Synthetic Experiments in the cyclo*Heptatrienone Series. Part VI.* Further Reactions of 3-Hydroxytropone.*

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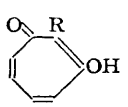
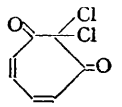
Reaction of 3-hydroxytropone with electrophilic reagents leads to substitution in the 2-position of the ring and 2-iodo-, 2-chloro-, 2-nitro-, 2-amino-, and 2-*p*-tolylazo-derivatives have been prepared. Dichlorination leads to a non-aromatic 1 : 3-diketonic derivative. The Sandmeyer reaction with 2-amino-3-hydroxytropone gives the 2-chloro-compound.

In Part IV (Johns, Johnson, and Tišler, *J.*, 1954, 4604) the preparation of 3-hydroxytropone (I; R = H) was described and it was of interest to compare the reactivity and stability of tropolone with those of 3-hydroxytropone where intramolecular hydrogen bonding between the hydroxyl and the carbonyl group does not exist. It is known that the stability of tropone itself is not as great as that of tropolone although both are derivatives of the aromatic *cyclo*heptatrienylium (tropylium) cation and thus the five-membered hydrogen-bonded ring in tropolone makes a significant contribution to its stability. The absence of intramolecular hydrogen bonding in 3-hydroxytropone has a marked effect on its physical properties (Part IV, *loc. cit.*) for the isomer is less volatile than tropolone, is more acidic, has a considerably higher m. p. (179—180°; tropolone 49°), and is insoluble in non-polar solvents.

The chemical reactions of tropolone, especially electrophilic substitutions and ring contractions to benzenoid compounds, have been studied in detail (review: Johnson, *J.*, 1954, 1331), particularly by Nozoe and his co-workers, but little has been reported so far on similar reactions with tropones lacking the 2-hydroxyl group.



(I)



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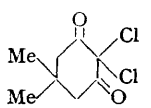


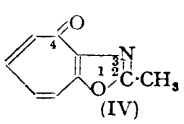
(III)

In 3-hydroxytropone (I; R = H) the combined directive influence of the two oxygen atoms renders the 2-position most favourable for electrophilic attack and it was found that bromination even in the presence of a moderate excess of bromine yielded the 2-bromo-derivative (I; R = Br), the structure of which was proved by *X*-ray examination and by conversion into the known 3-hydroxytropolone (I; R = OH) (Part IV, *loc. cit.*). Iodination of 3-hydroxytropone in acetic acid gave 3-hydroxy-2-iodotropone (I; R = I) although this derivative was not obtained by reaction with iodine in aqueous potassium iodide or from an attempted halogen exchange with the bromo-compound. The introduction of chlorine into a cooled solution of 3-hydroxytropone in acetic acid rapidly gave the colourless 2-chloro-derivative (I; R = Cl) which with diazomethane yielded the corresponding methyl ether. Both of these 2-chlorotropones have been prepared from 7-bromotropolone by Seto (*Sci. Rep. Tôhoku Univ.*, 1953, **37**, 275, 377). A yellow dichloro-compound, $C_7H_4O_2Cl_2$, was isolated as a by-product from the low-temperature chlorination of 3-hydroxytropone and it was the major product when the chlorination was carried out in warm carbon tetrachloride solution. It was also obtained in rather poor yield from the further chlorination of 2-chloro-3-hydroxytropone and reduction of the dichloro-compound with stannous chloride in acetic acid gave a small yield of the original monochloro-derivative. No pure product was isolated from a reduction of the dichloro-compound with zinc and acetic acid. The ultraviolet and infrared spectra indicated that the dichloro-compound no longer contained a tropone ring and the compound is probably represented as (II), 2 : 2-dichloro*cyclo*hepta-4 : 6-diene-1 : 3-dione. It formed a yellow solution in aqueous sodium

* Part V, *J.*, 1955, 309.

