

One-Pot Synthesis of 2*H*-Pyrans by Indium(III) Chloride-Catalyzed Reactions. Efficient Synthesis of Pyranocoumarins, Pyranophenalenones, and Pyranoquinolinones

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An efficient synthesis of 2*H*-pyrans is achieved by indium (III) chloride-catalyzed reactions of 1,3-dicarbonyl compounds with a variety of α,β -unsaturated aldehydes in moderate yields. This method has been applied to the synthesis of pyranocoumarins, pyranophenalenones, and pyranoquinolinone alkaloids.

Keywords : Indium(III) chloride, Pyranocoumarins, Pyranophenalenones, Pyranoquinolinones.

Introduction

2*H*-Pyrans are distributed in nature as a key unit of natural products.¹ They have a variety of interesting biological activities and potential medical applications.² Although several synthetic approaches of 2*H*-pyrans derivatives have been reported, general and efficient approaches still remain scarce.³ In previous work, the many steps and low yields which were required for preparation have prompted our research for better preparation of 2*H*-pyrans.

Indium(III) chloride has been used as an efficient catalyst in organic synthesis.⁴ Also, it has been proven that indium (III) chloride is a powerful reagent which is stable in water.⁵ Indium(III) chloride-catalyzed Mukaiyama aldol reaction,⁶ Mannich-type reaction,^{5c,7} Diels-Alder reaction,⁸ aziridination reaction,⁹ Fridel-Crafts reaction,¹⁰ Barbier reaction,¹¹ and Biginelli reaction¹² have been already reported by many groups. However, indium(III) chloride-catalyzed reaction of 1,3-carbonyl compounds to α,β -unsaturated aldehydes has not been examined. We report here a convenient and efficient one-pot synthesis of 2*H*-pyrans by a tandem Knoevenagel-electrocyclic reaction. The strategy that we have developed begins with the reaction of cyclic 1,3-dicarbonyl compounds **1-8** (Figure 1) and α,β -unsaturated aldehydes in the presence of indium(III) chloride.

Results and Discussion

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**2**) with

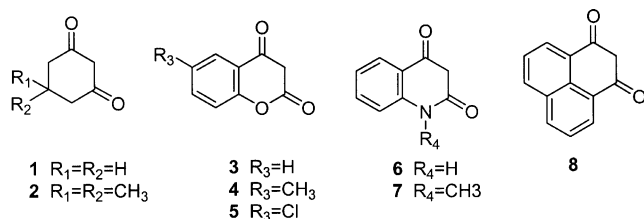
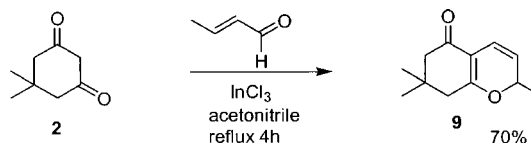


Figure 1



Scheme 1

crotonaldehyde in refluxing acetonitrile for 4h in the presence of 50 mol % of indium(III) chloride afforded 2*H*-pyran **9** in a 70% yield (Scheme 1). The formation of **9** is supported by the observation of a peak in the IR spectrum at 1651 cm⁻¹ (enone C=O) and the expected chemical shifts associated with two vinylic protons at δ 6.40 ($J = 10.0$ Hz) and at δ 5.24 ($J = 10.0$ Hz) ppm in the ¹H NMR spectrum. This reaction provides a concise synthetic route into the substituted 2*H*-pyrans as a one-pot reaction.

Next, additional reactions of 1,3-cyclohexanediones with several α,β -unsaturated aldehydes in the presence of indium (III) chloride were attempted. The results are summarized in Table 1. In entries 1-5, reactions with crotonaldehyde, 3-methyl-2-butenal, and *trans*-2-methyl-2-butenal afforded cycloadducts **10-14** in 50-61% yields. Interestingly, in the case of 1-cyclohexene-1-carboxaldehyde with a ring system (entries 6-7), the expected pyrans **15-16** were also produced in 74 and 64% yields, respectively.

