Unexpected dimerization reaction of 5-methyl-6,7-methylendioxy-1-tetralone in the presence of TMSCl-ethylene glycol

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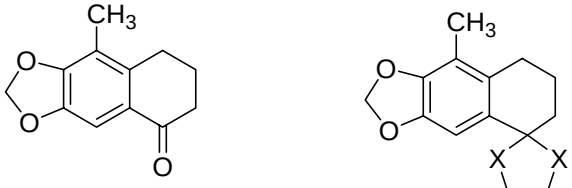
Dedicated to Professor Joan Bosch on his 60th birthday

Abstract
Unprecedented dimerization reactions of the title compound using TMSCl as reagent and ethylene glycol as solvent has been observed and rationalized.

Keywords: Dimerization, tetralone, trimethylsilyl chloride, ethylene glycol, Mukaiyama reaction

Introduction

During our approach to the synthesis of the hydrophenalene ring system of pseudopterosines,[1] it was necessary to protect the 1-tetralone derivative **1** as cyclic acetal **5** or dithiane **6**. Thus, the reaction of **1** with 1,2-ethanedithiol in presence of $BF_3 \cdot OEt_2$ afforded **6** (88% isolated yield).[2] In contrast, when **1** reacts with ethylene glycol (benzene, reflux) in the presence of TsOH, compound **5** was isolated with maximum (and difficult to reproduce) 47% yield (Figure 1).



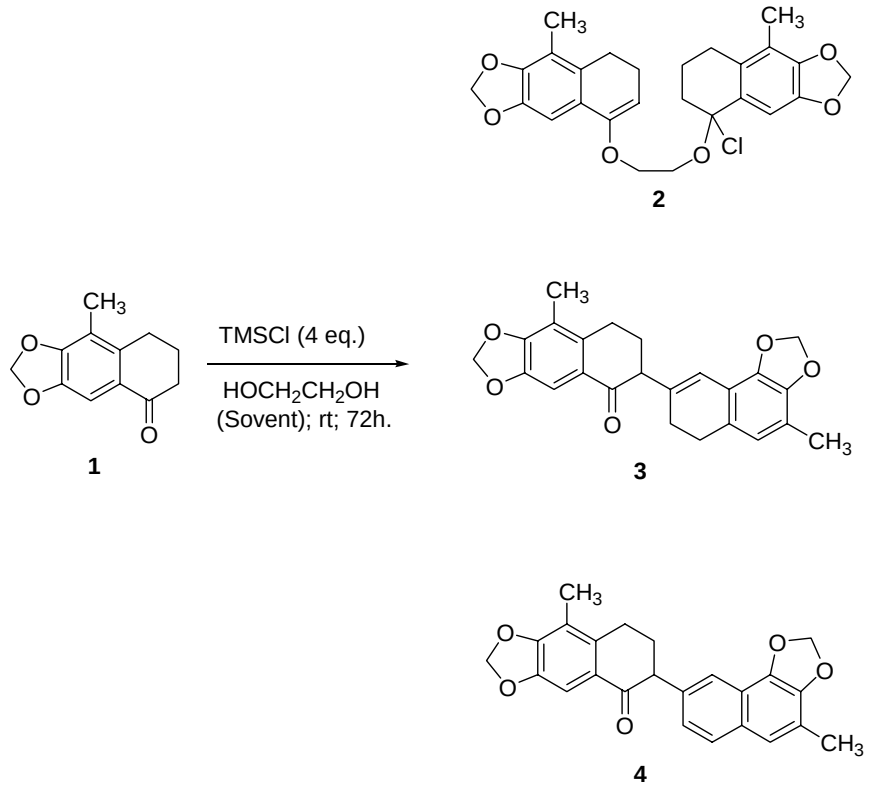
1

5, X = O
6, X = S

Figure 1

During the search for an alternative method for the preparation of **5,** the use of ethylene glycol as solvent in the presence of trimethylsilyl chloride[3] was considered as an appealing

