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Formation and Reduction of 2-Acyl-1-tetralones

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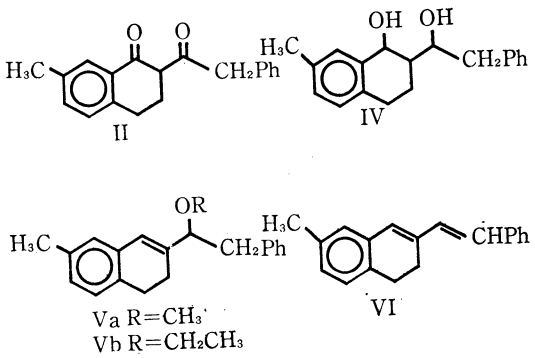
Following the synthesis of co-enzyme model compounds, we have attempted to synthesize the substituted polycyclenes from 7-methyl-1-tetralone (I), an important intermediate in the preparation of natural products. In the present paper we deal with the formation and reduction of 2-acyl-1-tetralone from I.

In the presence of sodium methoxide in methanol under nitrogen atmosphere, I could not be acylated with methyl acetate or phenyl acetate under any conditions and only afforded 7-methyl-1-naphthol, while sodium hydride in dimethyl sulfoxide (DMSO) gave 7-methyl-2-phenylacetyl-1-tetralone (II) in good yield besides the formation of methyl 2,4-diphenylacetoacetate (III), a self-condensation product of the ester. II and III were enolized in $CDCl_3$ and CCl_4 in 73 and 55% yield, respectively. They were determined by integral ratio of enolic hydroxyl and methine protons in the NMR spectra.

In the preparation of β-diols from β-diketones metallic sodium often gives unsatisfactory results particularly in β-diketones containing aroyl groups as the functional group.[1] Catalytic hydrogenation of aliphatic β-diketones in the presence of Raney nickel afforded β-diols in excellent yield, but this method requires high temperature and high pressure.[2] Thus it is desirable to find a mild reduction method of β-diketones to β-diols. Recent works[3] on reduction with the use of $LiAlH_4$ are valuable as regards the accomplishment of mild reduction. We attempted the reduction of II with $NaBH_4$ and found an interesting solvent effect in subsequent dehydration of β-diols (IV).

Reduction of II with $NaBH_4$ in ethanol followed by



treatment with hydrochloric acid afforded 2-(1-hydroxy-2-phenylethyl)-7-methyl-1,2,3,4-tetrahydro-1-naphthol (IV) (53%), 3-(1-ethoxy-2-phenylethyl)-6-methyl-1,2-dihydronaphthalene (Vb) (6%), and 3-styryl-6-methyl-1,2-dihydronaphthalene (VI) (5%). Since Vb and VI were expected from IV in the work up, treatment of IV with acid was investigated. On being treated with 9M H_2SO_4 in benzene–methanol, IV was converted into 3-(1-methoxy-2-phenylethyl)-6-methyl-1,2-dihydronaphthalene (Va) (78%) and VI (22%). When IV was treated with the same acid in 2-propanol (more bulky alcohol), only VI was obtained quantitatively. VI gave neither Va nor Vb. These results suggest that Va and Vb were formed from IV by the S_N2 acid-catalyzed substitution of hydroxyl group on the side chain after the completion of dehydration of hydroxyl group on the ring and that both V were irreversibly dealkoxylated to VI.

Experimental

Instruments for spectral measurements were Shimadzu IR 27 (IR), Hitachi 124 spectrophotometer (UV), Japan Electron Optics Model C-60 (NMR) and JMS-OISG (MS). Merck Art. 7734 was used for separation of products on a silica gel

1) E. Bauer, *C. R. Acad. Sci., Paris*, **154**, 1092 (1912).

2) P. S. Stutzman and H. Adkins, *J. Amer. Chem. Soc.*, **61**, 3303 (1939).