hydroxide but was decomposed when the solution was warmed. The formation of (II) is paralleled by the reaction of chlorine with other cyclic β-diketones, *e.g.*, dihydro-5 : 5-dimethylresorcinol gives (III) (Hirst and Macbeth, *J.*, 1922, **121**, 2169), but other attempts to simulate typical β-diketone reactions, *e.g.*, condensation with benzaldehyde, were negative. As with tropolone (Sebe *et al.*, *Proc. Japan Acad.*, 1952, **28**, 282; 1953, **29**, 107, 110) the Diels–Alder addition of maleic anhydride to 3-hydroxytropone did not occur except under forcing conditions necessary to overcome the aromatic character of the ring system. When the reactants were heated together at 100—120° in a sealed tube a dicarboxylic acid was obtained in small yield, which was probably an *exo*-adduct as there was no evidence of lactone formation even after repeated sublimation.

Attempted nucleophilic displacements of the halogen atoms in 2-bromo(or chloro)-3-hydroxytropone by cyanide or thiol groups were unsuccessful, as were experiments designed to bring about further electrophilic substitution, *e.g.*, diazonium coupling, nitration, and bromination. The alkaline ring contractions of 2-bromo-3-hydroxytropone as well as of 3-hydroxytropone itself were discussed in Part IV (*loc. cit.*) but at present 3-hydroxytropolone (I; R = OH) is the only compound of the general structure (I) which gives salicylic acid on alkaline rearrangement. Nitration of 3-hydroxytropone with a cooled mixture of nitric and sulphuric acid gave the pale yellow 2-nitro-derivative (I; R = NO_2). With a nitric–acetic acid mixture, the hydrobromide of 3-hydroxytropone gave the 2-bromo-derivative and from a similar reaction with the free base unchanged material was obtained. Hydrogenation of the nitro-compound in the prseence of Raney nickel yielded 2-amino-3-hydroxytropone (I; R = NH_2) which formed pale yellow needles and gave a crystalline sulphate. Acetylation of the amino-derivative with acetic anhydride gave a compound $C_9H_7O_2N$, probably the substituted oxazole (IV), formed by loss of acetic acid from the expected *ON*-diacetyl derivative. A Sandmeyer reaction on diazotised 2-amino-3-hydroxytropone gave the 2-chloro-compound, identical with that obtained from the direct chlorination of 3-hydroxytropone and thus confirmed the assigned position of the nitro-group in the nitration product. Reaction of 3-hydroxytropone with diazotised *p*-toluidine gave the red 2-*p*-tolylazo-derivative (I; R = *p*-$N_2 \cdot C_6H_4Me$) but an attempt to obtain the 2-amino-compound by hydrogenolysis of the azo-derivative was unsuccessful. No pure substitution products were obtained from the attempted nitrosation, sulphonation (with sulphamic acid), amination (with hydroxylamine), or hydroxylation (with potassium persulphate) of 3-hydroxytropone.


(IV)

Of the substitution products of 3-hydroxytropone which still retain the tropone ring those obtained so far are monosubstituted and have the substituent in the 2-position, except for 7-bromo-3-hydroxytropone (Part IV, *loc. cit.*), prepared by an indirect method, and it is of interest that in the one case, chlorination, where disubstitution of 3-hydroxytropone did occur, the aromatic ring system was destroyed. Orientation of the substitution products, as with the tropolones, by employing the alkaline rearrangement to derivatives of benzoic acid is not so useful in the 3-hydroxytropone series as many side reactions occur (Part IV, *loc. cit.*), and the orientations have been carried out by relating the products to the 2-bromo-derivative, the structure of which is known with certainty. With the exception of halogenation the experimental conditions required for the substitution reactions of 3-hydroxytropone are more critical than in the tropolone series because of the decreased stability of the parent compound and of the products.

Experimental

Ultraviolet spectra were determined in 95% EtOH and infrared spectra on Nujol mulls except where otherwise stated.