Next, reaction of 4-hydroxycoumarins **3-5** with α,β -unsaturated aldehydes was examined. The results are summarized in Table 2. Treatment of 4-hydroxycoumarin **3** with crotonaldehyde afforded the biologically interesting pyranocoumarin **17** in 59% yield (entry 1). Compound **17** has been clearly shown to be angular by their spectral analysis and by comparison with reported data in the literature.¹³ Reactions with other α,β -unsaturated aldehydes afforded pyranocoumarins **18-24** in 40-79% yields (entries 2-8). These reactions provide a rapid synthetic route toward pyranocoumarin derivatives, which have been widely found in nature.¹⁴

In order to extend the utility of these reactions, additional reactions were examined starting from 3-hydroxy-1*H*-

Table 1. Reaction of 1,3-cyclohexanediones and α,β -unsaturated aldehydes

Entry	1,3-dicarbonyl compound	α,β -unsaturated aldehyde	Product	Yield (%)
1				50
2				59
3				53
4				52
5				61
6				74
7				64

phenalen-1-one (**8**). Reaction with crotonaldehyde afforded pyranophenalenone **25** in 48 % yield (entry 1). Other similar results are summarized in Table 3. These reactions also provide a rapid synthetic route toward biologically interesting pyranophenalenone derivatives.

As an application of this methodology, one-pot synthesis of pyranoquinolinone alkaloids were investigated. Flindersine (**29**) and *N*-methylflindersine (**30**) have been primarily isolated from Rutaceous plants, *Fagara heitzii*,¹⁵ *Geijera balansae*,¹⁶ *Haplophyllum saveolens*,¹⁷ *Atalantia roxburghiana*,¹⁸ *Micromelum minutum*,¹⁹ and *Zanthoxylum coco*.²⁰ *N*-Methylflindersine (**30**) was also isolated from antifeedant active species,²¹ *Fagara chalybea*, *F. hostil*, *Xylocarpus granatum*, and *Orixa japonica*.²² The stems and leaves of *O. japonica* were formerly used in Japan as an insecticide for livestock.²² Reaction of 4-hydroxy-2(1*H*)-quinolone (**6**) with 3-methyl-2-butenal in the presence of 50 mol % of indium(III) chloride for 4 h at reflux in acetonitrile gave

Table 2. Reaction of 4-hydroxycoumarins and α,β -unsaturated aldehydes

Entry	1,3-dicarbonyl compound	α,β -unsaturated aldehyde	Product	Yield (%)
1				59
2				58
3				79
4				70
5				65
6				45
7				40
8				62

flindersine (**29**) in 41% (Scheme 2). Similarly, reaction of **7** with 3-methyl-2-butenal afforded *N*-methylflindersine (**30**)

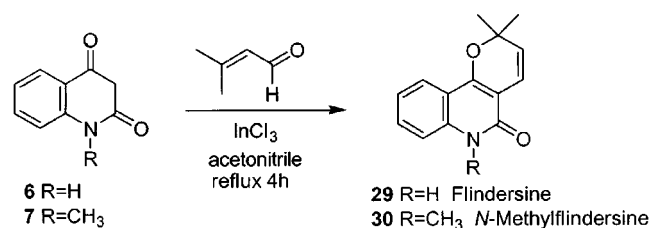
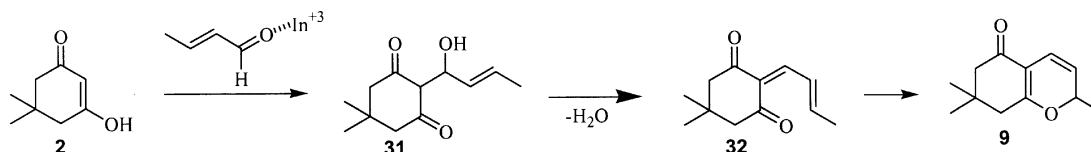
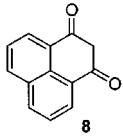
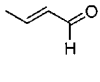
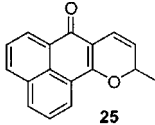
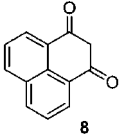
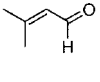
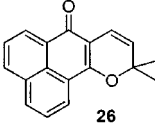
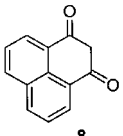
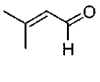
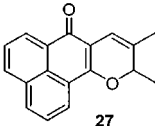
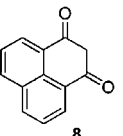
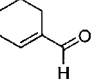
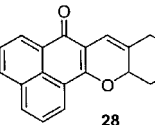