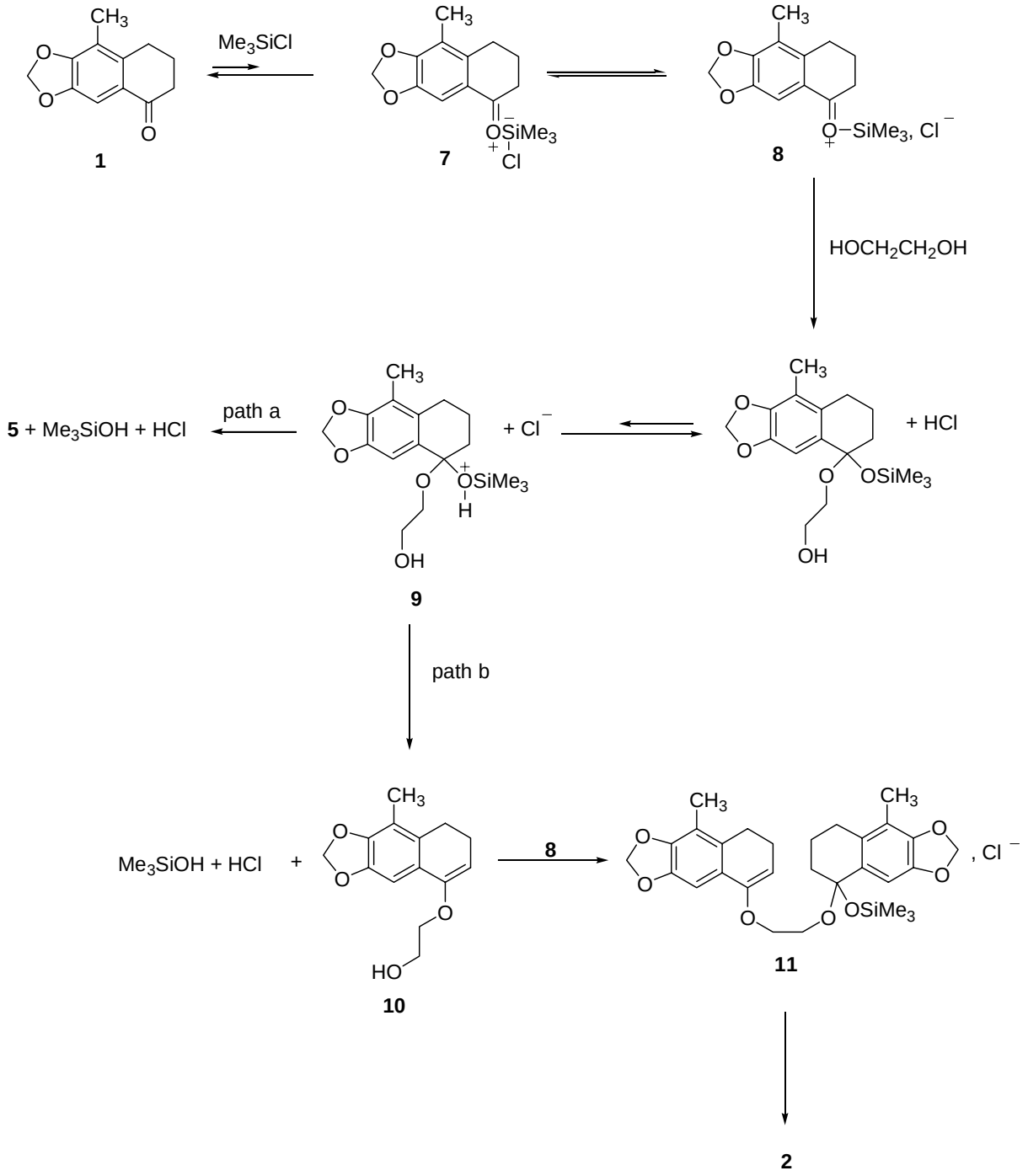
possibility. In this way, when **1** (2,0 mmol) was subjected to reaction with 8,2 mmol of TMSCl in 10 ml of ethylene glycol (rt, 72h), no traces of compound **5** were observed and instead a mixture of compounds **2**, **3** and **4** were isolated by column chromatography (SiO_2, hexane-AcOEt, 20:1). (Scheme 1)



