

SULFURIC ACID-ACETIC ANHYDRIDE PROMOTED REARRANGEMENT
OF α,β -UNSATURATED KETONES.

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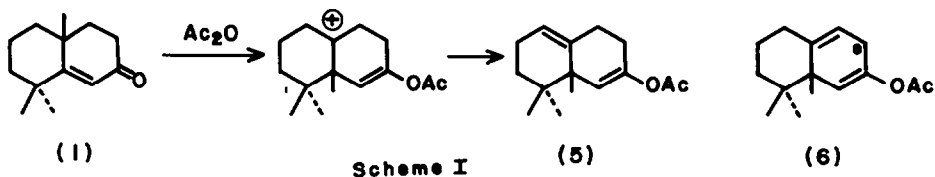
Abstract - The α,β -unsaturated ketones (1), (3), and (4) on treatment with sulfuric acid in acetic anhydride underwent molecular transformations yielding the products (5), (7) and (8), respectively.

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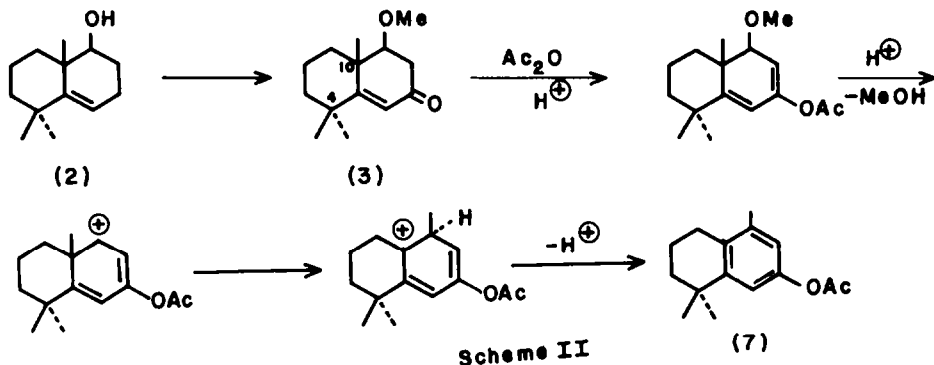
Under acidic conditions α,β -unsaturated ketones rearrange for many new products useful for many important synthetic reactions and for the construction of carbocyclic systems present in numerous natural products.¹ In connection with our studies on molecular rearrangement,² the reaction of some synthetically useful unsaturated ketones³ such as (1), (3), and (4) with sulfuric acid in acetic anhydride, a valuable reagent for synthetic reactions,⁴⁻⁶ was studied. The present paper documents the results of our investigation.⁷

Treatment of the ketone⁸ (1) with sulfuric acid in acetic anhydride provided primarily an olefinic acetate which exhibited a molecular ion at m/z 234 (M^+) in the mass spectrum and had adsorption at 1710 (CO) cm^{-1} in the IR spectrum. Its ¹H NMR spectrum exhibited acetate signals at δ 2.13 (3H,s), two vinyl protons at δ 5.26 and δ 5.61. The signals between δ 1.35-1.42 (2H,m) and δ 1.55-2.61 (m,6H) were assigned to methylene protons at C-3 and allylic protons at C-2, C-8, and C-9, respectively. On the basis of these spectroscopic data the olefinic acetate was assigned the structure (5), not the alternative structure (6) which contains four allylic and four methylene protons. The olefinic acetate (5) definitively resulted through the migration of the C-10 angular methyl group as depicted in Scheme I.

