (reflux, 8h) led to the decarbomethoxylated product **418** (63%).[221]
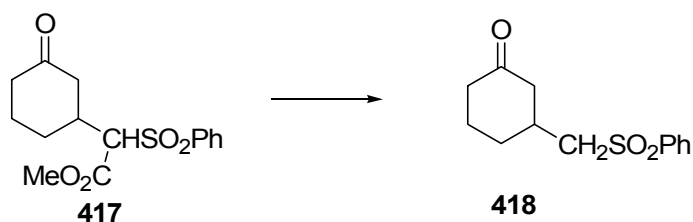
The 1,6-α-tolylsulfonyl ester **419** on treatment with DMSO and NaCl ($170^{\circ}C$, 18 h) led to decarbomethoxylation product **420** (99%).[222]
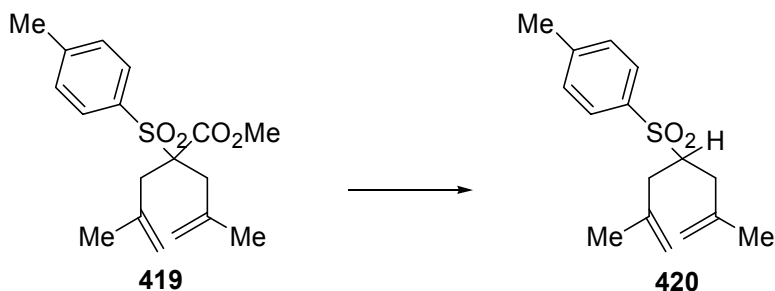
The α-carbomethoxy sulfone **421** on heating in DMSO, NaCl and water (160°C, 6 h) led to sulfone **422** (86%). [223]
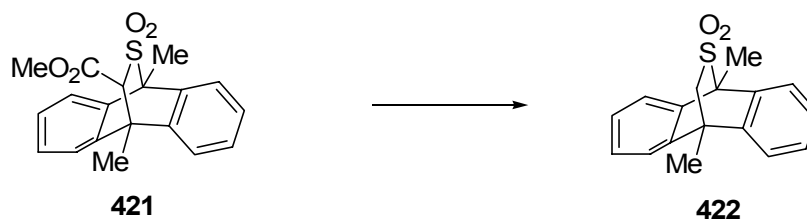
Without providing any experimental details, the demethoxycarbonylation of **423** was reported to afford a good yield of non-racemic **424**, an intermediate to be used in the synthesis of additional chiral analogues.[224]
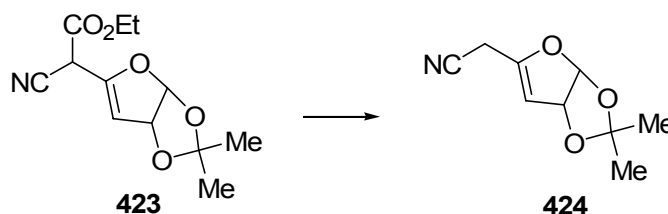
2.11. Sulfoximines

2.11.1. From α-carbomethoxy sulfoximines

The demethoxycarbonylations of both enantiomers of **425** using DMSO and NaCN (120°C) led to the corresponding sulfoximine enantiomers **426**.[225]
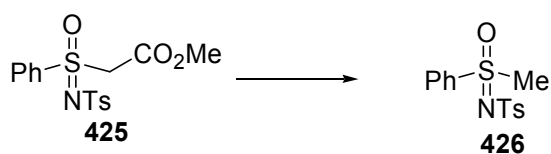
The diastereoisomeric chiral mixture of **427** on treatment with DMSO, NaCN (80°C, 48 h) led to optically active **428** (80%) as a diastereoisomeric mixture.[225]
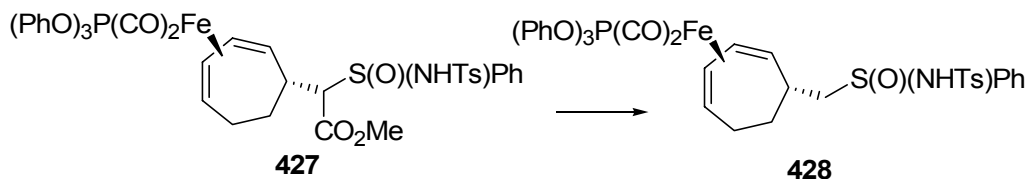
2.12. Chiral phosphine oxides
2.12.1. From P-chiral phosphinyl acetates
One illustrative example of the preparation of chiral phosphine oxides involves the treatment of (+)-(R) **429** with DMSO, LiCl which led to (-)-(S) **430** (34% yield).[226a,b]