3) a) L. Cazaux and P. Maroni, *Bull. Soc. Chim. Fr.*, **1972**, 773, 780; b) P. Maroni and J-P. Gorrichon, *ibid.*, **1972**, 785; c) P. Maroni and P. Tisnes, *ibid.*, **1972**, 794.

column by elution chromatography and Wakogel B-5 UA for thin layer chromatography (tlc).

Materials. 7-Methyl-1-tetralone (I) was synthesized in three steps from toluene and succinic anhydride, mp 31.5—32.5 °C (lit,[4] 33 °C).

7-Methyl-2-phenylacetyl-1-tetralone (II). I (0.04 mol) was treated with methyl phenylacetate (0.08 mol) and sodium hydride (0.08 mol) in DMSO (20 ml). After completion of the reaction, the mixture was poured into ice water (200 ml) containing 15 ml of concd. HCl and extracted with ether. The etheral extract was added dropwise to 200 ml of a hot aqueous cupric acetate solution (10%), and the mixture was stirred overnight. The precipitate was collected by filtration and washed with water, methanol and ether successively. For analytical use, a part of the precipitate was recrystallized from benzene–methanol as dark green crystals, mp 232—235 °C (decomp.). Found: Cu, 10.24%. Calcd for $C_{38}H_{34}O_4Cu$: Cu, 10.35%. UV: $\lambda_{max}(\varepsilon)$ (in methanol) 211 (40800), 253.6 (37700), 260 (35400), 334 (10200), 338.5 (3100), and 410 (2500) nm.

The copper chelate was treated with 10% sulfuric acid (60 ml) and the organic layer was extracted with benzene. After evaporation of the solvent, the residue was chromatographed on a silica gel column with benzene to give II (65%) and III (24%).

II was obtained as dark red plates, mp 56.5—58 °C. Found: C, 81.86; H, 6.71%. Calcd for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52%. UV: $\lambda_{max}(\varepsilon)$ (in methanol) 236 (11000), 245s (9200), 258 (6900), 310 (10700), and 347 (18400) nm. NMR ($CDCl_3$): 2.32 (3H, singlet, $-CH_3$), 7.28 (5H, s, phenyl protons), 7.72 (1H, broad s, isolated aromatic proton in tetralone ring), 7.10 (2H, multiplet, two neighboring aromatic protons in tetralone ring), 2.66 (centered) (4H, m, two methylene protons in tetralone ring), 3.80 (2H, s, benzyl protons in the chain), 3.97 (0.2667H, s, CO–CH–CO), and 16.50 (0.7333H, s, enol proton) ppm.

III was obtained as light yellow needles, mp 60—62.5 °C. Found: C, 76.19; H, 6.07%. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01%. MS (75 eV): parent peak at *m/e* 268 and base peak at *m/e* 91 ($C_7H_7^+$). UV: $\lambda_{max}(\varepsilon)$ (in methanol) 210 (13600), 254 (3700), and 264s (3370) nm. IR (KBr disk): ν_{max} 1770 (–COOMe) and 1740 (–CO–) cm^{-1}. NMR (CCl_4): 3.59 (3H, s, $-OCH_3$), 3.61 (2H, s, $-CH_2-$), 4.62 (0.455H, s, –CH–), and 13.05 (0.545H, s, enol proton) ppm.

Reduction of II with Sodium Borohydride. In Ethanol: Sodium borohydride was added at room temperature to I (6.13 mmol) in 60 ml of ethanol at once. The color of the orange-red solution gradually vanished. The reaction was accomplished after 8 hr. The solution was acidified with 6M hydrochloric acid and the solvent was removed under reduced pressure by repeated addition of methanol. The residue was chromatographed on a silica gel column with benzene to give IV (53.2%), Vb (6%), and VI (5%).

A part of IV crystallized during the course of chromatographic separation; fine white needles, mp 164—174.5 °C. Found: C, 80.76; H, 8.12%. Calcd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85%. Exact mass measurement: For parent peak, Found: 282.16121, Calcd for $C_{19}H_{22}O_2$: 282.16198. UV: $\lambda_{max}(\varepsilon)$ (in methanol) 262s (600), 264 (650), 269 (780), and 278.5 (760) nm. NMR ($CDCl_3$): 2.30 (3H, s, $-CH_3$) and 7.23 (5H, s, phenyl protons) ppm.

