The Structure of 4-(α-Ethylenedioxy)ethyltropolone Methyl Ether[1]

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4-Acetyltropolone[2] obtained by oxidation of β-dolabrin (4-isopropenyltropolone)[2] reacts with ethylene glycol in dehydrated benzene, in the presence of *p*-toluenesulfonic acid, and easily forms 4-(α-ethylenedioxy)ethyltropolone (I) as colorless prisms of m. p. 98°C. I easily reverts to 4-acetyltropolone on being heated with dilute mineral acid.

Methylation of I with an ether solution of diazomethane affords two kinds of methyl ethers in approximately 1:1 ratio, one a colorless needle (II), m. p. 110°C, and the other a colorless prism (III), m. p. 111°C. Admixture of II and III clearly indicates depression of the melting point. The ultraviolet spectra of II and III, shown in Fig. 1, clearly indicate the characteristic absorption of tropolone methyl ethers[3].

In order to establish the structure of these methyl ethers, the following reactions were examined.

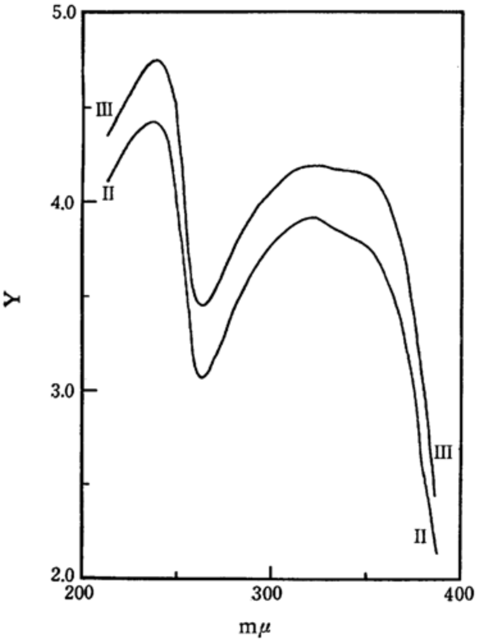

Fig. 1. Ultraviolet absorption spectra of II and III in methanol.
II: Y=log ε; III: Y=log ε+0.3

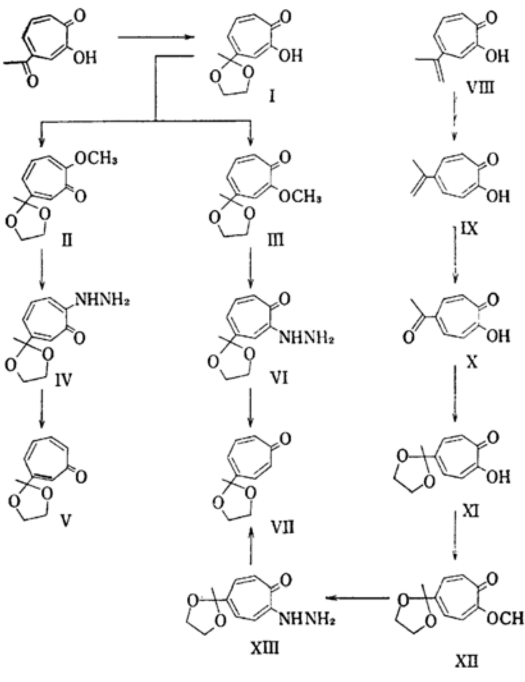

Fig. 2.

When II is heated with hydrazine hydrate in ethanol, a hydrazino derivative IV is obtained in a good yield as orange needles, m. p. 99°C. The cyclohexylidene compound of IV comes as yellow needles of m. p. 95~96°C. Decomposition of IV with aqueous solution of copper sulfate in dilute acetic acid affords *x*-(α-ethylenedioxy)ethyltropone (V) as colorless prisms, m. p. 72°C.

On the other hand, a similar derivation of the methyl ether III of m. p. 111°C to the hydrazinotropone derivative VI, m. p. 124°C, and its subsequent decomposition with copper sulfate gives *x′*-(α-ethylenedioxy)ethyltropone (VII) as colorless scales, m. p. 81.5°C.

The two kinds of tropone derivatives V and VII so obtained show infrared absorption spectra[4] (region of out-of-plane vibrations) indicated in Fig. 3.