3-Hydroxy-2-iodotropone.—3-Hydroxytropone (200 mg.) was suspended in glacial acetic acid (3 c.c.), and a solution of iodine (228 mg., 1·1 mol.) in acetic acid (15 c.c.) added to it. The mixture was heated on the water-bath for 10 min. and, after cooling, water (80 c.c.) was added and the whole kept overnight. The precipitated iodo-compound was separated and crystallised from ethanol, forming brownish needles (170 mg.), m. p. 163—164° (decomp.) (Found: C, 34·3;

H, 2·4; I, 50·8. $C_7H_5O_2I$ requires C, 33·9; H, 2·05; I, 51·2%). Light absorption: max. at 251, 312, 324, 360 mμ (log ε 4·29, 3·69, 3·63, and 3·58 respectively); in 0·1 N-sodium hydroxide: max. at 260, 311, 322, and 365—366 mμ (log ε 4·40, 3·76, 3·69, and 3·54 respectively). The infrared spectrum showed max. at 1637, 1534, 1515, 1410, 1364, 1272, 1258, 1214, 1036, 1015, 862, 835, 793, and 684 cm.$^{-1}$. The product could be sublimed at 140°/0·5 mm. but considerable decomposition ensued.

2-*Chloro*-3-*hydroxytropone and* 2 : 2-*Dichloro*-4 : 6-cyclo*heptadiene*-1 : 3-*dione*.—Chlorine was passed into a cooled (ice) solution of 3-hydroxytropone (195 mg.) in acetic acid (15 c.c.). The precipitate which was obtained at once was separated and crystallised from methanol, as colourless needles (226 mg., 88%), m. p. 210—215° (decomp.) [Seto, *loc. cit.*, gives m. p. 210—215° (decomp.)] (Found: C, 53·4; H, 3·6. Calc. for $C_7H_5O_2Cl$: C, 53·7; H, 3·2%). Light absorption: max. at 213, 254, 260, 274, and 310 mμ (log ε 4·10, 4·50, 4·52, 4·38, and 3·96 respectively); in 0·1N-sodium hydroxide: max. at 260, 270, and 308 mμ (log ε 4·51, 4·46, and 3·83 respectively) with an inflection at 340—354 mμ (log ε 3·40). Infrared spectrum: max. at 1645, 1538, 1527, 1420, 1311, 1282, 1266, 1227, 1049, 1036, 985, 920, 840, 799, 685, and 652 cm.$^{-1}$. A determination on a mull in hexachlorobutadiene showed additional bands at 1468 and 1379 cm.$^{-1}$.

Treatment of 2-chloro-3-hydroxytropone with diazomethane gave 2-chloro-3-methoxytropone which, after sublimation at 100°/0·5 mm. and crystallisation from ether–light petroleum (b. p. 40—60°) formed colourless crystals, m. p. 100—101° (Seto, *loc. cit.*, gives m. p. 102—103°) (Found: C, 56·45; H, 4·4. Calc. for $C_8H_7O_2Cl$: C, 56·3; H, 4·15%). Light absorption: max. at 217, 256, 264, 312, and 324 mμ (log ε 4·08, 4·41, 4·36, 3·69, and 3·65 respectively). The infrared spectrum showed max. at 1642, 1570, 1416, 1247, 1225, 1172, 1149, 1082, 1025, 936, 917, 866, 830, 797, and 789 cm.$^{-1}$. A determination on a hexachlorobutadiene mull showed additional maxima at 1477 and 1453 cm.$^{-1}$.

