

**847. Tropolones. Part VI.\* Further Reactions of Tropolone.**

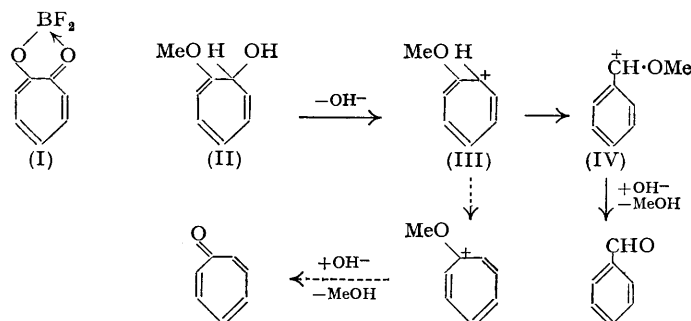
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The Friedel-Crafts, Gattermann, Kolbe-Schmidt, and chloromethylation reactions failed to give substitution products with tropolone. The Reimer-Tiemann reaction, however, gave a small yield of  $\gamma$ -formyltropolone. Lithium aluminium hydride reduction of tropolone led to traces of *cyclohept-4-ene-1 : 2-dione*, but tropolone methyl ether was converted into benzaldehyde by this reagent.

THE somewhat close parallel between the reactions of tropolone and of phenol (*e.g.*, halogenation, nitration, diazo-coupling) suggested investigation of the behaviour of tropolone in other electrophilic substitution reactions. *iso*Propylation of tropolone under Friedel-Crafts conditions was first attempted as all three possible monosubstitution products (the thujaplicins) were known. Treatment of tropolone in *iso*propyl chloride solution with aluminium chloride furnished a complex from which tropolone was regenerated by acid treatment. In an attempt to circumvent this difficulty tropolone methyl ether was similarly treated but tropolone was again recovered. C-Acetylation was attempted by using acetyl chloride and aluminium chloride, but once more tropolone was the sole isolable

\* Part V, *J.*, 1952, 2350.

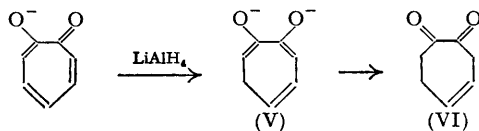
material. Similar results were obtained with acetic anhydride-stannic chloride and acetic anhydride-phosphoric acid, the latter reagents furnishing some *O*-acetyltropolone. Heating tropolone with a solution of boron trifluoride in acetic acid produced a complex to which structure (I) may be assigned. Analogous products have been obtained from both *o*-acylphenols and  $\beta$ -diketones, the chelate ring in these compounds being six-membered (Hauser and Man, *J. Org. Chem.*, 1952, **17**, 393; Kästner, "Newer Methods of Preparative Organic Chemistry," Interscience Publ., New York, 1948, pp. 282, 287). An obvious contributory factor to the failure of these substitution reactions is the ready co-ordination of the strongly electron-donating tropolone with the Lewis acid type of catalyst involved.



Tropolone was also recovered unchanged after being subjected to the Gattermann reaction with zinc cyanide and hydrogen chloride. Attempted chloromethylation, with either paraformaldehyde or chloromethyl methyl ether, gave only tropolone hydrochloride. Three procedures for the Kolbe-Schmidt carboxylation reaction led to recovery of the tropolone.

More success followed when tropolone was subjected to the Reimer-Tiemann reaction; heating with sodium hydroxide and chloroform gave a small yield of  $\gamma$ -formyltropolone the structure of which was established by oxidation to tropolone- $\gamma$ -carboxylic acid, prepared by Mr. D. K. V. Steel in this laboratory by a method which established the structure. This acid was obtained directly when carbon tetrachloride was employed in place of chloroform. An attempt to prepare the aldehyde by using the *N*-methylformanilide-phosphorus oxychloride procedure was unsuccessful.

In Part I (*J.*, 1951, 503) brief mention was made of the lithium aluminium hydride reduction of tropolone. Careful repetition of this work showed that the primary product rapidly resinified when the reaction mixture was hydrolysed. Distillation of the resulting tar gave a very small yield of a liquid which readily gave a bis-2:4-dinitrophenylhydrazone. The ultra-violet absorption curve of this derivative resembled very closely that of the bis-2:4-dinitrophenylhydrazone of *cycloheptane*-1:2-dione although the two compounds were clearly different. It is suggested, therefore, that the liquid reduction product was *cyclohept-4-ene*-1:2-dione (VI) produced by 1:4- or 1:6-addition of lithium aluminium hydride to the dienone system of the initially formed lithium tropolone derivative; hydrolysis of the resulting dienolate (V) would give the dione (VI) by ketonisation:



A similar mechanism has been proposed to account for the production of 3-hydroxy-1:4-diphenylbutan-1-one by reduction of dibenzoyl ethylene (Lutz and Gillespie, *J. Amer. Chem. Soc.*, 1950, **72**, 2002; cf. Cavalla and McGhie, *J.*, 1951, 834).