429   **430**
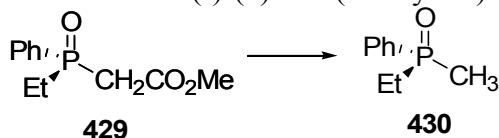
Treatment of α-substituted (-)-(S_P)-ethyl((menthoxycarbonyl)methyl)phenylphosphine oxides **431** with LiCl in aqueous DMSO (reflux, 8-18 h) led to the corresponding (-)-R_P-alkylethylphosphineoxides **432** in 54-70% yields in 100% enantiomeric purity.[227]

431   **432**

R = CD$_3$, CH$_3$CH$_2$; CH$_2$=CHCH$_2$; PhCH$_2$
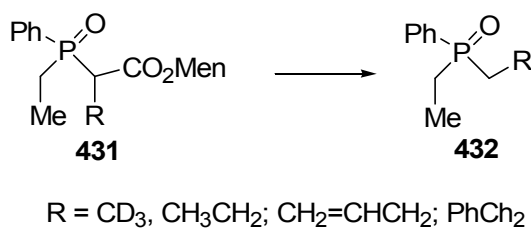
2.13. Ketophosphonates
2.13.1. From 2-acylphosphonoacetates
It has been reported that 2-acylphosphonoacetates such as **433** undergo deethoxy-carbonylations with water (oil bath, 120-140°C, 2-3 h) to afford β-ketophosphonates such as **434** (70%). A number of other substrates were also evaluated.[228]

433   **434**
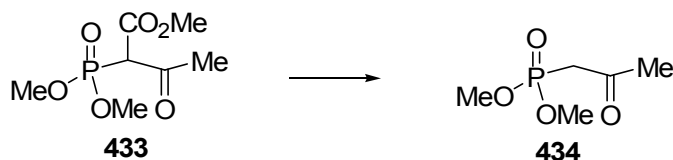
2.14. Nitro analogues
2.14.1. From α-nitro esters
Only one example of a dealkoxycarbonylation of an α-nitro ester could be found.

Treatment of α-nitro ester **435** with DMSO, NaCl and water (150°C, 4 h) led to deethoxycarbonylation to afford nitro derivative **436** (66%).[229]

435   **436**
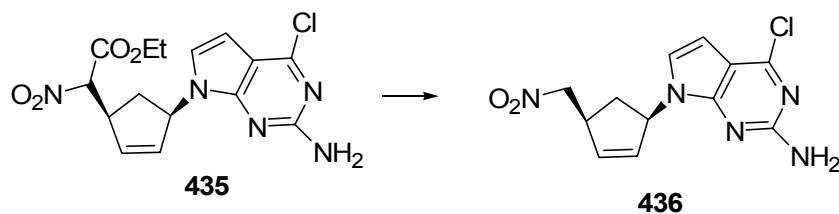
2.15. 2-Cyclohexenone derivatives
2.15.1. From 4-carbalkoxy-2-cyclohexanones

The chemoselective deethoxycarbonylation of the keto diester **437** on treatment with DMSO, LiCl and water (180-190°C, 5 h) led to **438** (70%).[230]
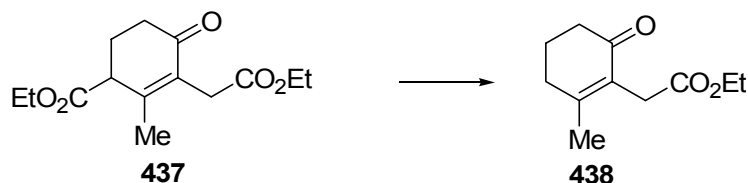
Upon heating **439** in DMSO, NaCl and water (140°C, 10 h, sealed tube), **440** (19%) was obtained, the product of a demethoxycarbonylation and a demethoxylation. This yield (40%) was improved with the use of MgCl$_2$.   The mesylate (OMs instead of OMe in **439**, α-position to the ester group) under the MgCl$_2$ -DMSO conditions led to **440** (89%). This intermediate was used in a synthesis of *Erythrina* and related alkaloids.[231]
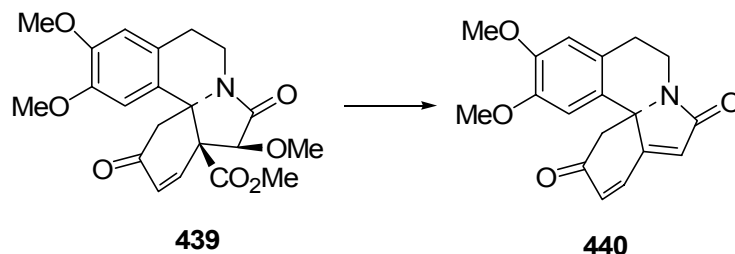
2.16. Heterocyclic vinylogous dethoxycarbonylation