Evaporation of the mother-liquors from the crystallisation of 2-chloro-3-hydroxytropone gave a solid residue which after sublimation at 75°/0·5 mm. gave a yellow crystalline product, m. p. 83°. Larger quantities (56%) of this material, 2 : 2-*dichloro*cyclo*hepta*-4 : 6-*diene*-1 : 3-*dione*, were obtained together with smaller amounts (23%) of 2-chloro-3-hydroxytropone when 3-hydroxytropone was chlorinated in carbon tetrachloride solution at 50°. The dichloro-compound formed bright yellow plates, m. p. 83°, after crystallisation from ether–light petroleum (b. p. 40—60°) (Found: C, 43·7; H, 2·4. $C_7H_4O_2Cl_2$ requires C, 44·0; H, 2·1%). Light absorption: max. at 286—288 mμ (log ε 3·84). Infrared spectrum: max. at 1704, 1686, 1631, 1595, 1420, 1282, 1198, 1127, 1010, 992, 959, 905, 883, 869, 787, and 726 cm.$^{-1}$. The same compound was also obtained (26%) from the chlorination of 2-chloro-3-hydroxytropone in carbon tetrachloride at 50°. It formed no precipitate with ethanolic silver nitrate and gave no ferric reaction, but liberated iodine from aqueous potassium iodide. The solution in cold aqueous sodium hydroxide was yellow but it rapidly darkened and decomposed on warming. On hydrogenation over platinum, 6·35 mols. of hydrogen were absorbed. Treatment with stannous chloride in glacial acetic acid (cf. Vorländer and Kohlmann, *Annalen*, 1902, **322**, 257) gave a small amount of 2-chloro-3-hydroxytropone.

3-*Hydroxy*-2-*nitrotropone*.—Nitric acid (*d* 1·42; 0·5 c.c.) was added dropwise to a cooled solution of 3-hydroxytropone (0·5 g.) in concentrated sulphuric acid (5 c.c.), and the mixture kept overnight. It was poured on ice (5 g.) and the yellow precipitate separated, dried, and extracted with ether. Concentration of the ethereal solution gave small pale yellow needles, m. p. 258—260° (decomp.) (0·38 g., 56%) (Found: C, 50·4; H, 3·4; N, 8·4. $C_7H_5O_4N$ requires C, 50·3; H, 3·0; N, 8·4%). Light absorption: max. at 213—214, 246, and 298—299 mμ (log ε 4·22, 4·47, and 3·62 respectively) with an inflection at 326—333 mμ (log ε 3·35); in 0·1N-sodium hydroxide: max. at 254 and 291 mμ (log ε 4·50 and 3·70 respectively). Infrared spectrum: max. at 1645, 1603, 1534, 1289, 1266, 1244, 1220, 1070, 1048, 990, 948, 843, 808, 689, and 651 cm.$^{-1}$. A determination on a mull in hexachlorobutadiene also showed bands at 1462 and 1379 cm.$^{-1}$. The *nitro-compound* was very soluble in acetone, soluble in alcohol and acetic acid, sparingly soluble in ether, and insoluble in *cyclo*hexane or light petroleum. It could be sublimed at 190°/0·5 mm. but the process was attended by considerable decomposition.

2-*Amino*-3-*hydroxytropone*.—An ethanolic solution of the foregoing nitro-compound (167 mg.) was hydrogenated in the presence of Raney nickel, and the reaction stopped after the absorption of the theoretical ($NO_2 \longrightarrow NH_2$) volume of hydrogen. The catalyst was separated, the solvent evaporated, and the residue made just alkaline with 2N-sodium hydroxide. After separation of any solid material the red solution was acidified with acetic acid, a yellow precipitate being obtained which was crystallised from water to give small yellow needles of *base*

(112 mg., 82%), m. p. 228° (decomp.) (Found : C, 61·05; H, 4·95; N, 10·3. $C_7H_7O_2N$ requires C, 61·3; H, 5·15; N, 10·2%). Light absorption : max. at 248, 262, 272, 336, and 409 mμ (log ε 4·48, 4·26, 4·28, 4·13, and 4·08 respectively) ; in 0·1N-sodium hydroxide : max. at 216, 260, 277, 342, and 413 mμ (log ε 4·13, 4·46, 4·32, 4·07, and 3·94 respectively). The infrared spectrum showed max. at 3448, 3300, 1595, 1536, 1499, 1399, 1274, 1235, 1198, 1156, 847, 784, and 763 cm.$^{-1}$ An additional band at 2915 cm.$^{-1}$ was revealed when the determination was carried out on a mull in hexachlorobutadiene. The amine gave a purple ferric reaction, and formed a crystalline *sulphate*, m. p. 247° (decomp.) (from water) (Found : C, 45·2; H, 4·4. $C_{14}H_{16}O_8N_2S$ requires C, 45·2; H, 4·3%). Light absorption : max. at 249, 272, 335, 386, and 410 mμ (log ε 4·77, 4·41, 4·31, 4·19, and 4·18 respectively), with an inflection at 260—264 mμ (log ε 4·48). Infrared spectrum : max. at 3413, 3175, 2469, 1610, 1585, 1529, 1316, 1294, 1274, 1227, 1064, 847, 782, and 728 cm.$^{-1}$. A determination on a mull in hexachlorobutadiene showed additional max. at 2899, 2740, 1456, and 1379 cm.$^{-1}$.

