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ACID INDUCED REARRANGEMENT OF β,γ-UNSATURATED KETONES

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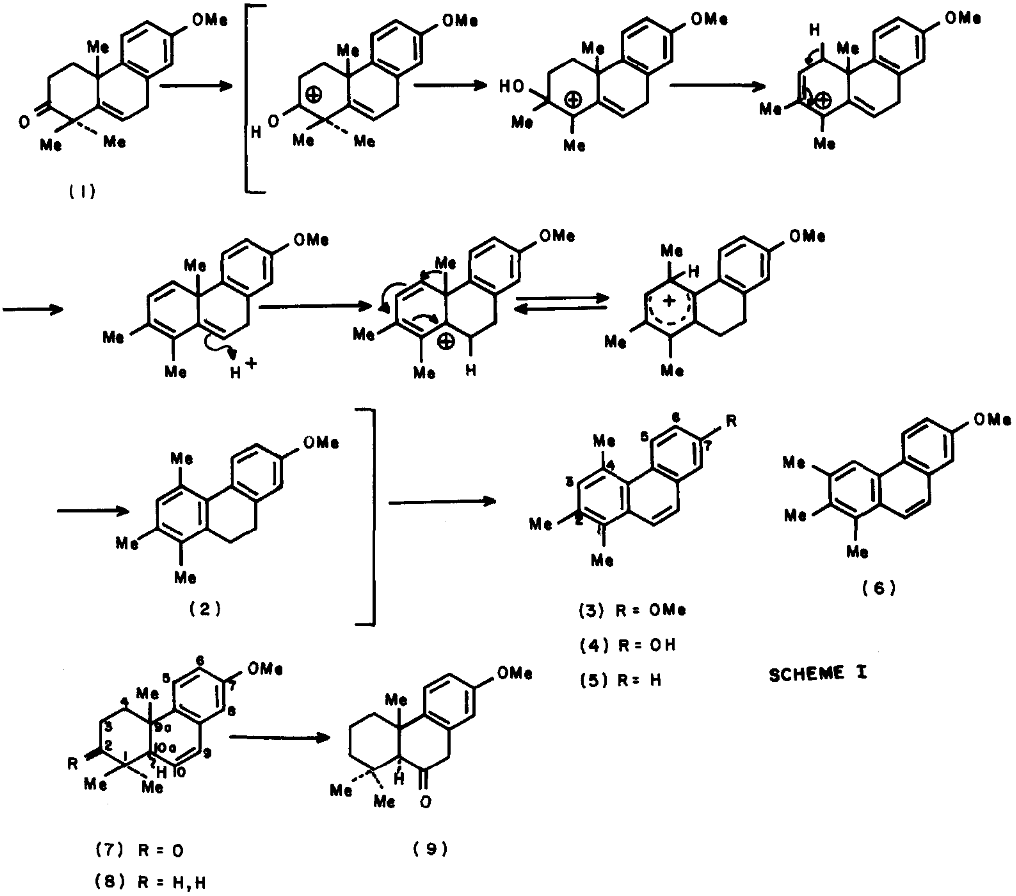
Abstract - The molecular rearrangement of the ketones (1), (10) and (19) to phenanthrene derivative (3) and decalin derivative (11) and (12) is respectively described.

The chemical literature reveals that a number of organic compounds suffer molecular rearrangement on treatment with p-toluenesulphonic acid in acetic acid or acetic anhydride.[1-3] During our investigations on the synthesis of terpenes we have observed that several β,γ-unsaturated ketones underwent interesting molecular transformations on treatment with p-toluenesulphonic acid in acetic acid. The present paper documents our results.[4]

The tricyclic ketone (1), prepared by the procedure of Turner[5] on heating with p-toluenesulphonic acid and acetic acid afforded a solid material (60%) and two oily materials in 5% and 20% yield. The solid material was assigned the structure (3) on the basis of spectral data. Its formation can be rationalized[3] as depicted in Scheme I which indicates transformation of ketone (1) to compound (2) which undergoes further transformation leading to phenanthrene (3). In order to confirm this structure, phenanthrene (3) was subjected to demethylation with boron tribromide in dichloromethane. The phenol (4) was obtained in satisfactory yield and on treatment with sodium borohydride and trifluoroacetic acid[6] yielded the known hydrocarbon[7] (5) as evidenced from its melting point. An alternative structure (6), instead of (3) was considered[3] for the solid compound but its conversion to (5) lent strong support in favor of structure (3).

