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Thionyl-chloride–pyridine-mediated rearrangement of tertiary alcohols

Ajoy K. Banerjee * and William Vera

Centro de Química, IVIC, Apartado 21827, Caracas 1020-A, Venezuela
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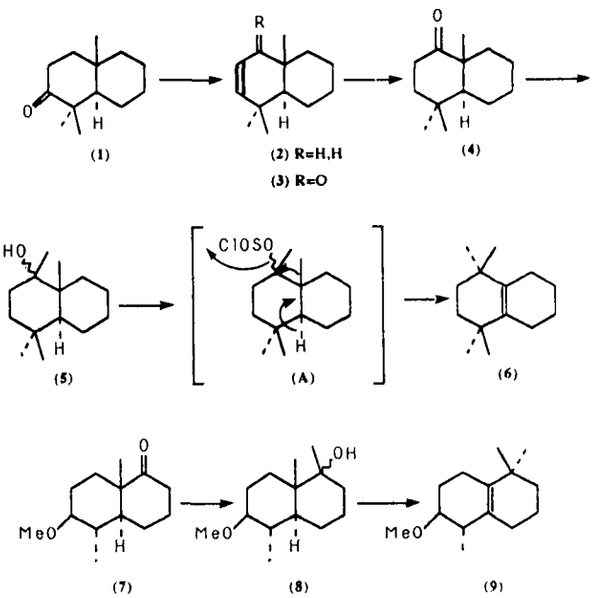
Abstract. Tertiary alcohols **5** and **8** undergo rearrangement on treatment with thionyl chloride and pyridine, yielding octahydronaphthalenes **6** and **9**, respectively. Alcohol **12** under similar treatment affords a mixture of tetrahydronaphthalene **14** and diene **15**, whereas alcohol **22** suffers no rearrangement but produces olefin **23**.

Thionyl chloride and pyridine have proved to be powerful reagents for the dehydration of alcohols[1,2]. An interesting rearrangement of a tertiary alcohol during its dehydration with thionyl chloride and pyridine was reported by *Welch*[3]. Difficulty in the dehydration of a tertiary alcohol with the same reagent was observed by *ApSimon*[4]. These observations encouraged us to synthesize several tertiary alcohols and study their behavior with thionyl chloride and pyridine. This work is the subject of the present paper[5].

Ketone **1**[6] on treatment with sodium borohydride in methanol afforded a mixture of alcohols whose tosyl [a] derivative, on heating with lithium bromide in dimethylformamide, afforded olefin **2** which was converted to α,β-unsaturated ketone **3** by oxidation with *tert*-butyl hydroperoxide in the presence of hexacarbonylchromium[7]. The reduction of the double bond was effected with Adams catalyst in acetic acid to obtain the saturated ketone **4**. This was made to react with methyllithium in ether to obtain the alcohol **5** which, on treatment with thionyl chloride and pyridine, underwent rearrangement affording octahydronaphthalene **6** in 58% yield. The transformation can be explained by assuming the formation of the derivative **A** from which the elimination of the chlorosulfite group (OSOCl) and 1,2 methyl-group shift occurred in a concerted manner leading to the formation of naphthalene **6**. This assumption has been made on the basis of a similar study from our laboratory[8] and other authors' work[9]. These works indicate that the elimination of leaving groups like tosylate and chlorosulfite takes place under a base-catalysed process by a concerted path. No definite proof was sought to confirm this assumption. The spectroscopic data m/z 192 (M^+) and δ 0.93 (s, 12H, 1,1,4,4-Me_4) support the structure of compound **6**.

Similarly, alcohol **8**, obtained from ketone **7**[10] by reaction with methyllithium in ether, underwent rearrangement on treatment with thionyl chloride and pyridine yielding octahydronaphthalene **9** in 50% yield. The spectral data [m/z 208 (M^+) and δ 0.93 (d, 3M, J 6 Hz, 5-Me), 1.17 (s, 6H, 1,1-Me_2) and 3.28 (s, 3H, OMe)] completely agree with the structure of naphthalene **9** (see Scheme 1).

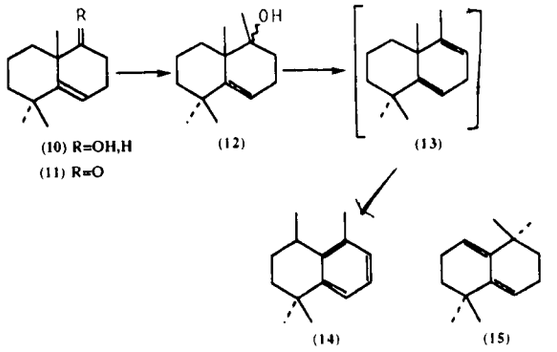


Scheme 1.