Scheme 2

Scheme 3

Table 3. Reaction of 3-hydroxy-1*H*-phenalen-1-one and α,β -unsaturated aldehydes

Entry	1,3-dicarbonyl compound	α,β -unsaturated aldehyde	Product	Yield (%)
1				48
2				90
3				40
4				60

in 40% yield. Spectral data of our synthetic materials are in agreement with those reported in the literature.²²

Although the exact mechanism of the reaction is still not clear, it is best described as shown in Scheme 3. The dione **2** first attacks aldehyde to yield the alcohol **31**, which is dehydrated on heating in acidic condition to give **32**. The intermediate **32** then undergoes electrocyclic reaction to give cycloadduct **9**.

Experimental Section

All experiments were carried out under a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points were determined with microcover glasses on a Fisher-Johns apparatus and are uncorrected. ¹H NMR spectra were recorded on a Bruker Model ARX (300 MHz) spectrometer. IR spectra were recorded on a JASCO FTIR 5300 spectrophotometer. Elemental analysis and HRMS spectra were obtained by Yeungnam University Instrumental Analysis Center and Korea Basic Science Institute

General Procedure for the Synthesis of 2*H*-Pyrans. To a solution of 1,3-dicarbonyl compound (1.0 mmol) and α,β -unsaturated aldehyde (2.0 mmol) in acetonitrile (10 mL) was added InCl₃ (111 mg, 0.5 mmol) at room temperature. The reaction mixture was refluxed for 4 h and then cooled to room temperature. Saturated sodium bicarbonate was added and the solution was extracted with ethyl acetate. Evaporation of solvent and purification by column chromatography on silica gel give products.

2,7,7-Trimethyl-2,6,7,8-tetrahydro-chromen-5-one (9)^{3f}.

Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**2**) (140 mg, 1 mmol) with crotonaldehyde (140 mg, 2 mmol) afforded **9** (135 mg, 70%) as a liquid: ¹H NMR (300 MHz) δ 6.40 (1H, d, J = 10.0 Hz), 5.24 (1H, dd, J = 10.0, 3.1 Hz), 4.96 (1H, m), 2.31-2.17 (4H, m), 1.36 (3H, d, J = 6.5 Hz), 1.03 (3H, s), 1.02 (3H, s); IR (neat) 2960, 1651, 1633, 14222, 1408, 1370, 1224, 1140, 1054, 947 cm⁻¹.

2-Methyl-2,6,7,8-tetrahydro-chromen-5-one (10)^{3f}. Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with crotonaldehyde (140 mg, 2 mmol) afforded **10** (82 mg, 50%) as a liquid: ¹H NMR (300 MHz) δ 6.43 (1H, d, J = 10.0 Hz), 5.26 (1H, dd, J = 10.0, 3.0 Hz), 4.99 (1H, m), 2.42-2.34 (4H, m), 2.02-1.90 (2H, m), 1.38 (3H, d, J = 6.5 Hz); IR (neat) 2933, 1650, 1639, 1612, 1454, 1403, 1256, 1232, 1192, 1136, 1068, 931 cm⁻¹.