In addition to the compound (3), and oily material (5%), not homogeneous in t.l.c. was obtained which exhibited a m/z 252 molecular ion (M^+) in its mass spectrum. Its NMR spectrum was not well defined. This oily material, on dehydrogenation with palladium-charcoal catalyst, yielded compound (3) in moderate yield. These results led us to conclude that the compound (2) was one of the components in the oily material.

The skeletal arrangements of ketone (1) also afforded another oily material (20%) which was assigned structure (7) on the basis of spectral data. The Clemmensen reduction of keto-olefin (7) yielded the already reported[9] olefin (8) whose identity was confirmed by comparing its spectral properties with an authentic specimen.[9] The transformation of olefin (8) to known ketone[9] (9) has also been reported. These data corroborate structure (7) for the major oily material.



(1)

(2)

(3) R = OMe

(4) R = OH

(5) R = H

(6)

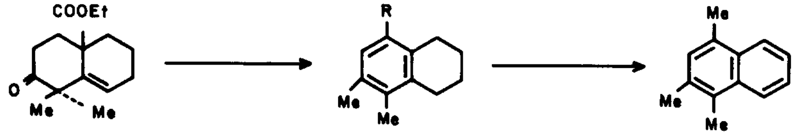
SCHEME I

(7) R = O

(8) R = H,H

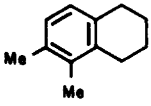
(9)

The bicyclic ketone (10), prepared by the procedure of Meyer[10], on similar treatment with p-toluenesulphonic acid and acetic acid afforded principally acid (12) (60%) instead of ester (11) which was anticipated by the mechanism depicted in Scheme I. There is no doubt that the ester (11) underwent hydrolysis to acid (12). In order to confirm the structure of the acid (12), it was subjected to esterification and then reduction with lithium aluminium hydride in tetrahydrofuran. The resulting alcohol was converted to its tosyl derivative with tosyl chloride and pyridine. The tosylate, on reduction with lithium triethylborohydride in tetrahydrofuran[11] followed by dehydrogenation with palladium charcoal, afforded trimethyl naphthalene (13) whose six step synthesis has already been reported.[12] The melting point of (13) was similar to the melting point reported in the literature.[12]

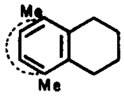


(10) (11) R = COOEt (12) R = COOH (13)

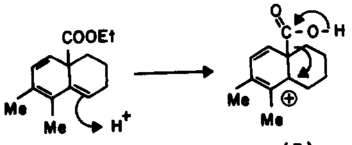
In addition to the acid (12), a tetrahydronaphthalene derivative (25%) was obtained which showed two overlapping spots in the t.l.c. In the mass spectrum, it had a m/z 160 molecular ion (M$^+$) and showed in chromatogram two peaks which indicated the tetrahydronaphthalene derivative was a 1:1.3 mixture of two compounds. The signals in the NMR spectrum at δ 2.01 (s, 6H) and 2.04 (s, 6H) indicated the presence of four methyl groups. The signals at δ 7.08 (s, 1H) and δ 6.78-6.92 (m, 3H) evidenced the presence of four aromatic protons. These spectroscopic data led us to conclude that the tetrahydronaphthalene derivative was a mixture of the compound (14) and isomeric compound (15)[3]. As acid (12) could be isolated after heating the ketone (10) with acid for three days, the formation of naphthalene (14) cannot be accounted for the decarboxylation of acid (12). The transformation of (1) to (2) leads one to deduce that ketone (10) also forms an intermediate (A) which undergoes hydrolysis to acid (B) and this further undergoes decarboxylation as shown yielding (14).