The above-mentioned observations on the dehydration of alcohols **5** and **8** support the observation of *Welch*[3].

An interesting rearrangement occurred when a similar experiment was attempted with tertiary alcohol **12** which was obtained by the conversion of alcohol **10**[11] with *Jones* reagent[12] to ketone **11**, followed by treatment with methyllithium in ether. Alcohol **12**, on treatment with thionyl chloride and pyridine, yielded an oily material which exhibited a mixture of two products of unequal intensity as evidenced on TLC. The mass spectrum showed the molecular ion m/z 173 (M^+-15) and 175 (M^+-15). The H-NMR spectrum exhibited signals at δ 7.12 (s, 3H, ArH), 4.61–5.23 (m, 2H, olefinic protons), 2.32 (s, 3H, Me), 1.01–1.22 (3s, 2H, 1d, J 6 Hz). All these spectroscopic data strongly supported the formation of tetrahydronaphthalene **14** (through intermediate **13**) and diene **15**. Their separation proved extremely difficult owing to close polarity. Therefore, neither very clean spectral data

[a] Tosyl = 4-methylbenzenesulfonyl-Me-ϵH_4-SO_2Cl.



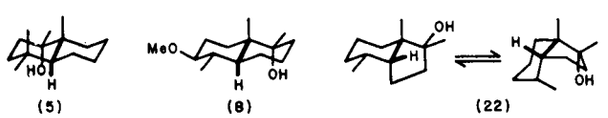
Scheme 2.

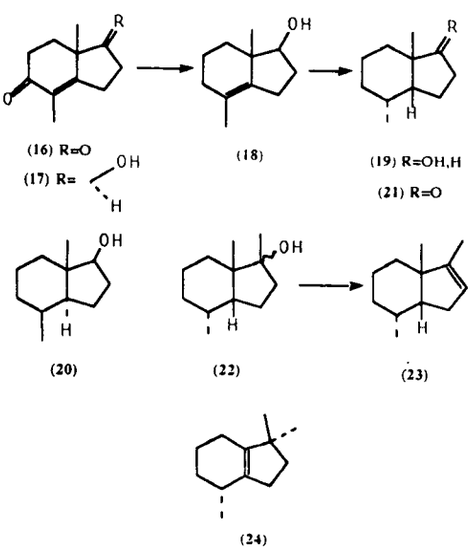
nor very satisfactory elemental analysis could be achieved (see Scheme 2).

The rearrangement of alcohol **12** to diene **15** is not difficult to explain on the basis of the rearrangement of alcohols **5** and **8**. The formation of tetrahydronaphthalene **14** from alcohol **12** is interesting and curious because the rearrangement involves dehydration, migration of the angular methyl group at the aliphatic ring, and dehydrogenation. The dehydrogenation action of thionyl chloride, already reported by *Buchi* and *Lukas*,[13] is not very common. The synthesis of diene **13** from **12** is conceivable but it was difficult to provide any concrete chemical evidence for the transformation of diene **13** to naphthalene **14**. On the basis of the computational calculation of the ΔH formation of the naphthalene **14** (ΔH_f −9.578 Kcal) and diene **13** (ΔH_f 23.1755 Kcal), it can be assumed that the formation of naphthalene **14** is thermodynamically more favorable than diene **13** and thus its partial transformation to naphthalene **14** occurs.

The last phase of our study involved the treatment of octahydroindanol **22** with thionyl chloride and pyridine. Dienone **16** which appeared to be a suitable starting material for the synthesis of alcohol **22** was prepared following the procedure of *Halsall*[14]. The condensation of 2-methyl-1,3-cyclopentadione and 1-chloro-3-pentanone, using toluene as solvent and tosylic acid as catalyst, afforded the dienone **16** (see Scheme 3).