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[1] Paper presented at the 12th Annual Meeting of the Chemical Society of Japan, Kyoto, April, 1959.

[2] T. Nozoe, K. Takase and M. Ogata, *Chem. and Ind.*, **1957**, 1070.

[3] M. Tsuboi, This Bulletin, **25**, 369 (1952).

[4] Infrared spectra were measured with a Perkin-Elmer model-21 spectrophotometer provided with a sodium chloride prism.

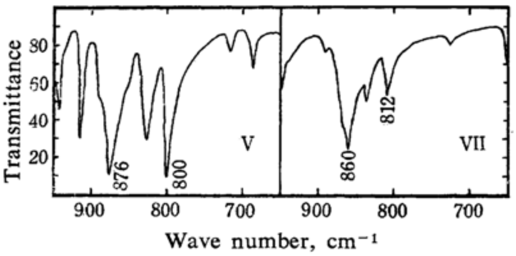

Fig. 3. Infrared absorption spectra of V and VII.

As had already been pointed out by Kitahara⁵⁾, the out-of-plane absorption of hydrogens in the seven-membered ring in the troponoid compounds is approximately in regularity with the number of adjacent hydrogen, as was found in benzenoid compounds.

The α-ethylenedioxyethyl group in the tropone derivatives obtained by the removal of methoxyl group from the methyl ethers II and III should be present in the 3- or 4-position. If it is in the 3-position, the number of adjacent hydrogen atoms would be one and four, and their absorptions should appear at 760~810 cm^{-1} (s) and at 860~900 cm^{-1} (m). If in the 4-position, the number of adjacent hydrogen atoms would be two and three, and their absorptions should appear at 770~820 cm^{-1} (s) and 820~860 cm^{-1} (s).

It is clearly seen in Fig. 3 that V shows marked absorptions at 800 and 876 cm^{-1}, while VII has absorptions at 812 and 860 cm^{-1}. Consequently, it would seem possible to conclude that V is a 3-substituted tropone and VII is a 4-substituted tropone.

In order to prove the above assumptions by organic chemical means, the following reactions were carried out.

β-Dolabrin (VIII) was converted by the known process⁶⁾ into γ-dolabrin (IX) and oxidized with hydrogen peroxide and then with periodic acid into 5-acetyltropolone (X)⁶⁾. Reaction of ethylene glycol on X in benzene, in the presence of p-toluenesulfonic acid, as in the case of 4-acetyltropolone, afforded 5-(α-ethylenedioxy)ethyltropolone (XI) as colorless needles, m. p. 104°C. Methylation of XI with an ether solution of diazomethane produced almost quantitatively the methyl ether (XII) of XI as colorless prisms, m. p. 115°C. Since XI is a 5-substituted tropolone, the structure of its methyl ether XII should be 2-methoxy-5-(α-ethylenedioxy)ethyltropone. XII forms a hydrazinotropone derivative XIII of m. p. 164°C (decomp.) with hydrazine hydrate.

Decomposition of XIII with copper sulfate in dilute acetic acid affords a tropone derivative of m. p. 81.5°C, whose structure would clearly be 4-(α-ethylenedioxy)ethyltropone considering the route of its synthesis.

Of the two kinds of tropone derivatives V and VII obtained in the present series of work and described above, the one with m. p. 81.5°C (VII) agreed with the product obtained by decomposition of XIII in mixed melting point, and in ultraviolet and infrared absorption spectra, indicating them to be the same substance. Consequently, it becomes clear that the structure of V is 3-(α-ethylenedioxy)ethyltropone. This fact agrees well with the results of infrared spectral analysis mentioned above.

From the foregoing experimental facts, it is concluded that the structure of II is 2-methoxy-6-(α-ethylenedioxy)ethyltropone and that of III is 2-methoxy-4-(α-ethylenedioxy)ethyltropone.

Experimental⁷⁾

4-(α-Ethylenedioxy)ethyltropolone (I).—A mixture of 4-acetyltropolone (2.9 g.), dehydrated benzene (100 ml.), ethylene glycol (30 ml.), and p-toluenesulfonic acid (0.3 g.) was refluxed with stirring and the water was removed by azeotropic distillation with benzene through a column 20 cm. in length. During this time, 50 ml. of benzene was supplemented twice and the whole reaction was carried out over 20 hr. The reaction mixture was then diluted with water and extracted with benzene. The benzene layer was extracted with 2 N sodium hydroxide, the aqueous layer was acidified with hydrochloric acid and the crystals that formed were collected. Low-pressure sublimation of this product afforded 3.25 g. of I, m. p. 95~97°C. Recrystallization of I from a mixed solvent of benzene and cyclohexane gave colorless prisms, m. p. 97.5~98°C.