2,2-Dimethyl-2,6,7,8-tetrahydro-chromen-5-one (11)^{3f}. Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **11** (105 mg, 59%) as a liquid: ¹H NMR (300 MHz) δ 6.38 (1H, d, J = 10.0 Hz), 5.21 (1H, d, J = 10.0 Hz), 2.39-2.34 (4H, m), 1.99-1.90 (2H, m), 1.37 (6H, s); IR (neat) 2926, 1645, 1611, 1455, 1399, 1375, 1266, 1188, 1130, 1010, 905 cm⁻¹.

2,2,7,7-Tetramethyl-2,6,7,8-tetrahydro-chromen-5-one (12). Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**2**) (140 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **12** (109 mg, 53%) as a solid: mp 38-40 °C; ¹H NMR (300 MHz) δ 6.36 (1H, d, J = 9.9 Hz), 5.19 (1H, d, J = 9.9 Hz), 2.23 (2H, s), 2.21 (2H, s), 1.35 (6H, s), 1.03 (6H, s); IR (KBr) 2959, 2870, 1645, 1633, 1586, 1454, 1416, 1351, 1324, 1299, 1251, 1206, 1131, 1090, 1047, 976, 928 cm⁻¹; HRMS m/z (M^+) calcd for C₁₃H₁₈O₂: 206.1306. Found: 206.1306.

2,3-Dimethyl-2,6,7,8-tetrahydro-chromen-5-one (13). Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with *trans*-2-methyl-2-butenal (168 mg, 2 mmol) afforded **13** (93 mg, 52%) as a liquid: ¹H NMR (300 MHz) δ 6.10 (1H, s), 4.77 (1H, q, J = 6.4 Hz), 2.35-2.27 (4H, m), 1.92-1.65 (2H, m), 1.65 (3H, s), 1.27 (3H, d, J = 6.4 Hz); IR (neat) 2940, 1645, 1615, 1452, 1403, 1383, 1234, 1193, 1169, 1070, 1010, 931 cm⁻¹; HRMS m/z (M^+) calcd for C₁₁H₁₄O₂: 178.0994. Found: 178.0991.

2,3,7,7-Tetramethyl-2,6,7,8-tetrahydro-chromen-5-one (14). Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**2**) (140 mg, 1 mmol) with *trans*-2-methyl-2-butenal (168 mg, 2 mmol) afforded **14** (126 mg, 61%) as a solid: mp 80-82 °C; ¹H NMR (300 MHz) δ 6.16 (1H, s), 4.80 (1H, q, J = 6.4 Hz), 2.28-2.20 (4H, m), 1.70 (3H, s), 1.31 (3H, d, J = 6.4 Hz), 1.05 (3H, s), 1.02 (3H, s); IR (KBr) 2963, 1645, 1634, 1622, 1558, 1471, 1455, 1418, 1404, 1387, 1373, 1260, 1238, 1067, 1030, 877 cm⁻¹; HRMS m/z (M^+) calcd for C₁₃H₁₈O₂: 206.1306. Found: 206.1305.

2,3,4,5,6,7,8,10a-Octahydro-xanthen-1-one (15). Reaction of 1,3-cyclohexanedione (**1**) (112 mg, 1 mmol) with 1-cyclohexene-1-carboxaldehyde (220 mg, 2 mmol) afforded **15** (152 mg, 74%) as a liquid: ¹H NMR (300 MHz) δ 6.05 (1H, s), 4.91 (1H, dd, J = 10.9, 4.9 Hz), 2.35-2.30 (6H, m), 1.95-1.24 (8H, m); IR (neat) 2942, 1645, 1518, 1404, 1171, 1073, 1019, 939, 869 cm⁻¹; HRMS m/z (M^+) calcd for

C₁₃H₁₆O₂: 204.1150. Found: 204.1150.