Scheme 1

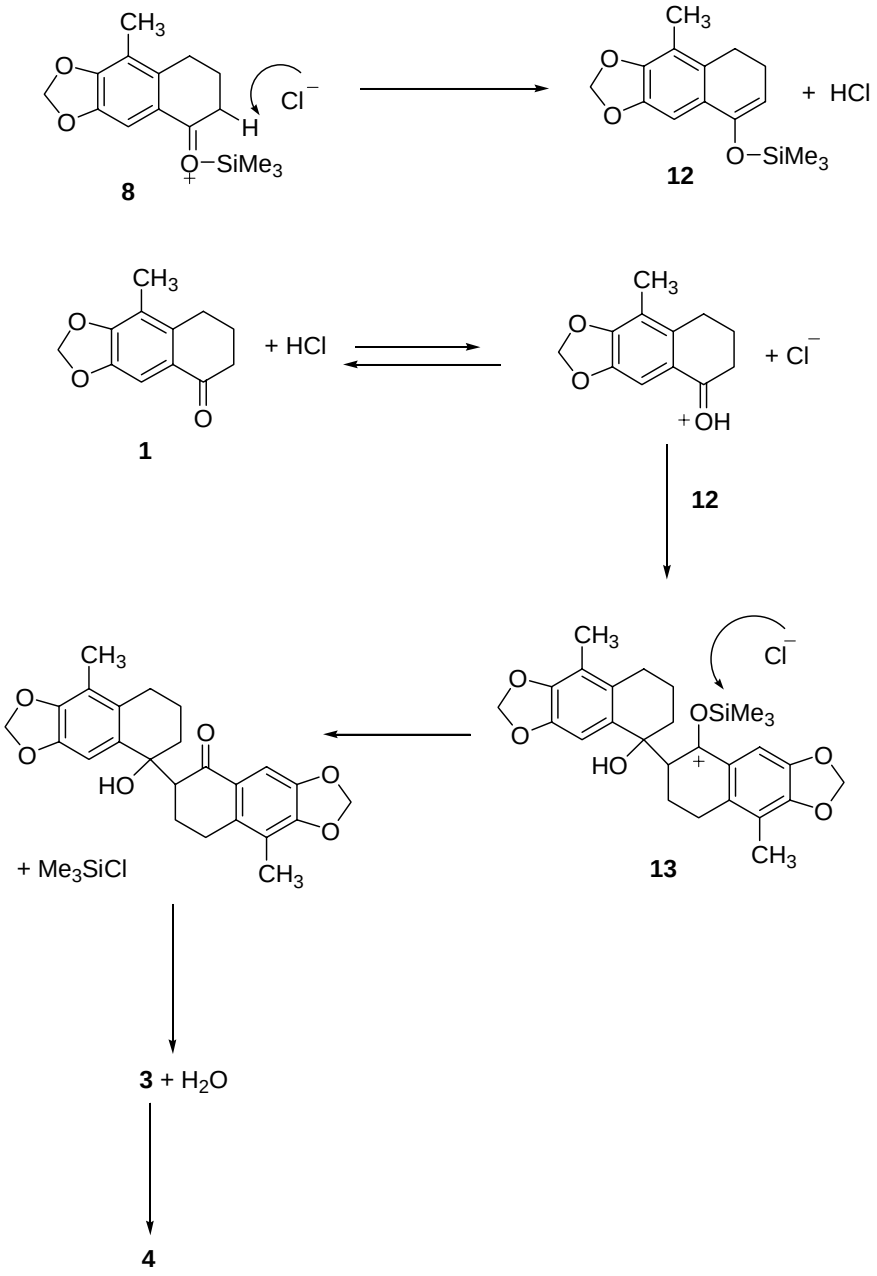
The structures of these new compounds were established on the basis of their spectroscopic (^{1}H-, ^{13}C-NMR, MS) and analytical data. Thus, in all cases the ^{1}H- and ^{13}C-NMR spectra show double signals which suggest the dimeric nature of these compounds. That was confirmed by MS as well as by the presence of chlorine in compound **2**.