Found: C, 63.00; H, 6.05. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81%.

Methylation of I.—To a suspension of I (3.2 g.) in ether (20 ml.), ether solution of diazomethane was added dropwise with ice-cooling, by which I gradually dissolved and needle crystals began to precipitate out. When the solution no longer colored with ferric chloride solution, the crystals were collected. Yield 1.45 g. M. p. 105~107°C.

The ethereal mother liquor was concentrated and a further crop (1.85 g.) of crystals, m. p. 95~106°C was obtained. Repeated fractional recrystallization from a mixed solvent of cyclohexane and benzene finally afforded II (1.1 g.) from the former as colorless needles, m. p. 109~110°C, and III (1.49 g.) chiefly from the latter as colorless prisms, m. p. 110~111°C. Admixture of II and III melting at 85~87°C.

Found (for II): C, 65.10; H, 6.29. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 236 (4.44), 322 (3.92).

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5) Y. Kitahara, *Sci. Repts. Tohoku Univ.*, [1] **39**, 275 (1956).

6) T. Nozoe, T. Mukai, K. Yamane, T. Asao and I. Murata, Paper presented at the 11th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1958.

7) All melting points are not corrected.

Found (for III): C, 65.01; H, 6.24. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 238 (4.48), 322 (3.91).

2-Hydrazino-6-(α-ethylenedioxy)ethyltropone (IV). —80% hydrazine hydrate (0.2 g.) was added to the solution on II (0.2 g.) dissolved in ethanol (0.5 ml.) and the mixture was heated at 90°C for 5 min. Evaporation of ethanol afforded crystals (0.2 g.) of m. p. 68~79°C which recrystallized from dilute ethanol to IV as orange needles, m. p. 98~99°C.

Found: C, 57.52; H, 6.35; N, 12.48. Calcd. for $C_{11}H_{14}O_3N_2$: C, 57.45; H, 6.35; N, 12.60%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 250 (4.41), 340 (4.07), 402 (4.03).

Cyclohexylidene Compound of IV. — Cyclohexanone (0.06 g.) was added to the solution of IV (0.12 g.) dissolved in ethanol (1 ml.) and the mixture was boiled for 5 min. Removal of ethanol afforded 0.11 g. of crystals, m. p. 93~95°C, which recrystallized from ethanol to yellow prisms, m. p. 95~96°C.

Found: C, 67.33; H, 7.22; N, 9.19. Calcd. for $C_{17}H_{22}O_3N_2$: C, 67.52; H, 7.33; N, 9.27%.

3-(α-Ethylenedioxy)ethyltropone (V). — A solution of IV (0.5 g.) dissolved in a mixture of acetic acid (3 ml.) and water (10 ml.) was boiled. A 10% aqueous solution of copper sulfate (30 ml.), preliminarily boiled, was added to the foregoing solution in one portion, by which a vigorous evolution of nitrogen gas occurred. The mixture was boiled for 15 min., the precipitate was filtered off, and the filtrate was extracted with chloroform. The reddish oil left after evaporation of chloroform was sublimed at a reduced pressure and gave 0.03 g. of crystals, m. p. 70~72°C. Recrystallization from a mixed solvent of benzene and cyclohexane gave V as colorless prisms, m. p. 71~72°C.

Found: C, 68.76; H, 6.32. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 227 (4.34), 305 (3.89).

2-Hydrazino-4-(α-ethylenedioxy)ethyltropone (VI). —To a solution of III (0.2 g.) dissolved in ethanol (0.5 ml.), 80% hydrazine hydrate (0.2 g.) was added and the mixture was heated at 90°C for 5 min. Removal of ethanol left 0.21 g. of crystals of m. p. 119~121°C which recrystallized from dilute ethanol to VI as yellow prisms, m. p. 123~124°C.

Found: C, 59.72; H, 6.36; N, 12.67. Calcd. for $C_{11}H_{14}O_3N_2$: C, 59.45; H, 6.35; N, 12.60%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 252 (4.37), 338 (4.02), 408 (4.00).