The deethoxycarbonylation of the heterocyclic susbstrate **441** to afford **442** (32%) was accomplished by treatment with DMSO, NaCl and water (145°C, 6 h).[232]
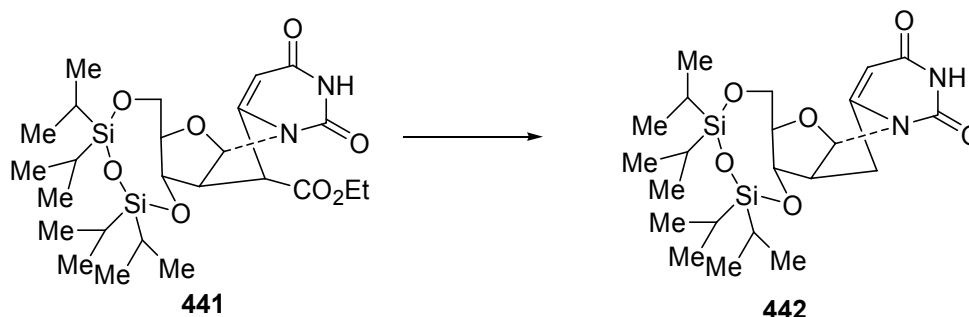
2.17. Tetra-demethoxycarbonylation

Treatment of **443** with DMSO, NaCl and water (140°C, 4 h) led to **444** (quantitatively). A rational mechanism is proposed.[233]
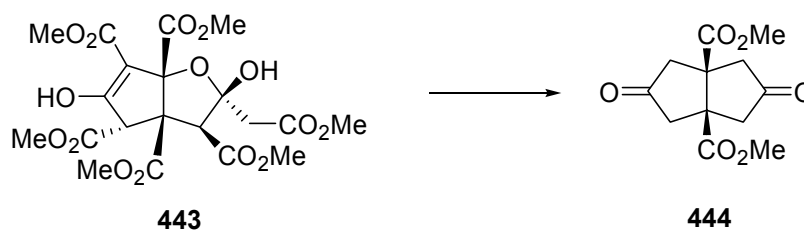
3. Conclusions

Dealkoxycarbonylations of a wide variety of substrates have been accomplished using NaCN, NaCl or LiCl and water in dipolar aprotic solvents such as DMSO and DMF. This procedure will continue to be useful in the dealkoxycarbonylations of activated ester functionalities.

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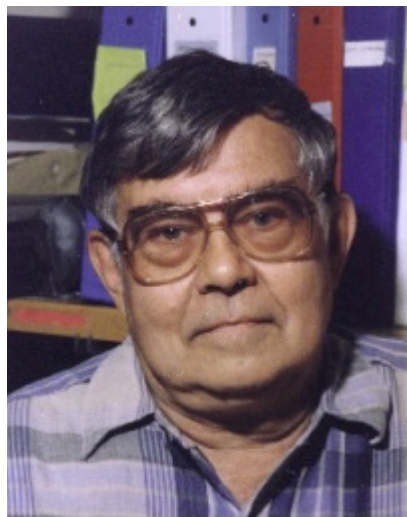
A. Paul Krapcho was born in Alden Station, PA on March 6, 1932. He did his undergraduate work at Penn State (B.S. in Chemistry, 1953) and graduate studies at Harvard University (Ph.D. 1957). He then spent the 2-year period of 1957-1959 teaching at Smith College and then held a post-doctoral position at Penn State from 1959-1960 (with Phil Skell). In 1960 he joined the faculty at the University of Vermont, where he is currently an Emeritus Professor of Chemistry still active in research. He has directed the research of numerous undergraduate and graduate students in projects related to natural product synthesis, solvolytic studies of spiro analogues, reaction mechanism studies of metal-ammonia reductions, chemistry of carbenes (or carbenoids), reactions of α-anions of acids and esters, and the preparation of anticancer heterocyclic analogues. Krapcho has been a Fulbright scholar at the University of Montpellier, France (1968-1969), a research scholar at Stanford University (1976-1977) and an invited lecturer at Addis Ababa University in Ethiopia (1981). He was a research scholar at Duke University (1983-1984), the University research scholar in Physical Sciences (1990), a visiting Professor at the University of Auckland Medical School in Auckland, New Zealand (Spring 1991) and, for a short period, at Humboldt University in Berlin, Germany (1998). He has been involved over the past 15 years in a collaborative anticancer drug development program initially with the Vermont Cancer Center, and then with Novuspharma SpA of Milan, Italy (recently merged with CTI) and the University of Padova, Padova, Italy. These projects deal with the synthesis of telomerase inhibitors. Recently (2005-present) he was awarded a Dreyfus Senior Scientist Mentor grant. Krapcho is a Scientific Editor for ARKIVOC (2000-present) and a Co-Editor-in-Chief of Mini-Reviews in Medicinal Chemistry (2001-present).