Under the same conditions the ketone (3), prepared by methylation and oxidation of the alcohol⁸ (2), underwent an interesting rearrangement yielding a tetralene derivative which had a molecular ion m/z 232 (M^+) in the mass

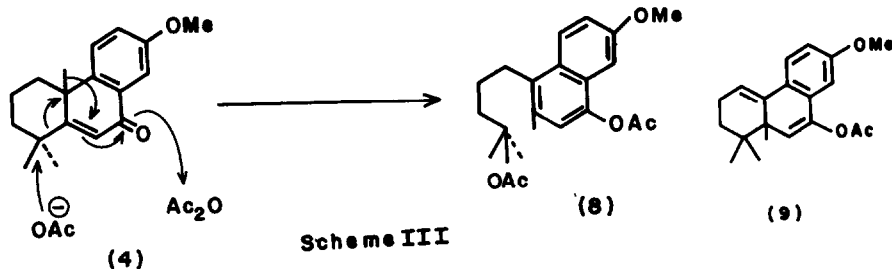


spectrum and showed absorption at $1730 (\text{C}=\text{O}) \text{ cm}^{-1}$ in the IR spectrum. The tetralene derivative exhibited in the ^1H NMR spectrum two methyl groups at δ 1.26 (6H), one acetyl group at δ 2.22 (3H), one aromatic methyl group at δ 2.28 (3H), and two aromatic protons centered at δ 6.72 (1H), and 6.91 (1H). These spectroscopic data led us to propose the structure (7) for the tetralene derivative whose formation can be best explained by the well established pattern of the dienone-phenol rearrangement depicted in Scheme II. It can be observed that the beta-methoxy ketone apparently did not obscure its basic and unsurprising nature. We believe that owing to the steric interaction between 9-methoxy and 10-methyl groups, the ketone (3) did not undergo similar rearrangement as the ketone (1).



Our experiment was next extended to the tricyclic ketone (4)¹⁰ which under the above mentioned conditions underwent ring cleavage affording an oily diacetate which had a molecular ion m/z 312 ($\text{M}^+ - \text{AcOH}$) and showed absorption at $1735 (\text{C}=\text{O}) \text{ cm}^{-1}$ in the IR spectrum. The singlet signals at δ 1.31 (6H) and 2.43 (3H) indicated the presence of two methyl groups and one aromatic methyl group. The signals between δ 2.08-2.10 (6H) and δ 7.02-7.43 (4H) were assignable to two acetate groups and aromatic protons, respectively. On the basis of these spectroscopic data, the structure (8) was assigned to the diacetate. There is no doubt that owing to the molecular rigidity of the ketone (4), it is difficult to explain the formation of diacetate by the mechanistic evidence proposed in Schemes I and II. The formation of the diacetate (8) can be explained by the ease of elimination of tertiary carbonium ions as suggested in Scheme III. The mechanism also receives support

from the work of Kropp.¹¹ The ketone (4), though was expected to yield the acetate (9) according to Scheme I, afforded principally the diacetate (8). In addition of the diacetate, another oily material in very poor yield was obtained and this did not exhibit the vinyl proton signals in the ^1H NMR spectrum which indicated the absence of the acetate (9).



EXPERIMENTAL¹²

General Procedure - To a solution of α,β -unsaturated ketone in acetic anhydride, was added sulfuric acid-acetic anhydride (1:1) and the mixture was left standing at room temperature for 3 h. The reaction mixture was poured on cold water containing sodium bicarbonate and then extracted with ether. The ethereal extract was washed with brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure. The resulting product was chromatographed over silica gel (Merck). The unsaturated ketones were not recovered.

Acetate (5) - Ketone (1) (580 mg) in acetic anhydride (20 ml) was treated with 2 ml of sulfuric acid-acetic anhydride. The usual workup yielded an oily material which on chromatographic purification (eluant benzene: ether 8:2) afforded the oily acetate (5) (348 mg, 48%); IR: 1710 (C=O) cm^{-1} ; NMR: δ 1.13 (s, 6H), 1.26 (s, 3H) (4,4,5-Me), 1.35-1.42 (m, 2H) (3-H), 1.55-2.61 (m, 6H, C-2, C-8 and C-9), 2.13 (s, 3H, OAc), 5.26 (m, 1H) and 5.61 (s, br, 1H) (vinyl protons), MS: m/z 234 (M^+) and 192 ($\text{M}^+ - \text{CH}_2\text{CO}$). (Found: C, 76.69; H, 9.42. Calc. for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46%).