3,3-Dimethyl-2,3,4,5,6,7,8,10a-octahydro-xanthen-1-one (16). Reaction of 5,5-dimethyl-1,3-cyclohexanedione (**2**) (140 mg, 1 mmol) with 1-cyclohexene-1-carboxaldehyde (220 mg, 2 mmol) afforded **16** (149 mg, 64%) as a liquid: ¹H NMR (300 MHz) δ 6.05 (1H, s), 4.92 (1H, dd, *J* = 10.9, 4.9 Hz), 2.37-2.05 (6H, m), 1.95-1.20 (6H, m), 1.04 (3H, s), 1.03 (3H, s); IR (neat) 2955, 1644, 1630, 1617, 1404, 1258, 1231, 1146, 1074, 1041, 1008, 945 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₅H₂₀O₂: 232.1463. Found: 232.1464.

2-Methyl-2H-pyrano[3,2-*c*]chromen-5-one (17). Reaction of 4-hydroxycoumarin (**3**) (162 mg, 1 mmol) with crotonaldehyde (140 mg, 2 mmol) afforded **17** (127 mg, 59%) as a solid: mp 55-56 °C; ¹H NMR (300 MHz) δ 7.75 (1H, dd, *J* = 7.8, 1.6 Hz), 7.5 (1H, m), 7.28-7.23 (2H, m), 6.55 (1H, d, *J* = 10.0 Hz), 5.55 (1H, dd, *J* = 10.0, 3.2 Hz), 5.27 (1H, m), 1.52 (3H, d, *J* = 6.6 Hz); IR (KBr) 3069, 2982, 2930, 1707, 1642, 1609, 1566, 1493, 1454, 1418, 1377, 1327, 1271, 1217, 1192, 1165, 1113, 1040, 1019, 922 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₃H₁₀O₃: 214.0630. Found: 214.0631.

2,9-Dimethyl-2H-pyrano[3,2-*c*]chromen-5-one (18). Reaction of 4-hydroxy-6-methyl-coumarin (**4**) (176 mg, 1 mmol) with crotonaldehyde (140 mg, 2 mmol) afforded **18** (133 mg, 58%) as a solid: mp 123-125 °C; ¹H NMR (300 MHz) δ 7.53 (1H, s), 7.29 (1H, d, *J* = 8.3 Hz), 7.16 (1H, d, *J* = 8.3 Hz), 6.56 (1H, d, *J* = 9.1 Hz), 5.55 (1H, dd, *J* = 9.1, 3.1 Hz), 5.28 (1H, m), 2.39 (3H, s), 1.53 (3H, d, *J* = 6.5 Hz); IR (KBr) 2986, 1713, 1645, 1572, 1495, 1427, 1371, 1304, 1269, 1219, 1202, 1127, 1084, 1028, 924 899 922 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₄H₁₂O₃: 228.0786. Found: 228.0790.

2,2-Dimethyl-2H-pyrano[3,2-*c*]chromen-5-one (19). Reaction of 4-hydroxycoumarin (**3**) (162 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **19** (181 mg, 79%) as a liquid: ¹H NMR (300 MHz) δ 7.78 (1H, dd, *J* = 7.8, 1.6 Hz), 7.50 (1H, m), 7.30-7.23 (2H, m), 6.53 (1H, d, *J* = 9.9 Hz), 5.52 (1H, d, *J* = 9.9 Hz), 1.47 (6H, s); IR (neat) 3073, 2978, 2930, 1715, 1642, 1566, 1493, 1458, 1416, 1362, 1327, 1281, 1217, 1192, 1157, 1115, 1038, 992, 909 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₄H₁₂O₃: 228.0786. Found: 228.0790.