Cyclohexylidene Compound of VI. — Cyclohexanone (0.06 g.) was added to the solution of VI (0.12 g.) dissolved in ethanol (1 ml.) and the mixture was boiled for 5 min. Evaporation of ethanol afforded crystals (0.12 g.) of m. p. 122~124°C which were recrystallized from a mixed solvent of cyclohexane and benzene to yellow needles, m. p. 124~125°C.

Found: C, 67.72; H, 7.03; N, 9.29. Calcd. for $C_{17}H_{22}O_3N_2$: C, 67.52; H, 7.33; N, 9.27%.

4-(α-Ethylenedioxy)ethyltropone (VII).—A solution of VI (0.5 g.) dissolved in a mixture of acetic acid (3 ml.) and water (10 ml.) was boiled, and a boiled 10% aqueous solution (30 ml.) of copper sulfate was added to it in one portion. The mixture was further boiled for 2 min., the precipitate was filtered off, and the filtrate was extracted with chloroform. The oil obtained by the evaporation of the chloroform was extracted with petroleum ether and crystals (0.13 g.) of m. p. 78~80°C were obtained. Sublimation under reduced pressure and recrystallization of the sublimate from a mixed solvent of benzene and cyclohexane afforded VII as colorless scales, m. p. 80.5~81.5°C. This substance contained 1 mol. of crystal cyclohexane.

Found: C, 73.18; H, 8.62. Calcd. for $C_{11}H_{12}O_3 \cdot C_6H_{12}$: C, 73.88; H, 8.75%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 236 (4.54), 313 (3.97).

5-Acetyltropolone (X).—Prepared from β-dolabrin (VIII) by the method already described in the literature7).

5-(α-Ethylenedioxy)ethyltropolone (XI).—A mixture of X (0.5 g.), dehydrated benzene (15 ml.), ethylene glycol (5 ml.), and *p*-toluenesulfonic acid (0.05 g.) was heated and the water which formed was removed azeotropically with benzene. After heating for 25 hr., the mixture was diluted with water and extracted with chloroform. The chloroform layer was extracted with 2 N sodium hydroxide and the alkali solution was acidified with hydrochloric acid. The crystals that precipitated out were collected and sublimed under reduced pressure to form crystals (0.51 g.) of m. p. 98~102°C. Recrystallization from a mixed solvent of cyclohexane and benzene afforded XI as colorless needles, m. p. 103~104°C.

Found: C, 63.20; H, 5.46. Calcd. for $C_{11}H_{11}O_4$: C, 63.45; H, 5.81%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 237 (4.41), 327 (4.02), 367 (3.86).

2-Methoxy-5-(α-ethylenedioxy)ethyltropone (XII). —Ether solution of diazomethane was added to XI (0.4 g.) suspended in ether (10 ml.) to effect methylation. When the solution no longer colored with ferric chloride, the crystals that precipitated out and those obtained by concentration of the filtrate were combined and recrystallized from benzene to XII as colorless prisms, m. p. 114~115°C.

Found: C, 65.31; H, 5.98. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 235 (4.45), 320 (4.08).

2-Hydrazino-5-(α-ethylenedioxy)ethyltropone (XIII).—To a solution of XII (0.5 g.) dissolved in ethanol (2 ml.), 80% hydrazine hydrate (0.3 g.) was added and the mixture was boiled for 5 min. The crystals that precipitated out on cooling the mixture were collected and the crude crystals (0.45 g.) of m. p. 160°C (decomp.) were recrystallized from ethanol to XIII as yellow scales, m. p. 164°C (decomp.).

Found: C, 59.80; H, 5.80; N, 12.56. Calcd. for $C_{11}H_{14}O_3N_2$: C, 59.45; H, 6.35; N, 12.60%. Ultraviolet $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 248 (4.38), 345 (4.18), 408 (4.06).

Synthesis of VII from XIII.—XIII (0.45 g.) was decomposed with aqueous solution of copper sulfate as in the case of IV and VI and the crystals (0.03 g.) of m. p. 78~79.5°C thereby obtained were recrystallized from a mixed solvent of cyclohexane and benzene to VII of m. p. 80~81.5°C, undepressed on admixture with VII obtained from VI, but mixed melting point of 46～52°C was indicated on admixture with V.

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