(14)

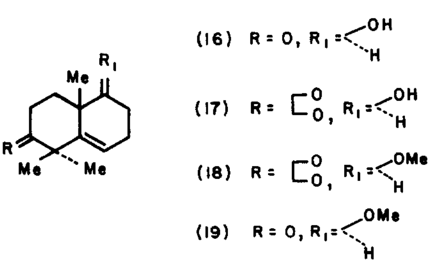


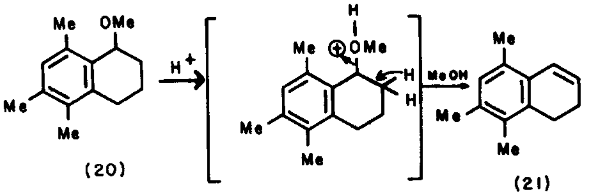
(15)



(A) (B)

The acid induced rearrangement was then attempted with bicyclic ketone (19) which was prepared from known ketone[13] (16). Ketalization of ketone (16) produced compound (17) and this on treatment with methyl iodide in the presence of sodium hydride afforded (18) which, on heating with acetic acid, gave (19). Heating (19) with p-toluenesulphonic acid and acetic acid under the above mentioned conditions led to the formation of a complex mixture from which (21) not completely homogeneous, was isolated (42%) after laborious purification by thin layer chromatography. The expected product (20) (following the mechanism of Scheme I) could not be obtained owing to the rearrangement of (20) to (21) as shown. The spectral data nicely support the structure of (21). In order to confirm the structure, (21) was subjected to dehydrogenation with palladium charcoal. The trimethyl naphthalene (13) was obtained in moderate yield and confirmed by comparison with the authentic specimen already described.





(20)

(21)

In addition of (21), another oily material (39%) was obtained which had a m/z 170 molecular ion (M^+) in the mass spectrum indicating the formation of trimethyl naphthalene (13) whose origin can be accounted for by the aromatization of (21). This was confirmed by comparing its t.l.c. behavior with an authentic specimen described before. The oily material, in addition of (13), exhibited the presence of two products in t.l.c. and therefore the NMR spectrum of the oily material was very complicated. No attempt was made to isolate these two additional components.

We believe that during the acid rearrangement of (19), in addition to the naphthalene (13), other isomeric naphthalenes were formed. Unfortunately we experienced difficulties in ascertaining the correct position of methyl groups in these isomerci naphthalenes.

Experimental

Mps were determined on a Kofler hot stage apparatus and are uncorrected unless otherwise stated. IR spectra were taken on a Perkin-Elmer spectrometer for KBr or liquid films. ^{1}H NMR spectra were obtained for solutions in $CDCl_3$ and CCl_4 with a Varian A-90 spectrometer. Chemical shifts are reported as units using TMS as internal standard. The form of signals is expressed s:singlet, d:doublet and t:triplet. Mass spectra were recorded on Du Pont 21-492B and Hitachi Perkin Elmer RMU-6H at 70 ev using a direct inlet system. Column chromatography was carried out with Neutral Brockman alumina and silica gel (BDH). TLC plates were coated with silica gel having a thickness of ca. 0.2 mm and the spots were located by exposing the dried plates to iodine vapor. DC-plates precoated SiF (20 x 20 cm^{-1}) layer thickness (1 mm) were used for preparative thin layer chromatography. Unless otherwise stated all organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. Microanalysis were carried out in Mikroanalytisches Labor Pascher, Germany.

7-Methoxy-1,2,4-trimethyl phenanthrene (3) - To the ketone (1) (1 g) dissolved in acetic acid (35 ml, 99%) was added p-toluenesulphonic acid (250 mg) and the solution heated under reflux for 70 hr. The dark colored solution was cooled, concentrated, diluted with water and extracted with ether. The organic extract was washed, dried and evaporated. The oily material obtained on chromatographic purification over silica gel (hexane;benzene 40:60) afforded phenanthrene (3) (552 mg, 60%), m.p. 162-163°C (from benzene), UV (methanol): 256 (ε 19230), NMR: δ 2.40 (s, 3H, Me), 2.65 (s, 3H, Me), 2.93 (s, 3H, Me), 3.81 (s, 3H, OMe) and 7.01-8.24 (m, 6H, aromatic protons), MS: m/z 250 (M^+) (Found: C, 86.33; H, 7.23. Calc. for $C_{18}H_{18}O$: C, 86.36; H, 7.25).