2,2,9-Trimethyl-2H-pyrano[3,2-*c*]chromen-5-one (20). Reaction of 4-hydroxy-6-methyl-coumarin (**4**) (176 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **20** (170 mg, 70%) as a solid: mp 107-109 °C; ¹H NMR (300 MHz) δ 7.55 (1H, s), 7.30 (1H, d, *J* = 8.4 Hz), 7.17 (1H, d, *J* = 8.4 Hz), 6.50 (1H, d, *J* = 10.0 Hz), 5.49 (1H, d, *J* = 10.0 Hz), 2.39 (3H, s), 1.53 (6H, s); IR (KBr) 2976, 2922, 1711, 1651, 1576, 1462, 1418, 1354, 1316, 1279, 1194, 1154, 1127, 1107, 1046, 1024, 941, 920 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₅H₁₄O₃: 242.0943. Found: 242.0946.

9-Chloro-2,2-dimethyl-2H-pyrano[3,2-*c*]chromen-5-one (21). Reaction of 6-chloro-4-hydroxy-coumarin (**5**) (197 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **21** (171 mg, 65%) as a solid: mp 122-124 °C; ¹H NMR (300 MHz) δ 7.74 (1H, s), 7.45 (1H, d, *J* = 8.7 Hz), 7.23 (1H, d, *J* = 8.7 Hz), 6.50 (1H, d, *J* = 10.2 Hz), 5.55 (1H, d, *J* = 10.2 Hz); IR (KBr) 2974, 2933, 1718, 1651, 1603, 1562, 1485, 1416, 1351, 1311, 1263, 1144, 1119, 1005, 911 cm⁻¹;

Anal. Calcd for C₁₄H₁₁ClO₃: C, 64.01; H, 4.22. Found: C, 64.51; H, 4.28.

2,3-Dimethyl-2H-pyrano[3,2-*c*]chromen-5-one (22). Reaction of 4-hydroxycoumarin (**3**) (162 mg, 1 mmol) with *trans*-2-methyl-2-butenal (168 mg, 2 mmol) afforded **22** (103 mg, 45%) as a solid: mp 59-60 °C; ¹H NMR (300 MHz) δ 7.73 (1H, dd, *J* = 7.8, 1.6 Hz), 7.46 (1H, m), 7.29-7.21 (2H, m), 6.31 (1H, s), 5.09 (1H, q, *J* = 7.9 Hz), 1.73 (3H, s), 1.46 (3H, d, *J* = 7.9 Hz); IR (KBr) 3061, 2984, 2926, 2859, 1707, 1644, 1570, 1495, 1427, 1372, 1269, 1219, 1202, 1155, 1127, 1084, 1028, 924, 901 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₄H₁₂O₃: 228.0786. Found: 228.0786.

2,3,9-Trimethyl-2H-pyrano[3,2-*c*]chromen-5-one (23). Reaction of 4-hydroxy-6-methyl-coumarin (**4**) (176 mg, 1 mmol) with *trans*-2-methyl-2-butenal (168 mg, 2 mmol) afforded **23** (97 mg, 40%) as a solid: mp 93-95 °C; ¹H NMR (300 MHz) δ 7.52 (1H, s), 7.29 (1H, d, *J* = 10.1 Hz), 7.17 (1H, d, *J* = 10.1 Hz), 6.30 (1H, s), 5.05 (1H, q, *J* = 7.8 Hz), 2.39 (3H, s), 1.84 (3H, s), 1.46 (3H, d, *J* = 7.8 Hz); IR (KBr) 2983, 2926, 28611710, 1660, 1620, 1607, 1575, 1499, 1439, 1400, 1324, 1300, 1207, 1167, 1124, 1063, 991, 975, 926, 816 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₅H₁₄O₃: 242.0943. Found: 242.0945.

2-Methyl-9,10,11,11a-tetrahydro-8H-chromeno[4,3-*b*]chromen-6-one (24). Reaction of 4-hydroxy-6-methyl-coumarin (**4**) (176 mg, 1 mmol) with 1-cyclohexene-1-carboxaldehyde (220 mg, 2 mmol) afforded **24** (167 mg, 62%) as a solid: mp 125-128 °C; ¹H NMR (300 MHz) δ 7.48 (s, 1H), 7.27 (1H, d, *J* = 10.1 Hz), 7.14 (1H, d, *J* = 10.1 Hz), 6.19 (1H, s), 5.18 (1H, dd, *J* = 13.5, 6.5 Hz), 2.38 (3H, s), 2.38-1.27 (8H, m); IR (KBr) 2922, 1709, 1493, 1426, 1329, 1204, 1115, 1053, 1015, 963, 936, 891 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₇H₁₆O₃: 268.1099. Found: 268.1096.