Selective reduction of the saturated carbonyl group of **16** with sodium borohydride afforded alcohol **17**. The β-configuration of the hydroxyl group was assumed on the basis of analogy[15]. *Huang–Minlon*-modified Wolff–Kishner reduction[16] produced alcohol **18** which was subjected to hydrogenation with Adams catalyst. It was supposed that *cis*-fused alcohol **19** would be the major product[17,18] along with some presumably *trans*-fused, alcohol **20**. The formation of **20** was less likely, as a molecular-model study indicated strong repulsion of the two methyl groups. Alcohol **19** exhibited molecular ion 168 (M^+) in the mass spectrum. It was converted to ketone **21** with *Jones* reagent[12] and this was made to react with methyllithium in ether to obtain tertiary alcohol **22** which did not undergo similar rearrangement with thionyl chloride and pyridine as observed with alcohols **5** and **8**. The major product obtained (59%) was identified as olefin **23** which exhibited molecular ion 164 (M^+) in the mass spectrum and presented signals at δ 1.52 (s, 3H, Me) and δ 5.27 (broad s, 1H) indicating the presence of vinyl-methyl and olefinic proton, respectively. Apart from olefin **23**, no other products could be isolated in acceptable quantity and purity and, therefore, their structures could not be determined. It was curious that alcohols **5** and **8** underwent rearrangement with thionyl chloride and pyridine while under the same reaction condition, alcohol **22** yielded olefin **23**, but not olefin **24**. In our opinion a more reasonable explanation of the differences in behavior may be sought in the difference in orientation of the various bonds involved in the rearrangement. The *trans*-juncture of the rings in compounds **5** and **8** enables an antiperiplanar arrangement of the migrating methyl group and the hydrogen at the bridgehead position, thereby fulfilling the stereoelectronic requirement for a more or less synchronous elimination–rearrangement reaction. A similar orientation can not be realized in compound **22** as a result of the *cis*-juncture of the rings.





Scheme 3.

Experimental section

Unless otherwise stated, IR spectra were obtained on a Nicolet FT. NMR spectra recorded on Varian A-90 spectrometer were taken in $CDCl_3$ using Me_4Si as an internal standard. Mass spectra were carried on a Dupont 21-492B. Methyllithium in ether (1.4 M), 1-chloro-3-pentanone and 2-methyl-1,3-cyclopentanedione were purchased from Aldrich Chemical Company. The expression 'work-up' indicates that the solution was diluted with water, extracted with ether, washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Column chromatography was carried out on silica gel 60 (Merck). Microanalysis were carried out in our Institute (IVIC) and Franz Pascher Microanalytiches laboratorium, Bonn, Germany.

1,4,4a,5,6,7,8,8a-hydro-1,1,4a-trimethylnapthalene (**2**)

To a solution of ketone 1 (500 mg) in methanol (15 ml) was added sodium borohydride (400 mg). The mixture was stirred at room temperature for 10 h. Work-up afforded alcohols (510 mg). IR: 3350 (OH) cm^{-1}.

To the crude alcohols (510 mg) dissolved in pyridine (6 ml) was added to chloride (400 mg). The mixture was stirred at room temperature for 24 h and then poured on ice. Workup afforded the tosylate (535 mg) which was used for the next step.

A mixture of the tosylate (535 mg) and anhydrous lithium bromide (610 mg) in dimethylformamide (6 ml) was heated in an oil bath at 110–120°C for 2 h. Workup followed by chromatographic purification (eluent hexane/ether (4/6) afforded olefin **2**; 320 mg, 70% from 1; IR: 1602 (C = C) cm^{-1}. NMR: δ 0.98, 1.02, 1.04, 3 s, 9H, 3 Me_3; 5.37 m, 2H, 2-H and 3-H, MS: m/z 178 (M^+). Anal. calcd. for $C_{13}H_{22}$: C 87.56, H 12.44; found: C 87.48, H, 12.39%.

4a,5,6,7,8,8a-Hexahydro-4,4,8a-trimethylnaphthalene-1(4H)-one (**3**)

To a solution of olefin **2** (300 mg) in dry acetonitrile (3 ml) were added *tert*-butyl hydroperoxide (3 ml) and hexacarbonylchromium (100 mg). The mixture was refluxed for 30 h. After work-up the product was chromatographed (eluent hexane ether 8/2) to obtain ketone **3** (129 mg, 40%). IR: 1680 (α,β-unsaturated ketone) cm^{-1}. NMR: δ 1.01, 1.03, 1.05, 3s, 9H, 3 Me; 5.67, d, 1H, *J* 9 Hz; 6.27, d, 1H, *J* 9 Hz, 2-H and 3-H. MS: *m/z* 192 (M^+). Anal. calcd. for $C_{13}H_{20}O$: C 81.20, H 10.48; found: C 81.14, H, 10.29%.

3,4,4a,5,6,7,8,8a-octahydro-4,4,8a-trimethyl-naphthalen-1(2H)-one (**4**)

Ketone **3** (125 mg) in acetic acid (15 ml) was stirred for 10 h in hydrogen over platinum oxide (270 mg) at room temperature. Work-up yielded the oily ketone **4** (94 mg, 75%). IR: 1715 (CO) cm^{-1}. NMR: δ 0.85, 0.93, 1.22, 3 s, 9H, 3 me; MS: *m/z* 194 (M^+). Anal. calcd. for $C_{13}H_{22}O$: C 80.35, H 11.41; found: C 80.28, H 11.37%.

