Aspects of the Chemistry of Methyl 3-Hydroxycyclohexa-1,5-diene-1-carboxylate: a Methyl Benzoate Hydrate

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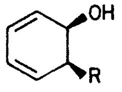
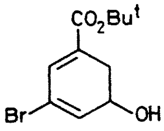
Summary Methyl 3-hydroxycyclohexa-1,5-diene-1-carboxylate (**10**) is prepared in two steps from methyl cyclohexa-2,5-diene-1-carboxylate (**7**), and its dehydration, hydrolysis, acetylation, reduction, and epoxidation are reported, together with its Diels–Alder reaction with 4-phenyl-1,2,4-triazoline-3,5-dione.



(1) R = H
(2) R = Me
(3) R = OH



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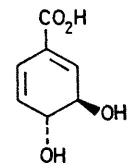

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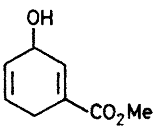


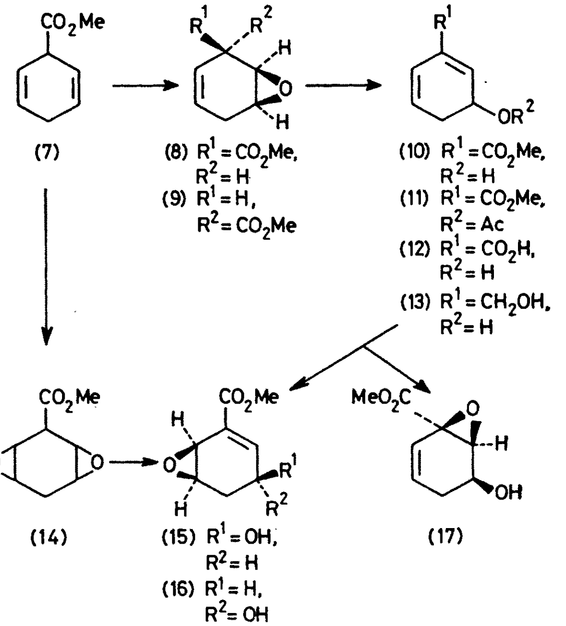
(6)

The arene hydrates are an interesting group of compounds which have been known for some time. Examples include the rather unstable cyclohexa-2,4-dienol (**1**),[1] its *cis*-6-methyl analogue (**2**),[2] and cyclohexa-3,5-diene-*cis*-1,2-diol (**3**).[3] More recently the hydroxy-ester, t-butyl 5-bromo-3-hydroxycyclohexa-4,6-diene-1-carboxylate (**4**) was reported,[4] and syntheses have been developed to 3-hydroxycyclohexa-1,5-diene-1-carboxylic acid (**12**),[5] its *trans*-3,4-dihydroxy analogue (**5**),[5,6] and to the non-conjugated ester, methyl 3-hydroxycyclohexa-1,4-diene-1-carboxylate (**6**).[7] However, despite the unusual structures of these arene hydrates, their chemistry, apart from dehydration to the corresponding aromatic compound, has not been widely studied. We report a new synthesis of the 3-hydroxycyclohexa-1,5-diene-1-carboxylate system, together with some aspects of its chemistry.

Epoxidation of methyl cyclohexa-2,5-diene-1-carboxylate (**7**) using *m*-chloroperoxybenzoic acid, gave a mixture of the *cis*- and *trans*-monoepoxides (**8**) and (**9**), in the ratio 35 : 65, respectively,† together with a small amount of unchanged starting material, and some bis-epoxides.‡ From this mixture the monoepoxides could be isolated by distillation (60%; b.p. 61—70 °C at 0·25 mmHg). The crude monoepoxide mixture was quantitatively isomerized to methyl 3-hydroxycyclohexa-1,5-diene-1-carboxylate (**10**) by treatment with triethylamine in chloroform (10 min; 20 °C), and a sample of the product was purified by column chromatography for characterization. The methyl benzoate hydrate (**10**) could be distilled, b.p. 82—84 °C at 0·02 mmHg, but the distillation was accompanied by some decomposition. The crude product was sufficiently pure to be used in all subsequent investigations.