It is of interest that the two bis-2:4-dinitrophenylhydrazones mentioned above exhibit a maximal absorption in the ultra-violet (3560 Å) which corresponds to that of

an unconjugated mono-derivative (cf. Braude and Jones, *J.*, 1945, 498). This must mean that the two hydrazone groupings are so far from possessing the coplanar configuration necessary for complete conjugation that they behave as discrete chromophores. This result is in harmony with the observation that the planes of the carbonyl groups of 3 : 3 : 7 : 7-tetramethylcycloheptane-1 : 2-dione are inclined at right angles (Leonard and Mader, *J. Amer. Chem. Soc.*, 1950, **72**, 5388).

Reduction of tropolone methyl ether with lithium aluminium hydride gave a completely different and surprising result, for a substantial yield of benzaldehyde was obtained. This may be explained by postulating that the primary reduction product (II) undergoes anionotropy with concomitant Wagner-Meerwein rearrangement of the resulting seven-membered carbonium ion (III) to the more stable benzenoid carbonium ion (IV). Although it would seem feasible for the anionotropy to take the alternative course shown to produce cyclohepta-2 : 4 : 6-trien-1-one (tropone), none of the latter compound could be isolated. The conversion of tropolone methyl ether into benzaldehyde recalls the formation of *o*-chlorobenzaldehyde by treatment of tropolone with thionyl chloride (*J.*, 1952, 2350).

#### EXPERIMENTAL

*Attempted C-Acetylation of Tropolone.*—(a) A mixture of tropolone (200 mg.), acetic anhydride (200 mg.), and syrupy phosphoric acid (40 mg.) was heated at 110° for 3 hours. Water was cautiously added to the cooled solution, and the product isolated with ether. Evaporation gave a residue which was sublimed under reduced pressure to yield (i) tropolone (110 mg.) and (ii) an oil, b. p. 80° (bath-temp.)/10 mm. The latter soon solidified and crystallised from light petroleum (b. p. 60—80°) to give *O*-acetyltropolone (60 mg.) as prisms, m. p. 67° (Kofler block) (Found : C, 65.1; H, 5.0. Calc. for C<sub>9</sub>H<sub>8</sub>O<sub>3</sub> : C, 65.6; H, 4.9%). (b) Tropolone (150 mg.) was dissolved in glacial acetic acid (1 c.c.) and boron trifluoride-ether (1 c.c.) added; an immediate precipitation occurred. The mixture was heated in a sealed tube at 70° for 5 hours, and, after cooling, the crystalline precipitate was filtered off. Crystallisation from acetic acid or light petroleum (b. p. 100—120°) yielded the *complex* (I) (110 mg.) as large plates, m. p. 151° (Found : C, 49.7; H, 3.3. C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>F<sub>2</sub>B requires C, 49.5; H, 2.95%). The complex gave no colour with ferric chloride but was hydrolysed to tropolone with boiling dilute sulphuric acid. Use of aluminium chloride or stannic chloride as catalyst led to recovery of the tropolone.

*Reimer-Tiemann Reaction.*—A mixture of tropolone (500 mg.), water (12 c.c.), and 10*N*-sodium hydroxide solution (4 c.c.) was warmed until solution was complete, and chloroform (0.5 c.c.) was then added. The resulting dark red solution was heated by steam and a further quantity of chloroform (1 c.c.) added during 1 hour. After a further 2 hours' heating the cooled mixture was acidified to Congo-red with dilute sulphuric acid, and an amorphous brown precipitate (50 mg.), m. p. >300°, filtered off. The filtrate was extracted continuously with ether for 24 hours. Drying (Na<sub>2</sub>SO<sub>4</sub>) and removal of solvent furnished a yellow gum which, on being fractionally sublimed under reduced pressure, gave tropolone (100—200 mg.), subliming at 60—80° (bath-temp.)/18 mm., and a yellow solid (20—25 mg.), subliming at 100—120° (bath-temp.)/18 mm. Repeated crystallisation of the latter product from ethanol gave *γ*-formyltropolone as bright yellow needles, m. p. 181° (decomp.), which slowly decomposed on exposure to light (Found : C, 64.0; H, 4.2. C<sub>8</sub>H<sub>6</sub>O<sub>3</sub> requires C, 64.0; H, 4.0%).