Further elution with hexane:benzene (45:55) afforded the oily compound (2), (47 mg, 5%), MS: 252 (M^+). The compound (2) on heating with palladium charcoal (10 mg) on a metal bath for 40 min yielded the phenanthrene (3) (12 mg) whose identity was confirmed by comparing with an authentic specimen. Evaporation of the elute hexane:benzene (30:70) afforded the oily compound (7) (54 mg, 20%), IR: 1710 cm^{-1} (CO), NMR: δ 0.92-1.09 (18H, 1-Me and 4a-Me), 1.88 (1H, d, J=6 Hz), 2.18 (1H, d, J=3 Hz) (10a-H), 3.86 (6H, s, OMe) and 6.55-7.45 (m, aromatic protons, 6H), MS: m/z 270 (M^+) (Found: C, 79.92; H, 8.18. Calc. for $C_{18}H_{18}O$: C. 79.96; H, 8.20).

1,2,4-Trimethyl Phenanthrene (5) - To a solution of the phenanthrene (3) (500 mg) in dichloromethane (10 ml), cooled at -25°C, was added boron tribromide in dichloromethane (1 ml, 1.0 M solution in dichloromethane) (Aldrich). The solution was kept in the cooling bath for 1 hr and allowed to attain room temperature. Workup followed by the filtration through a column of silica gel afforded the phenol (4) which showed almost complete absence of the methoxy signal in the NMR spectrum and was used without further purification for the next step.

To a suspension of sodium borohydride (102 mg) pellets in trifluoroacetic acid (20 ml) at 0°C under nitrogen was added a solution of the phenol (4) in dichloromethane (10 ml), stirred for 28 hr, diluted with water, treated with sodium hydroxide (pellets) and extracted with ether. The ether extract was concentrated which on chromatographic purification over silica gel (hexane:ether 80:20) afforded phenanthrene (5) (88 mg, 20%), m.p. 54-55°C (from EtOH-Pet. Ether) (lit.[7] 56°C), NMR: δ 2.42 (s, 3H, Me), 2.65 (s, 3H, Me), 2.95 (s, 3H, Me) and 7.01-8.26 (m, 7H), MS: m/z 220 (M^+) (Found: C, 92.64; H, 7.32. Calc. for $C_{17}H_{16}$: C, 92.68; H, 7.32). Its picrate derivative melted at 150-152°C (lit.[7] 151°C).

Olefin (8) - The keto-olefin (7) (50 mg) was refluxed for 5 hr with amalgamated zinc (2.2 g), water (3 ml) and hydrochloric acid (6 ml). The ethereal extract of the resulting material was concentrated and chromatographed over silica gel (eluant hexane) to obtain the olefin (8) (35 mg, 75%) whose spectral properties were identical with those reported.[9]

1,2-Dimethyl-4-carboxylic acid-5,6,7,8-tetrahydronaphthalene (12) - A solution of the ketone (10) (1 g) in acetic acid (30 ml, 99%) and p-toluenesulphonic acid (250 mg) was heated under reflux for 45 min, diluted with water and extracted with ether. The organic extract on chromatographic purification over silica gel (hexane) gave the tetrahydronaphthalene (14) and (15) (169 mg 25%), NMR: δ 2.01 (s, 6H), 2.04 (s, 6H) (4 Me), 6.78-6.92 (m, 3H) and 7.08 (s, 1H) (aromatic protons) MS: m/z 160 (M^+).

Further elution (hexane:ether 1:2) yielded the acid (12) (489 mg, 60%), m.p. 216-217°C (from ether), IR: 1675 cm^{-1} (CO), NMR: δ 2.10 (s, 3H, Me), 2.20 (s, 3H, Me), 1.66-1.76 (m, 4H), 2.43-2.93 (m. 4H) (methylene and benzyl protons respectively) and 7.42 (s, 1H, aromatic protons), MS: m/z 204 (M^+) and 159 (M^+-COOH) (Found: C, 76.39; H, 7.86. Calc. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90).

1,2,4-Trimethylnaphthalene (13) - The acid (12) (400 mg) with diazomethane gave the ester derivative (425 mg) which in tetrahydrofuran (30 ml) was heated for 6 hr with lithium aluminium hydride (100 mg), cooled, treated with water (1 ml), filtered, dried and concentrated to yield an alcohol (410 mg), IR: 3460 cm^{-1} (OH).