10-Methyl-10H-11-oxa-benzo[de]anthracen-7-one (25). Reaction of 3-hydroxy-1H-phenalen-1-one (**8**) (196 mg, 1 mmol) with crotonaldehyde (140 mg, 2 mmol) afforded **25** (120 mg, 48%) as a solid: mp 94-96 °C; ¹H NMR (300 MHz) δ 8.59 (1H, dd, *J* = 7.3, 1.2 Hz), 8.19 (1H, dd, *J* = 7.3, 1.1 Hz), 8.10 (1H, dd, *J* = 8.1, 1.1 Hz), 8.01 (1H, dd, *J* = 8.2, 1.1 Hz), 7.69 (1H, dd, *J* = 8.1, 7.3 Hz), 7.59 (1H, dd, *J* = 8.2, 7.3 Hz), 6.88 (1H, d, *J* = 9.9 Hz), 5.61 (1H, dd, *J* = 9.9, 3.3 Hz), 5.25 (1H, m), 1.54 (3H, d, *J* = 6.6 Hz); IR (KBr) 3059, 2976, 2926, 1633, 1577, 1509, 1427, 13081, 1358, 1323, 1225, 1193, 1156, 1126, 1021, 913, 877, 846 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₇H₁₂O₂: 248.0837. Found: 248.0839.

10,10-Dimethyl-10H-11-oxa-benzo[de]anthracen-7-one (26). Reaction of 3-hydroxy-1H-phenalen-1-one (**8**) (196 mg, 1 mmol) with 3-methyl-2-butenal (168 mg, 2 mmol) afforded **26** (237 mg, 90%) as a solid: mp 85-88 °C; ¹H NMR (300 MHz) δ 8.59 (1H, dd, *J* = 7.3, 1.2 Hz), 8.21 (1H, dd, *J* = 7.3, 1.1 Hz), 8.10 (1H, dd, *J* = 8.1, 1.1 Hz), 8.01 (1H, dd, *J* = 8.2, 1.1 Hz), 7.69 (1H, dd, *J* = 8.1, 7.3 Hz), 7.60 (1H, dd, *J* = 8.2, 7.3 Hz), 6.83 (1H, d, *J* = 9.9 Hz), 5.56 (1H, d, *J* = 9.9 Hz), 1.54 (6H, s); IR (KBr) 2975, 2927, 1632, 1578, 1506, 1458, 1425, 1387, 1331, 1259, 1152, 1127, 898 cm⁻¹; HRMS *m/z* (M⁺) calcd for C₁₈H₁₄O₂: 262.0993. Found: 262.0994.

9,10-Dimethyl-10H-11-oxa-benzo[de]anthracen-7-one

(27). Reaction of 3-hydroxy-1*H*-phenalen-1-one (**8**) (196 mg, 1 mmol) with 3-methyl-2-butanal (168 mg, 2 mmol) afforded **27** (105 mg, 40%) as a solid: mp 136-139 °C; ¹H NMR (300 MHz) δ 8.59 (1H, d, *J* = 7.3 Hz), 8.17 (1H, d, *J* = 7.3 Hz), 8.10 (1H, d, *J* = 7.8 Hz), 7.99 (1H, d, *J* = 7.8 Hz), 7.69 (1H, dd, *J* = 7.8, 7.3 Hz), 7.57 (1H, dd, *J* = 7.8, 7.3 Hz), 6.61 (1H, s), 5.06 (1H, q, *J* = 6.4 Hz), 1.89 (3H, s), 1.45 (3H, d, *J* = 6.4 Hz); IR (KBr) 3075, 2978, 2930, 1713, 1644, 1566, 1493, 1456, 1414, 1362, 1327, 1281, 1248, 1217, 1157, 1115, 1038, 989, 909 cm⁻¹; HRMS *m/z* (*M*⁺) calcd for C₁₈H₁₄O₂: 262.0994. Found: 262.0993.

