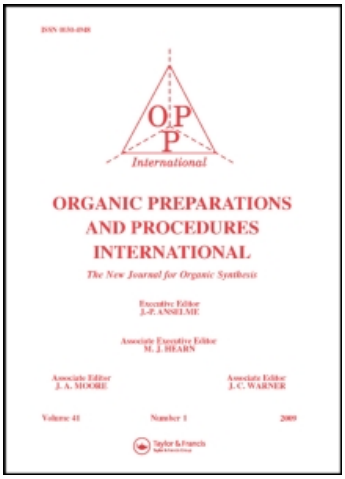

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A CONVENIENT SYNTHESIS OF 3-HYDROXYTROPONE

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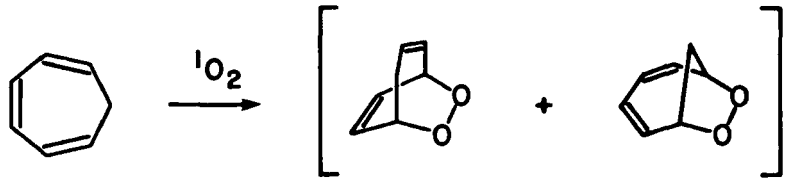
Several synthetic routes to 3-hydroxytropone (β-tropolone) (5) have been reported, but none appears to offer convenient, reliable access to this interesting compound.[1] The first syntheses involved reactions of activated arenes, such as resorcinol dimethyl ether or veratrole, with ethyl diazoacetate.[2] Several further steps were required to adjust the functionality and oxidation level of the ring-expanded products, and the overall yields were low. An alternative route from 3,4,5-trimethoxybenzoic acid proceeded *via* a Birch reduction to a 1,4-dihydroarene and reduction of the carboxyl group followed by ring expansion by solvolysis of the tosylate of the resulting homo-allylic alcohol.[3] Oxidation and demethylation of the mixture of 1,3-dimethoxycycloheptatrienes formed was reported to give 3-hydroxytropone (5) in 28% average overall yield.[3] This route involves six steps, for some of which the reported mass yields exceeded 100%. Finally, a short, potentially attractive route utilized dihalocarbene addition to the dihydroarenes formed by Birch reduction of 2-methoxy-,[4] 2-isopropoxy-[5] or 2-(2'-tetrahydropyranyloxy)-anisole[5] followed by ring expansion with concomitant dehydrohalogenation and dealkylation. However, repeated attempts by ourselves and others[1] have failed to reproduce the yields quoted for this route.

We have therefore developed a short and reliable synthesis of 3-hydroxytropone (5) starting from cheap, readily available cyclohepta-1,3,5-triene (1). Photooxygenation of the triene 1 in carbon tetrachloride with singlet oxygen as described by Adam and Balci[6] gives a mixture composed primarily of approximately equal amounts of the [4+2]- and [6+2]-adduct endoperoxides 2 and 3. Direct methanolysis of the mixture isomerizes the latter adduct 3 to the ketol 4,[7] while adduct 2 remains unchanged.[7,8] The ketol 4 readily dehydrates to tropone,[7] but can be isolated from the mixture by flash chromatography on silica gel in 25% overall yield from cycloheptatriene. The ketol 4 is also available directly from sensitized photooxygenation of cycloheptatriene in methanol.[8]



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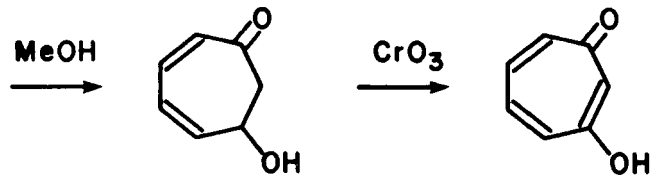

4 5

Oxidation of the allylic alcohol function of the ketol 4 with dichlorodicyanobenzoquinone, chloranil or manganese dioxide was slow and accompanied by dehydration to tropone and by decomposition. Pyridine dichromate in dimethylformamide effected smooth oxidation, but isolation of the product from the polar solvent proved difficult. However, oxidation

of the ketol 4 with Jones' reagent furnished the required 3-hydroxytropone (5) in 80% yield.

EXPERIMENTAL

^{1}H-NMR spectra were determined on Varian HA-100 and Jeol JNM-MH-100 spectrometers, and mass spectra were run on a GEC-AEI MS 902 instrument. Melting points were taken on a Kofler hot-stage apparatus and are uncorrected.

6-Hydroxycyclohepta-2,4-dien-1-one (4).- Singlet oxygen addition to cyclohepta-1,3,5-triene (1) (7.36 g, 80 mmol) was carried out as described by Adam and Balci.[7] After evaporation of the solvent the crude product mixture was dissolved in methanol (80 ml) and kept at room temperature for 2 h.[7] Removal of the solvent and flash chromatography of the product on silica gel in methanol/dichloromethane (5:95) gave the ketol 4 as a pale yellow liquid (2.49 g, 25%).

^{1}H-NMR ($CDCl_3$): δ 5.8 - 6.8 (m, 4H, =CH), 4.68 (bd, 1H, J = 13 Hz, CHOH), 3.08 and 2.78 ppm (dd, 1H, J = 16, 13 Hz and dm, 1H, J = 16 Hz, CH_2).

These values, with the exception of δ 3.08, agree with the data of Asao et al.,[8] but differ from those cited by Adam and Balci.[6]

3-Hydroxytropone (5).- To the ketol 4 (330 mg, 2.7 mmol) in acetone (10 ml) was added Jones' reagent (2.7 M, 1.2 ml) dropwise with stirring at 0°. After 15 min. excess of reagent was destroyed with isopropanol. The reaction mixture was diluted with water (10 ml), the organic solvent evaporated and the cooled residual aqueous solution adjusted to pH 4 with aqueous 2N sodium hydroxide. Inorganic salts were removed by centrifugation and washed successively with water and methanol. After removal of the methanol, the washings were combined with the aqueous supernatant, saturated with sodium chloride and continuously extracted with ethyl acetate. Evaporation and recrystallization from ethyl

acetate gave 3-hydroxytropone (5) (260 mg, 80%), mp. 179-181° (dec.), lit.[2] mp. 179-180° (dec.), lit.[3] mp. 183-183.5°; the spectral data were in accord with those of the literature.[2,3]

^{1}H-NMR (CD_3OD): δ 7.04 (m, 4H, H-4-7), 6.58 ppm (m, 1H, H-2); MS (70 eV) *m/e* (relative intensity): 122 (M^+, 67), 94 (M^+ - CO, 100), 66 (M^+ - 2CO, 60).

REFERENCES

1. F. Pietra, Chem. Revs., 73, 293 (1973).
2. R. B. Johns, A. W. Johnson and M. Tisler, J. Chem. Soc., 4605 (1954).
3. O. L. Chapman and P. Fitton, J. Am. Chem. Soc., 83, 1005 (1961); 85, 41 (1963).
4. A. J. Birch and J. M. H. Graves, Proc. Chem. Soc., 282 (1962).
5. A. J. Birch and R. Keeton, Aust. J. Chem., 24, 331 (1971).
6. W. Adam and M. Balci, Angew. Chem. Int. Ed. Engl., 17, 954 (1978); J. Am. Chem. Soc., 101, 7537 (1979).
7. W. Adam and M. Balci, ibid., 101, 7542 (1979).
8. T. Asao, M. Yagihara and Y. Kitahara, Bull. Chem. Soc. Japan, 51, 2131 (1978).

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