Sandmeyer Reaction with 2-Amino-3-hydroxytropone.—A diazotised solution of 2-amino-3-hydroxytropone sulphate (184 mg.) was added dropwise to an ice-cold solution of cuprous chloride (100 mg.) in hydrochloric acid. After being stirred at 0° for 10 min. the product was heated to 30—35° on the water-bath. The precipitate which was obtained was separated and crystallised from methanol, as colourless needles (78 mg., 64%), m. p. 210—212° (decomp.), not depressed on admixture with an authentic sample of 2-chloro-3-hydroxytropone.

Acetylation of 2-Amino-3-hydroxytropone.—The base (100 mg.) was heated under reflux with fused sodium acetate (0·5 g.) and acetic anhydride (5 c.c.) for 1 hr. The product was cooled, diluted with water (50 c.c.), and continuously extracted with ether for 2 days. Removal of the ether from the dried extract gave a residue which was sublimed at 140°/0·5 mm. to give colourless crystals (32 mg.), m. p. 153°, of *2-methyl-4-oxo*cyclo*heptaoxazole* (Found : C, 66·7; H, 4·2; N, 8·75. $C_9H_7O_2N$ requires C, 67·1; H, 4·4; N, 8·7%). Light absorption : max. at 228, 307, and 334 mμ (log. ε 4·35, 3·89, and 3·87 respectively) with an inflection at 344—347 mμ (log ε 3·80). The infrared spectrum showed max. at 1626, 1590, 1575, 1527, 1272, 1250, 1212, 1151, 1078, 1063, 1036, 964, 946, 875, 847, 813, 777, 719, and 682 cm.$^{-1}$. A small quantity of a second substance, m. p. 139°, was isolated from the crystallisation but the amount obtained was insufficient to permit identification.

3-Hydroxy-2-p-tolylazotropone.—*p*-Toluidine (300 mg.) was diazotised and added to an alkaline solution of 3-hydroxytropone (370 mg.) and the mixture kept for ½ hr. It was then acidified with glacial acetic acid, and the solid separated. For purification it was dissolved in a small volume of cold 3N-sodium hydroxide, the solution filtered, and the filtrate diluted with water (5 c.c.) and acidified with 3N-hydrochloric acid. The *azo-compound* was obtained as small red needles (127 mg.), m. p. 154°. The purification was repeated before analysis (Found : N, 11·6. $C_{14}H_{12}O_2N_2$ requires N, 11·7%).

Reaction of 3-Hydroxytropone with Maleic Anhydride.—3-Hydroxytropone (0·122 g.) and freshly distilled maleic anhydride (0·1 g.) were heated together in a sealed tube at 100—120° for 6 hr. The product was dissolved as far as possible in 3N-sodium hydrogen carbonate solution, and the neutral material extracted into ether. The aqueous layer was acidified and continuously extracted with ether for 2 days. The solvent was removed from the dried ethereal extract, and the solid residue sublimed twice at 170°/0·5 mm., being obtained as a colourless solid (28 mg., 12%) (Found : C, 55·5; H, 4·0. $C_{11}H_{10}O_6$ requires C, 55·5; H, 4·2%).

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