A probable reaction for the formation of the major product **2** is depicted in Scheme 2. Reaction of **1** with Me_3SiCl[4] should afford five-coordinate complex **7** which can exist in equilibrium with cation **8**.[5] The nucleophilic attack of ethylene glycol on **8** should give intermediate **9**. Now two possible reaction paths are conceivable for **9**. Path a) involves the intramolecular addition of the remaining OH group to give the expected and not observed compound **5**. Alternatively, chloride ion may act as basic reagent inducing β-elimination reaction (path b) giving intermediate **10** which, by intramolecular reaction with **8** (nucleophilic addition to carbonyl-activated group) of **1** afforded **11**. Final nucleophilic substitution reaction of chlorine anion on **11**, should give **2**.



Scheme 2

Regarding the formation of compounds **3** and **4**, these may be formed *via* a Mukaiyama-type aldol reaction[6] between silylenolether **12** (arising from **8** *via* Cl^- induced enolization) and protonated ketone **1**, to give intermediate **13** which, after recovering of catalyst (Me_3SiCl) and dehydration should afford compound **3**. Further aromatization of **3** (probably during the work-up of the reaction) gave **4** (Scheme 3).



Scheme 3

In summary, the results here presented constitute a convenient procedure for the synthesis of dimeric structures of tetralone derivatives avoiding the use of any organometallic catalytic reagent.

Experimental Section

General Procedures. The reaction was carried out under a positive pressure of dry Ar using freshly distilled solvents under anhydrous conditions. Reagents and solvents were handled by

using standard syringe techniques. Ethylene glycol and TMSCl were commercial and used as received. 5-Methyl-6,7-methylendioxy-1-tetralone (1) was synthesized as previously described.[7] IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^{1}H-NMR and ^{13}C-NMR were obtained on Varian XL-300 and Bruker AM-300 spectrometers. Silica gel Merck (230-400 mesh) and Merck $60F_{254}$ plates were used for conventional and analytical (TLC) chromatography respectively.

Reaction of 5-Methyl-6,7- methylendioxy-1-tetralone with ethylene glycol and TMSCl (1) 190 mg. Trimethylsilyl chloride (1.04 ml; 8.2 mol) was added to a suspension of **1** (408 mg; 2,0 mmol) in ethylene glycol (10 ml) at room temperature (22-24 ºC) under Ar. After stirring the resulting mixture at rt for 72 h, dilution with Et_2O (20 ml), addition of a solution of $NaHCO_3$ (5%) and decantation of the organic phase, the aqueous layer was extracted with Et_2O (3 x 5 ml). The combined organic extracts were washed with H_2O, a saturated solution of NaCl and dried over $MgSO_4$. After removing the solvent *in vacuo*, 382 mg of an orange oil was isolated and chromatographed twice (SiO_2, hexane-AcOEt 20:1). The following fractions were isolated and characterized.

8-{-2-[(5-chloro-9-methyl-5,6,7,8-tetrahydronaphto [2,3 [1,3]dioxol-5-yl)oxy] ethoxy}-4-methyl-5,6-dihydronaphto [2,3-d] [1,3]dioxole (2)
87 mg as a pale yellow oil. ^{1}H-NMR **(**$CDCl_3$, ppm): δ 1.60-1.75 (m, 2H, CH_2); 2.13 (s,3H, CH_3); 2.21 (s,3H, CH_3); 2.10-2.25 (m, 2H, CH_2); 2.49 (t, 2H, J=7.5Hz, CH_2); 2.58 (t, 2H, J=7.8 Hz, CH_2); 2.95 (m, 2H, CH_2); 3.76 (t, 2H, J=5.9Hz, OCH_2); 4.47 (t, 2H, J=5.9 Hz, OCH_2); 5. 79 (t, 1H, J=4.5 Hz, =CH); 5.89 (s, 2H, OCH_2O); 5.95 (s, 2H, OCH_2O); 6.73 (s, 1H, CH); 7.35 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$, ppm): δ 11.4 (CH_3); 11.7 (CH_3); 22.9 (CH_2); 23.9 (CH_2); 29.6 (CH_2); 33.7 (CH_2); 41.8 (CH_2); 64.2 (OCH_2CH_2O); 100.3 (OCH_2O);101.2 (OCH_2O); 109.9 (CH); 108.2 (CH); 116.7 (C); 118.5 (C); 122.2 (C); 122.6 (C); 128.8 (C); 129.6 (C); 136.3 (C); 139.8 (C); 144.4 (C); 147.7 (C); 144.8 (C); 149.6 (C); 166.8 (C). IR ($CHCl_3$, cm^{-1}) ν max: 2780; 1590; 930 (C-O-C); 750 (C-Cl). MS 437(1); 472(3); 471(3, M^+); 470(10); 221(10); 215(19); 213(27); 201(30); 202(100); 199(25); 193(28); 189(26); 187(35); 149(37); 115(22). Elem. Anal**:** Calcd. for $C_{26}H_{27}ClO_6$: C, 66.31; H, 5.78. Found: C, 66.56; H, 5.88.