Ketone (3) - A solution of the alcohol (2) (1.95 g) in tetrahydrofuran (20 ml) was added dropwise to a suspension of sodium hydride (1.82 g) in tetrahydrofuran (20 ml). The mixture was warmed for 10 min followed by the addition of methyl iodide (10 ml) and the mixture was then heated under reflux for 6 h, cooled, diluted with water, extracted with ether, dried, and evaporated. The residue on chromatographic purification (eluant benzene: ether 7:3) yielded the oily methoxy compound (1.67 g, 80%).

The methoxy compound (1.62 g) dissolved in dichloromethane (30 ml) was added to a suspension of dry chromium trioxide (4 g) in dry pyridine (15 ml) and dry dichloromethane (25 ml), cooled to 0°C . The resulting mixture was stirred at 0°C for 5 min and 24 h at room temperature. The deep orange colored solution was decanted from the precipitated dark resinous material, and evaporated. The residue was dissolved in ether, washed with 2% hydrochloric acid, dried, and evaporated. The resulting material, on chromatographic purification (eluant benzene: ether 6:4), afforded the oily ketone (3) (690 mg, 40%); IR: 1665 (C=O) cm^{-1} ; NMR: δ 1.16 (s, 3H), 1.24 (s, 3H), 1.28 (s, 3H) (4, 4, 10-Me), 1.44-1.63 (m, 6H) (C-1, C-2 and C-3), 2.32-2.62 (m, 2H, C-8), 3.35 (s, 3H, OMe), 3.24 (m, 1H, 9-H), and 6.01 (s, 1H, vinyl proton); MS: m/z 222 (M^+). (Found: C, 75.54; H, 9.91. Calc for $\text{C}_{14}\text{H}_{22}\text{O}_2$: C, 75.63; H, 9.97%).

Tetralene (7) - Ketone (3) (600 mg) in acetic anhydride (15 ml) was treated with 3 ml of sulfuric acid-acetic anhydride. The usual workup yielded a deep yellow oily material which on chromatographic purification (eluant benzene)

afforded the tetralene (7) (376 mg, 60%); IR 1735 (CO) cm^{-1} ; NMR: δ 1.26 (s, 6H, 4-Me), 1.61-2.01 (m, 4H), 2.52-2.62 (m, 2H, benzyl protons), 2.22 (s, 3H, OAc), 2.28 (s, 3H, aromatic Me), 6.72 (s, broad, 1H) and 6.91 (s, broad, 1H) (aromatic protons); MS: m/z 232 (M^+) and 190 ($\text{M}^+ - \text{CH}_2\text{CO}$). (Found: C, 77.48; H, 8.63. Calc. for $\text{C}_{15}\text{H}_{20}\text{O}_2$: C, 77.55; H, 8.68%).

Diacetate (8) - Ketone (4) (300 mg) in acetic anhydride (10 ml) was reacted with 2 ml of sulfuric acid-acetic anhydride. The usual workup followed by chromatographic purification (eluant benzene:ether 70:30) afforded the oily diacetate (8) 251 mg, 61%, IR: 1730 (CO) cm^{-1} ; NMR: δ 1.31 (s, 6H, 4-Me), 1.42-1.74 (m, 4H) (C-2 and C-3), 2.61-2.91 (m, 2H) (C-1, benzyl protons), 2.08-2.10 (2s, 6H, 4-OAc and 7-OAc), 2.43 (s, 3H, aromatic Me), 3.65 (s, 3H, OMe) and 7.02-7.43 (m, 4H, aromatic protons); MS: m/z 312 ($\text{M}^+ - \text{AcOH}$). (Found: C, 70.87; H, 7.52. Calc. for $\text{C}_{22}\text{H}_{26}\text{O}_5$: C, 70.94; H, 7.58%).

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