10,11,12,12a-Tetrahydro-9*H*-13-oxa-benzo[de]naphthacen-7-one (28). Reaction of 3-hydroxy-1*H*-phenalen-1-one (**8**) (196 mg, 1 mmol) with 1-cyclohexene-1-carboxaldehyde (220 mg, 2 mmol) afforded **28** (173 mg, 60%) as a liquid: ¹H NMR (300 MHz) δ 8.55 (1H, d, *J* = 7.3 Hz), 8.13 (1H, d, *J* = 7.3 Hz), 8.07 (1H, d, *J* = 8.1 Hz), 7.97 (1H, d, *J* = 8.1 Hz), 7.67 (1H, dd, *J* = 8.1, 7.3 Hz), 7.57 (1H, dd, *J* = 8.1, 7.3 Hz), 6.51 (1H, s), 5.17 (1H, dd, *J* = 11.1, 5.1 Hz), 2.51-1.34 (8H, m); IR (neat) 3060, 2933, 2857, 1632, 1577, 1422, 1383, 1296, 1198, 1026, 941, 861 cm⁻¹; HRMS *m/z* (*M*⁺) calcd for C₂₀H₁₆O₂: 288.1150. Found: 288.1146.

Flindersine (29)²². Reaction of 4-hydroxy-2(1*H*)-quinolone (**6**) (161 mg, 1 mmol) with 3-methyl-2-butanal (168 mg, 2 mmol) afforded **29** (94 mg, 41%) as a solid: mp 195 °C; ¹H NMR (300 MHz, CDCl₃) δ 11.5 (1H, s), 7.87 (1H, d, *J* = 8.1 Hz), 7.46 (1H, dd, *J* = 8.2, 7.4 Hz), 7.31 (1H, d, *J* = 8.2 Hz), 7.17 (1H, dd, *J* = 8.1, 7.4 Hz), 6.75 (1H, d, *J* = 9.9 Hz), 5.54 (1H, d, *J* = 9.9 Hz), 1.53 (6H, s); IR (KBr) 3152, 2975, 1651, 1630, 1599, 1499, 1433, 1411, 1361, 1278, 1132, 872 cm⁻¹.

***N*-Methylflindersine (30)**²³. Reaction of 4-hydroxy-1-methyl-2(1*H*)-quinolone (**7**) (175 mg, 1 mmol) with 3-methyl-2-butanal (168 mg, 2 mmol) afforded **30** (97 mg, 40%) as a solid: mp 80 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.93 (1H, d, *J* = 8.0 Hz), 7.51 (1H, dd, *J* = 8.3, 7.3 Hz), 7.28 (1H, d, *J* = 8.3 Hz), 7.19 (1H, dd, *J* = 8.0, 7.3 Hz), 6.73 (1H, d, *J* = 10.0 Hz), 5.51 (1H, d, *J* = 10.0 Hz), 3.67 (3H, s), 1.49 (6H, s); IR (KBr) 2976, 1645, 1505, 1464, 1418, 1360, 1325, 1211, 1154, 1123, 1092, 1044, 1005, 987, 895 cm⁻¹.

Conclusion

The indium(III) chloride-catalyzed reactions of 1,3-dicarbonyl compounds with α,β-unsaturated aldehydes are carried out in refluxing acetonitrile to yield the 2*H*-pyrans. These methods have been applied to the synthesis of biologically interesting pyranocoumarins and pyranophenalenones, and naturally occurring pyranoquinolinone alkaloids such as flindersine (**29**) and *N*-methylflindersine (**30**) in moderate yields.

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