9,9'-dimethyl-7,7',8,8'-tetrahydro-5,6'-binaphto[2,3-d][1,3]-dioxol-5'(6'H)-one (3)
16 mg as pale yellow oil. ^{1}H-NMR **(**$CDCl_3$, ppm) δ 2.17 (s, 6H, 2xCH_3); 2.10-2.82 (m, 8H, 4xCH_2); 3.69 (dd, 1H, J=7.2 and 4.5 Hz, CH); 5.66 (t, 1H, J=4.5 Hz, =CH); 5.89 (d, 2H, J=1.1 Hz, OCH_2O); 6.00 (s, 2H, OCH_2O); 6.56 (s, 1H, CH); 7.45 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$, ppm): δ 11.5 (CH_3); 11.9 (CH_3); 23.0 (CH_2); 23.8 (CH_2); 24.7 (CH_2); 28.2 (CH_2); 50.1 (C); 100.5 (OCH_2O); 101.4 (OCH_2O); 102.3 (CH); 104.5 (CH); 116.6 (C); 117.9 (C); 124.6 (CH); 127.9 (C); 128.0 (C); 130.0 (C); 135.3 (C); 139.7 (C); 145.0 (C); 146.0 (C); 150.7 (C); 198.9 (C=O). IR ($CHCl_3$, cm^{-1}) ν max: 3040; 1720 (C=O); 1660 (C=C); 930 (C-O-C). MS: 391 (10); 390(37, M^+); 388 (19); 205(13); 204 (67); 203 (27); 202 (44); 199 (19); 190 (19); 189 (64); 187 (38); 186

(24); 177 (30); 175 (25); 174 (17); 149 (100); 148 (86). Elem. Anal**:** Calcd. for $C_{24}H_{22}O_5$: C, 78.83; H, 5.69. Found: C, 73.46; H, 5.32.

9,9'-dimethyl-7',8'-dihydro-5,6'-binaphto [2,3-d] [1,3]-dioxol-5'(6'H)-one (4)
8 mg as reddish oil. ^{1}H-NMR **(**$CDCl_3$, ppm) δ 2.20 (s, 3H, CH_3); 2.48 (s, 3H, CH_3); 2.20-2.92 (m, 4H, 2 x CH_2); 4.32 (m, 1H, CH); 5.99 (s, 2H, OCH_2O); 6.02 (s, 2H, OCH_2O); 6.73 (s, 1H, CH); 7.03 (d, 1H, CH); 7.32 (dd, 1H, CH); 7.50 (s, 1H, CH); 7.78 (s, 1H,CH). IR ($CHCl_3$, cm^{-1}) ν max 2980, 1720 (C=O); 940 (C-O-C). MS: 389 (2); 388 (6, M^+); 386 (2); 220 (7); 189 (22); 167 (15); 148 (27); 113 (12); 111 (12); 96 (12); 91(16). Elem. Anal**:** Calcd. for $C_{24}H_{20}O_5$: C, 74.21;H, 5.19. Found: C, 74.40; H, 5.12.

Acknowledgements

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