1,2,3,4,5,6,7,8-Octahydro-1,1,4,4-tetramethylnaphthalene (**6**)

To ketone **4** (100 mg) dissolved in ether (25 ml) and cooled to 0° was added methyllithium in ether (8 ml). The mixture was stirred at room temperature for 25 h. Work-up, followed by chromatographic purification (eluent ether/hexane 1/1) yielded pure, tertiary alcohol **5** (90 mg; 77%). IR: 3380 (OH) cm^{-1}.
Alcohol **5** (90 mg) dissolved in pyridine was treated with freshly distilled thionyl chloride (2 ml) and the mixture stirred at room temperature for 20 h. Work-up followed by chromatographic purification (eluent hexane) afforded naphthalene **6** (57 mg, 58%) (from ketone **4**). IR: 1627 (C = C) cm^{-1}. NMR: δ 0.93, s, 12H, 1,1,4,4-Me_4; 1.10–1.83, 6 CH_2, 12H. MS: *m/z* 192 (M^+). Anal. calcd. for $C_{14}H_{24}$: C 87.42, H 12.58; found: C 87.38, H 12.56%.

1,2,3,4,5,6,7,8-Octahydro-6-methoxy-1,1,5-trimethylnaphthalene (**9**)

To a solution of ketone **7** (256 mg) in ether (5 ml) was added methyllithium in ether (8 ml). The mixture was stirred for 24 h at room temperature. The usual workup followed by chromatographic purification (eluant ether/hexane 1/1) yielded alcohol **8** (224 mg, 81%). IR: 3343(OH) cm^{-1}.
To alcohol **8** (224 mg) dissolved in pyridine (9 ml) was added freshly distilled thionyl chloride. The mixture was stirred at room temperature for 20 h. Workup and chromatographic purification (eluent: hexane) gave naphthalene **9** (100 mg, 50%). IR: 1632 (C = C) cm^{-1}. NMR: δ 0.93, d, 3H, *J* 6 Hz, 5-Me; 1.17, s, 6H, 1,1-Me_2; 1.31–2.01 12H, 6-H, 5-H, 5CH_2; 3.28, s, 3H, OMe. MS: *m/z* 208 (M+). Anal. calcd. for $C_{14}H_{24}O$: C 80.71, H 11.61; found: C 80.58, H 11.52%.

5,5,8a-Trimethyl-3,5,6,7,8,8a-hexahydronaphthalen-1(2H)-one (**11**)

To alcohol **10** (300 mg) in acetone (6 ml) was added Jones reagent and the mixture was stirred at 0°C for 20 min. Work-up and chromatographic purification (hexane/ether, 6/4) yielded ketone **11** (266 mg, 90%). IR: 1708 (CO) cm^{-1}. NMR: δ 1.01, s, 3H; 1.03, s, 3H; 1.05, s, 3H, 5,5,8a-Me_3; 5.36 (t, 1H, *J* 4 Hz). MS: 192 (M^+). Anal. calcd. for $C_{13}H_{20}O$: C 81.20, H 10.48; found: C 81.12, H 10.42%.

1,1,4,5-Tetramethyl-1,2,3,4-tetrahydronaphthalene (**14**) *and 1,1,5,5-tetramethyl-1,2,3,5,6,7-hexahydronaphthalene* (**15**)

To a solution of ketone **11** (265 mg) in ether (6 ml) was added methyllithium in ether (8 ml). The mixture was stirred for 24 h at room temperature. Work-up followed by chromatographic purification (eluant ether/hexane 1/1) yielded alcohol **12** (238 mg, 85%). IR: 3345 (OH) cm^{-1}.
To alcohol **12** (238 mg) dissolved in pyridine (10 ml) was added freshly distilled thionyl chloride (3 ml) and the mixture was stirred at room temperature for 20 h. Work-up followed by repeated chromatographic purification (eluent hexane), afforded a mixture of tetrahydronaphthalenes 14 and 15 (132 mg). MS: 173 (M^+ – Me) and 175 (M^+ – Me). NMR: δ 1.01–1.22, 3s, 1d; 7 Me, 21H, *J* 6 Hz; 1.31–2.21, 13H, 6CH_2 and 4-H; 2.32; s, 3H, Me; 4.61–5.23, m, 2H olefinic protons; 7.12 s, 3H, aromatic protons.