*Tropolone-γ-carboxylic Acid.*—(a) *γ*-Formyltropolone (24 mg.) was added to a suspension of freshly precipitated silver oxide (68 mg.) in 4*N*-sodium hydroxide solution (0.5 c.c.), and the mixture heated by steam for 30 minutes. The cooled, filtered solution was acidified with dilute sulphuric acid and extracted continuously with ether for 16 hours. Evaporation gave a yellow solid (12 mg.), m. p. 250—270°, which on crystallisation from glacial acetic acid afforded tropolone-*γ*-carboxylic acid as fine yellow needles, m. p. 288° (decomp.; sealed tube), undepressed on admixture with an authentic specimen (Cook, Loudon, and Steel, future communication). When crystallised from water the acid formed a *monohydrate*, yellow prisms, m. p. 222—225° (Found : C, 52.1; H, 4.4. C<sub>8</sub>H<sub>6</sub>O<sub>4</sub>·H<sub>2</sub>O requires C, 52.2; H, 4.3%). Treatment of the acid with ethereal diazomethane gave the corresponding methyl ether methyl ester which crystallised from benzene as fine white needles; m. p. and mixed m. p. 184.5°.

(b) A mixture of tropolone (100 mg.), potassium hydroxide (300 mg.), ethanol (0.5 c.c.), water (0.5 c.c.), and carbon tetrachloride (100 mg.) was heated at 100° in a sealed tube for 16 hours. Cooling and acidification followed by continuous ether-extraction and fractional sublimation gave tropolone (60 mg.) and a pale yellow solid subliming at 180° (bath-temp.)/0.4

mm. Crystallisation of this latter from water gave tropolone- $\gamma$ -carboxylic acid hydrate (3 mg.), m. p. and mixed m. p. 222—225°.

*Attempted Reaction with N-Methylformanilide.*—A mixture of tropolone (200 mg.), *N*-methylformanilide (550 mg.), and phosphorus oxychloride (500 mg.) was kept at room temperature for 16 hours. The product was poured into water and extracted with ether. The extract was then shaken out with 1% sodium hydroxide solution; acidification and ether-extraction furnished tropolone (100 mg.). In one experiment evaporation of the alkali-washed extract gave an oil possessing carbonyl activity which gave a 2:4-dinitrophenylhydrazone, scarlet needles, m. p. 206° (from butanol), having the composition of the derivative of a formyltropolone (Found: C, 50.8; H, 3.0.  $C_{14}H_{10}O_6N_4$  requires C, 50.9; H, 3.0%). This result could not be repeated, however.

*Reduction of Tropolone with Lithium Aluminium Hydride.*—A solution of tropolone (900 mg.) in dry ether (5 c.c.) was added to a slurry of lithium aluminium hydride (1 g.) in ether (40 c.c.). The initial yellow precipitate rapidly redissolved. The mixture was heated under reflux for 30 minutes, cooled, and decomposed with ice-cold dilute sulphuric acid. The initial yellow colour of the solution rapidly darkened to deep red; this could not be prevented either by working under nitrogen or carrying out the decomposition with ice alone. Isolation with ether yielded a dark red gum which on distillation at 80—100°/18 mm. gave a pale yellow oil (100 mg.) and a brown resin (600 mg.). The oil afforded a bis-2:4-dinitrophenylhydrazone which, after chromatographic purification (benzene-alumina), crystallised from benzene in red prisms, m. p. 183—185° (Found: C, 47.5; H, 3.35; N, 23.15.  $C_{19}H_{16}O_8N_8$  requires C, 47.1; H, 3.35; N, 23.15%). Light absorption in chloroform: Max. at 3560 ( $\epsilon = 36,500$ ), inflexion at 3960 Å ( $\epsilon = 29,000$ ).

The bis-2:4-dinitrophenylhydrazone of cycloheptane-1:2-dione, after chromatographic purification (benzene-alumina) crystallised from benzene as red needles which contained benzene of crystallisation (Found: C, 53.8; H, 4.4; N, 20.1.  $C_{19}H_{18}O_8N_8 \cdot C_6H_6$  requires C, 53.2; H, 4.3; N, 19.85%). Drying at 140°/18 mm. gave the solvent-free compound, m. p. 213° (Found: C, 47.55; H, 4.1; N, 22.65.  $C_{19}H_{18}O_8N_8$  requires C, 46.9; H, 3.75; N, 23.0%). Light absorption in chloroform: Max. at 3520 ( $\epsilon = 34,000$ ), inflexion at 3900 Å ( $\epsilon = 27,500$ ).

*Reduction of Tropolone Methyl Ether with Lithium Aluminium Hydride.*—A solution of anhydrous tropolone methyl ether (1 g.) was added to lithium aluminium hydride (1 g.) in ether (20 c.c.). After the initial vigorous reaction heating was continued for 30 minutes and the mixture then decomposed with ice. Ether-extraction gave an oil smelling strongly of benzaldehyde. Treatment of the product with excess of ethanolic 2:4-dinitrophenylhydrazine sulphate gave a derivative which was washed and dried. The product (0.9 g.; m. p. ca. 200°) was purified by chromatography (benzene-alumina), yielding benzaldehyde 2:4-dinitrophenylhydrazone, m. p. 236° undepressed on admixture with an authentic sample. The filtrate from the preparation of the derivative was neutralised with ammonia and several times extracted with ether. Evaporation gave a minute amount of yellow oil which did not give a picrate or hydrochloride.

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