The alcohol (400 mg) in pyridine (8 ml) was stirred with p-toluenesulphonyl chloride (300 mg) for 20 hr, added water (30 ml) and extracted with methylene chloride, washed with 1% HCl and dried to give the tosyl derivative (492 mg) which in tetrahydrofuran (10 ml) was treated with lithium triethylborohydride (10 ml, 1M in tetrahydrofuran) (Aldrich), stirred at room temperature for 2.5 hr, was added water (1.5 ml), sodium hydroxide (10 ml, 3N) and hydrogen peroxide (10 ml, 30%). Workup and purification over silica gel (eluant hexane) afforded an oil (103 mg), MS: m/z 174 (M^+). Heating this oil (100 mg) with palladium charcoal (40 mg) for 40 min followed by purification over silica gel (eluant hexane) gave trimethyl naphthalene (13) (55 mg), m.p. 53-55°C (from methanol), lit.[12] 54-55°C (Found: C, 91.66; H, 8.25. Calc. for $C_{13}H_{14}$: C, 91.71; H, 8.29).

3,3-Ethylenedioxy-4,4,10-trimethyl-9-methoxy-$\Delta^{5,6}$-Octalin (18) - A solution of ketone (16) (600 mg), ethylene glycol (4 ml) in benzene (10 ml) and p-toluenesulphonic acid (8 mg) was heated at reflux for 22 hr and cooled. Workup and purification over silica gel (eluant hexane:ether 4:1) gave the ketal (620 mg, 85%), IR: 3470 cm^{-1} (OH), NMR: δ 1.16 (s, 3H), 1.10 (s, 3H), 1.23 (s, 3H) (4,4,10-Me), 3.84 (m, 4H, ketal) and 5.55 (m, 1H, vinyl proton).

To sodium hydride (520 mg) in tetrahydrofuran (5 ml) was added a solution of ketal (17) (610 mg) in tetrahydrofuran (5 ml), warmed for 10 min, added methyl iodide (2 ml), and refluxed for 6 hr. Workup afforded the octalin (18) (578 mg, 90%), m.p. 96-98°C (from ether), NMR: δ 1.06 (s, 3H), 1.16 (s, 3H), 1.24 (s, 3H) (4,4,10-Me), 3.34 (s, 3H, OMe), 3.84 (s, 4H, ketal) and 5.45 (t, 1H, 6-H), MS m/z 266 (M^+) (Found: C, 72.11; H, 9.82. Calc. for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84).

3-Keto-4,4,10-trimethyl-9-methoxy-$\Delta^{5,6}$-Octalin (19) - The ketal (18) (500 mg) in acetic acid (80%, 5 ml) was heated for 4 hr. Workup and purification over silica gel (eluant hexane:ether 7:3) afforded the ketone (19) (383 mg, 92%), IR: 1710 cm^{-} (CO), NMR: δ 1.20 (s, 3H), 1.24 (s, 3H), 1.36 (s, 3H) (4,4,10-Me), 3.42 (s, 3H, OMe) and 5.65 (t, 1H, 6-H), MS: m/z 222 (M^+), 207 (M^+-Me) and 167 (M^+-3Me) (Found: C, 81.74; H, 10.74. Calc. for $C_{14}H_{22}O_2$: C, 81.50; H, 10.75)

1,2,4-Trimethyl-$\Delta^{5,6}$-7,8-dihydronaphthalene (21) - The ketone (19) (400 mg) in acetic acid (12 ml) was heated under reflux for 40 hr with p-toluenesulphonic acid (90 mg). Workup and purification by thin layer chromatography gave the naphthalene (21) (130 mg, 42%), NMR: δ 1.93 (s, 3H), 2.06 (s, 3H), 2.26 (s, 3h), (1,2,4-Me), 2.45-2.72 (4H) (two benzylic and two allylic protons), and 6.85-7.15 (3H) (two olefinic and aromatic protons, MS: m/z 172 (M^+). The naphthalene (21) (100 mg) on heating with palladium charcoal (45 mg) for 40 min yielded the already mentioned 1,2,4-trimethyl naphthalene (13) (44 mg, 45%).

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