2,3,7,7a-tetrahydro-4,7a-dimethyl-1H-indene-1,5(6H)-dione (**16**)

To a solution of 2-methylcyclopentane-1,3-dione (10.38 g) in dry toluene (400 ml) was added freshly distilled 1-chloro-3-pentanone (16.86 g) and tosylic acid (520 mg). The mixture was refluxed for 48 h in a Dean–Stark apparatus. The solution was concentrated, washed with sodium bicarbonate solution (5%) and then with brine. On distillation work-up afforded the dione **16** (11.92 g, 72%); b.p. 100–105°C/0.8 mmHg. IR: 1660 (C=C–C=O), 1710 (CO) cm^{-1}. NMR: δ 1.17, s, 3H, 7a-Me; 1.68, s, 3H, 4-Me. MS: 178 (M^+). Anal. calcd. for $C_{11}H_{14}O_2$: C 74.13, H 7.92; found: C, 73.92, H 7.81%.

1,2,3,6,7,7a-Hexahydro-1β-hydroxy-4-7a-dimethyl-1H-indene-6-one (**17**)

To a solution of dione **16** (6 g) in ethanol (100 ml), cooled to 0°C, was added a solution of sodium borohydride (3.21 g) in ethanol (150 ml). The mixture was stirred at 0°C for 1 h. Work-up and chromatographic purification (eluent ether/hexane 2/8) produced **17** (5.49 g, 90%). IR: 3280 (OH), 1680 (CO) cm^{-1}. NMR: δ 1.17, s, 3H, 7a-Me; 1.65, s, 3H, 4-Me; MS: *m/z* 180 (M^+) and 162 ($M^+ - H_2O$). Anal. calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95; found: C 73.18, H 8.84%.

2,3,5,6,7,7a-Hexahydro-4,7a-dimethyl-1H-inden-1-ol (**18**)

A solution of **17** (5.06 g), hydrazine hydrate (97%, 17.5 ml) and potassium hydroxide (17.5 g) in diethylene glycol (300 ml) was heated at 112°C (bath temperature) in a nitrogen atmosphere for 1 h; the bath temperature was raised to 215°C and maintained at this temperature for a further 3 h. Work-up followed by chromatographic purification (eluent ether/hexane, 4/6) afforded alcohol **18** (4.04 g, 87%). IR: 3275 (OH) cm^{-1}. NMR: δ 0.95, s, 3H, 7a-Me; 1.63, s, 3H, 4-Me). MS: *m/z* 166 (M^+) and 151 (M^+ – Me), 133 (M^+ – Me – H_2O). Anal. calcd. for $C_{11}H_{18}O$: C 79.46, H 10.92; found: C 79.34, H 10.81%.

Octahydro-4,7a-dimethyl-1H-inden-1-one (**21**)

Alcohol **18** (4 g) in acetic acid (100 ml) was stirred under hydrogen with PtO_2 (950 mg). Work-up afforded alcohol 19 (3.64 g, 90%). IR: 3330 (OH) cm^{-1}. MS: 168 (M^+) and 150 ($M^+ - H_2O$).
Alcohol 19 (3.62 g) in acetone (8 ml) was oxidized with Jones reagent (2 ml). Work-up and chromatographic purification of the resulting product (eluent hexane/ether 3/7) yielded ketone **21** (3.44 g, 86%) (from **18**). IR: 1710 (CO) cm^{-1}. NMR: δ 0.95, d, 3H, 4-Me, *J* 6 Hz; 1.03, s, 3H, 7a-Me. MS: *m/z* 166 (M^+). Anal. calcd. for $C_{11}H_{18}O$: C 79.46, H 10.92; found: C 79.34, H 10.03%.

3a,4,5,6,7,7a-Hexahydro-3,3a,7-trimethyl-1H-indene (**23**)

Ketone **21** (3 g) in dry ether (10 ml) was treated with methyllithium (17 ml) and the mixture stirred for 20 h at room temperature. Work-up afforded alcohol **22** (2.90 g, 90%). IR: 3268 (OH) cm^{-1}. MS: *m/z* 182 (M^+), 164 ($M^+ - H_2O$).
Alcohol **22** (2.90 g) was dissolved in pyridine (40 ml) and treated with thionyl chloride (4 ml) and the mixture stirred overnight at room temperature. Work-up followed by chromatographic purification (eluent hexane) yielded olefin (**23**) (1.74 g, 59%) (from **21**). NMR: δ 0.98, d, 3H, 7-Me, *J* 6 Hz; 1.01–1.95, 10H, 4 CH_2, C-H, 7a-H; 1.10, s, 3H, 3a, 6-Me; 1.52, s, 3H, 3-Me; 5.27, s, 1H, 8-H. MS: 164 (M^+). Anal. calcd. for $C_{12}H_{20}$: C 87.73, H 12.27; found: C 87.62, H 12.18%.

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