Vb was obtained as colorless oily liquid showing fluorescence. Found: C, 86.17; H, 8.03%. Calcd for $C_{21}H_{24}O$: C, 86.25; H, 8.27%. Exact mass measurement: For parent peak, Found: 292.17921, Calcd for $C_{21}H_{24}O$: 292.18272. IR (NaCl plates): ν_{max} 1085 (C–O–C) and 700 (–Ph) cm^{-1}. NMR ($CDCl_3$): 1.14 (3H, triplet, $J=12.0$ Hz, $-OCH_2\underline{CH_3}$), 2.27 (3H, s, Ar–CH_3), 3.33 (2H, quartet, $J=12.0$ Hz, $-OC\underline{H_2}-CH_3$), 4.00 (1H, t, $J=11.0$ Hz, –CH–O–), 6.21 (1H, s, –C–CH–), 6.95 (2H, broad s, two adjacent aromatic protons), and 7.22 (5H, s, phenyl protons) ppm.

VI was obtained as light yellow amorphous solid, mp 118—126 °C. Found: C, 91.71; H, 6.94%. Calcd for $C_{19}H_{18}$: C, 92.36; H, 7.37%. Exact mass measurement: For parent peak, Found: 246.13723, Calcd for $C_{19}H_{18}$: 246.14085. IR (KBr disk): ν_{max} 960 (C=CH) cm^{-1}. UV: $\lambda_{max}(\varepsilon)$ (in methanol) 213 (16500), 230 (11000), 237s (9900), 245 (9800), 252s (7900), 261 (6600), 309s (18000), 325 (31000), 340 (40000), and 358 (29700) nm. NMR ($CDCl_3$): 2.29 (3H, s, Ar–CH_3) and 2.65 (centered) (4H, AA'BB', $-CH_2CH_2-$) ppm, (aliphatic protons): (olefinic and aromatic protons) = 7: 11.

In Methanol: IV was vigorously stirred in benzene–methanol (3: 2 v/v) with sulfuric acid (9M) until no IV was detected on tlc. The mixture was extracted with benzene after neutralization with sodium bicarbonate on a silica gel column with benzene to give Va (78%) and VI (22%).

Va was obtained as colorless oily liquid showing fluorescence. Found: C, 86.28; H, 7.95%. Calcd for $C_{20}H_{22}O$: C, 86.28; H, 7.97%. IR (NaCl plates): ν_{max} 1095 (C–O–C) and 700 (–Ph) cm^{-1}. UV: $\lambda_{max}(\varepsilon)$ (in methanol) 266 (12000), 274 (11000), and 303 (1700) nm. NMR ($CDCl_3$): 2.26 (3H, s, Ar–CH_3), 3.23 (3H, s, $-OCH_3$), 3.90 (1H, t, $J=11.5$ Hz, –CH–O–), 6.23 (1H, s, C=CH), 6.81 (1H, s, isolated aromatic protons), 6.96 (2H, s, two adjacent aromatic protons), and 7.22 (5H, s, –Ph) ppm.

In Benzene: IV was vigorously stirred in benzene with 9M sulfuric acid until no IV was detected on tlc. The same work up as in methanol gave VI quantitatively.

In 2-Propanol: As the same operation as in methanol was carried out in 2-propanol. VI was quantitatively obtained after the work up. No alkoxylated product was detected.

Reaction of Va with Acid. To Va in methanol was added a small amount of concd. sulfuric acid and the mixture was allowed to stand at room temperature for 24 hr. From the solution VI crystallized quantitatively. Even when the solution containing only VI was allowed to stand further, no detectable amount of Va was found on tlc, indicating that formation of VI from Va was irreversible.

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4) F. Krollpfeiffer and W. Schaefer, *Ber.*, **56**, 620 (1923).