Treatment of the methyl benzoate hydrate (**10**) with methanol and concentrated hydrochloric acid (2:1) rapidly gave methyl benzoate (5 min; 20 °C), acetylation with acetic anhydride in pyridine–ether gave the acetate (**11**), and hydrolysis (KOH, dioxan–water; 30 min, 20 °C, acidify to pH 6) gave the crystalline hydroxy-acid (**12**) (m.p. 89 °C).[5] However, preliminary attempts to reduce the methyl benzoate hydrate (**10**) to 3-hydroxymethylcyclohexa-2,4-dienol (**13**) using di-isobutylaluminium hydride have not been too promising. The ^{1}H n.m.r. spectrum of the crude product indicates the presence of the desired benzyl alcohol hydrate (**13**), but attempts to isolate a pure sample of this compound have been thwarted by accompanying dehydration to benzyl alcohol. Attempts to trap (**13**) *via* a Diels–Alder reaction with 4-phenyl-1,2,4-triazoline-3,5-dione were unsuccessful; benzyl alcohol was the only isolable product. However, the methyl benzoate hydrate, (**10**) did undergo a Diels–Alder reaction with 4-phenyl-1,2,4-triazoline-3,5-dione to give a mixture of the adducts (**18**) in good yield.

Epoxidation of methyl benzoate hydrate (**10**) using *m*-chloroperoxybenzoic acid gave the *cis*-epoxide (**15**), and a mixture of the *trans*-epoxide (**16**) and *cis*-epoxide (**17**), which could not be separated, in the ratio of 50:15:35, respectively. Epoxidation using t-butyl hydroperoxide and $Mo(CO)_6$[8] gave the same epoxides, but in a slightly different ratio, (**15**):(**16**):(**17**) = 65:20:15. The *cis*- and *trans*-epoxides (**15**) and (**16**) were also prepared by treatment of methyl cyclohexa-2,5-diene-1-carboxylate (**7**) with excess of *m*-chloroperoxybenzoic acid to give a mixture of the bis-epoxides (**14**) which were isomerized using triethylamine in chloroform. In this way, a mixture of epoxides (**15**) and (**16**) was obtained in the ratio 30:70, respectively. Treatment of the methyl benzoate hydrate (**10**), or the mixture of epoxides (**15**) and (**16**), with excess of *m*-chloroperoxybenzoic acid, gave the unchanged *cis*-epoxide (**15**), together with a low yield of a single hydroxy-bis-epoxide identified as (**19**).



(**7**)

(**8**) $R^1 = CO_2Me$, $R^2 = H$
(**9**) $R^1 = H$, $R^2 = CO_2Me$

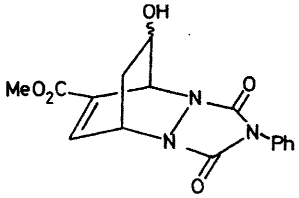
(**10**) $R^1 = CO_2Me$, $R^2 = H$
(**11**) $R^1 = CO_2Me$, $R^2 = Ac$
(**12**) $R^1 = CO_2H$, $R^2 = H$
(**13**) $R^1 = CH_2OH$, $R^2 = H$

(**14**)

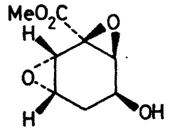
(**15**) $R^1 = OH$, $R^2 = H$
(**16**) $R^1 = H$, $R^2 = OH$

(**17**)

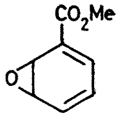
The structures assigned to these epoxides were consistent with their spectroscopic data. Configurations were assigned to the epoxides (**15**) and (**16**) on the basis that epoxidation of the methyl benzoate hydrate (**10**) would be expected to give more of the *cis*-isomer (**15**), whereas bis-epoxidation of the diene (**7**) would be expected to give more of the *trans*-bis-epoxide, and hence more of the *trans*-epoxide (**16**) after isomerization. Moreover the isomer to which we have assigned the *cis*-configuration (**15**) is capable of internal hydrogen bonding, and is the faster moving on t.l.c. The *cis*-configuration was assigned to the third monoepoxide (**17**), and the configuration shown assigned to the hydroxy-bis-epoxide (**19**), on the basis of the well known *cis*-directing effect of an allylic hydroxy group in epoxidation reactions. Attempts to dehydrate the hydroxy-epoxides (**15**) and (**16**) to the benzene oxide (**20**)[9] by treatment of the corresponding mesylates with base have so far been unsuccessful; only aromatic products have been obtained.



(**18**)



(**19**)



(**20**)

We thank the Malaysian Government for a grant (to (H.M.S.).

(*Received*, 22*nd September* 1978; *Com.* 1023.)

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† Stereochemistry confirmed by hydrogenation to the known saturated epoxides, (see S. G. Davies and G. H. Witham, *J.C.S. Perkin I*, 1977, 572; S. A. Cerefice and E. K. Fields, *J. Org. Chem.*, 1976, **41**, 355).

‡ Satisfactory spectroscopic and analytical or accurate mass data have been obtained for all new compounds.

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