Aromatisation of Some Cyclohexadienes through Methoxycarbonyl Migration or Alkyl Elimination

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Treatment of methyl 1,2-dimethyl- or 1-ethyl-2-methyl-cyclohexa-2,5-diene-1-carboxylate with triphenylmethyl tetrafluoroborate caused aromatisation to the methyl 2,3-dialkylbenzoates by migration of the methoxycarbonyl group. The corresponding 1-isopropyl- and 1-benzyl-cyclohexadienes gave methyl *o*-toluate under the same conditions.

MIGRATIONS of alkoxycarbonyl groups have been reviewed,[1] and a small number of ester shifts have been reported [2-8] subsequently. We now describe a new carbonium ion rearrangement where an ester group migrates in preference to a methyl or ethyl group. In contrast, if the alkyl group is isopropyl or benzyl, the ester group does not migrate and the alkyl group is eliminated. The cyclohexadienes (1)—(4) were prepared from *o*-toluic acid by successive Birch reduction,[9] alkylation to give the acids (5)—(8), and esterification with diazomethane.

Treatment of methyl 1,2-dimethylcyclohexa-2,5-diene-1-carboxylate (1) with triphenylmethyl tetrafluoroborate in dry acetonitrile at room temperature gave only methyl 2,3-dimethylbenzoate (11). This compound was identified unambiguously by its n.m.r. spectrum, which showed non-equivalent aromatic methyl groups and three strongly interacting aromatic protons, one of which gave a signal at lower field. In a similar way the ethylcyclohexadiene ester (2) gave both benzoates (12) and (13). The 100 MHz but not the 60 MHz n.m.r. spectrum of the mixture showed resolved quartets due to the

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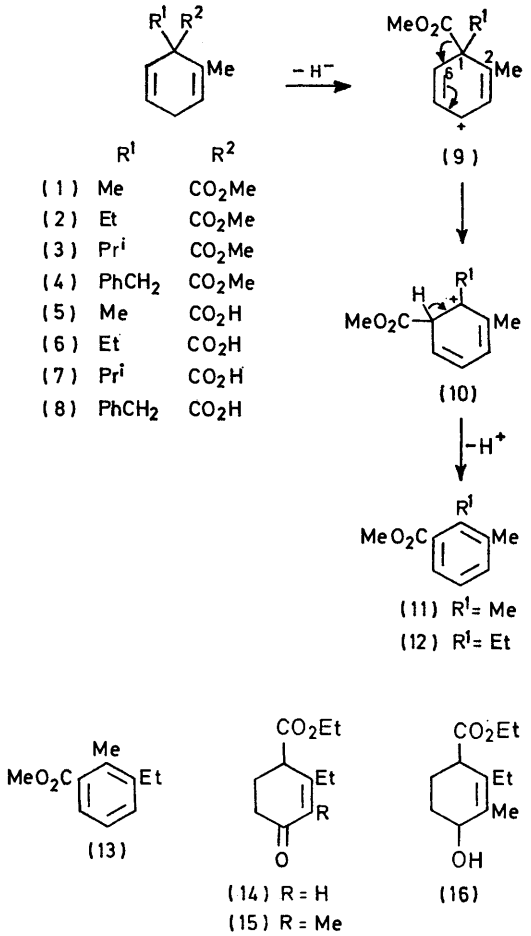
methylene groups of the constituents, and comparison with the spectra of the authentic esters (12) and (13) confirmed the results of g.l.c. analyses, which suggested that these compounds were the only constituents of the mixture and were present in the ratio 2 : 1.



The ester migrations presumably occur when the triphenylmethyl tetrafluoroborate abstracts a hydride ion [10] to yield the carbonium ion (9). A 1,2-ester shift then occurs as indicated and is followed by the loss of a proton to give the highly stabilised aromatic product. Some of the ester (11) could be formed by successive shifts of the ester group to positions 2 and 3, as it has been shown that the ester group of the ethyl analogue (2) moves in both directions. On the assumptions that intermediates of type (10) rapidly lose a proton to give the aromatic ester [*e.g.* (11)] and do not isomerise competitively back to structures such as (9), and that the ester group of (9) will have an equal probability of moving in either direction, the expected ratio of the esters (12) to (13) would be about 2 : 1. This is close to that observed and shows that encouragement to the ester group of methyl 1,2-dimethylcyclohexa-2,5-diene-1-carboxylate (2) to move to position 2, because of enhanced charge localisation caused by the methyl group, must be roughly balanced by the steric effect of the same group.

The only detectable product from triphenylmethyl tetrafluoroborate and the esters (3) and (4) was methyl *o*-toluate, elimination of the relatively stable isopropyl and benzyl cations from the postulated intermediate (9) presumably being easier than migration of these groups or the ester group. Attempts to rearrange the 2-methoxy-analogue of the cyclohexadiene (1) by proton removal caused only conjugation of the double bonds, or aromatisation by elimination of the ester group to give 2-methoxytoluene.[11]

Authentic methyl 2-ethyl-3-methylbenzoate (12) was prepared by well known procedures from 2-bromoethylbenzene involving the Tiffeneau reaction.[12] The 3-ethyl-2-methyl isomer (13) was synthesised from ethyl propionylacetate, which was more easily obtained than the corresponding methyl ester. Michael addition to methyl vinyl ketone, followed by cyclisation with piperidine–acetic acid, gave the ketone (14); sodium hydroxide or piperidine alone is reported [13] to cause cyclisation in the alternative mode. Alkylation, as for [14] Hagemann's ester, gave the ketone (15). Reduction with sodium borohydride yielded the alcohol (16), which was dehydrated and aromatised by hot palladised charcoal to the ethyl ester corresponding to the benzoate (12); attempted dehydration by oxalic acid in toluene followed by aromatisation was unsuccessful. Alkaline hydrolysis and treatment with diazomethane then gave methyl 2-ethyl-3-methylbenzoate (12).

EXPERIMENTAL

The instruments used have been described previously.[15] N.m.r. data for compounds (1)—(4), (14)—(16), 3-ethyl-2-methyl-benzyl alcohol and -benzoic acid, and 2-ethyl-3-methylbenzoic acid; mass spectral data for compounds (2), (12)—(15), and ethyl 5-oxo-2-propionylhexanoate; and analytical data for new compounds are available in Supplementary Publication No. SUP 21127 (5 pp.).†

General Method for the Preparation of 1,2-Disubstituted Cyclohexa-2,5-diene-1-carboxylic Acids.—*o*-Toluic acid (10 g, 0·074 mol) was dissolved in freshly distilled liquid ammonia (500 ml) kept at −70° by an acetone–solid carbon dioxide bath. Small pieces of lithium (1·41 g, 0·2 mol usually needed) were added to the stirred solution until it remained blue. The alkyl halide (0·35 mol) was added dropwise over 30 min, at which point the colour changed from blue through yellow to white. Stirring was continued at −70° for 15 min. The ammonia was allowed to evaporate slowly overnight. The solid residue was acidified with aqueous hydrochloric acid (10%) and extracted with ether. Evapor-

† For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1973, Index issue.

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ation of the washed and dried extracts gave the cyclohexadiene-1-carboxylic acid, obtained as prisms from light petroleum (charcoal). The methyl esters were obtained with diazomethane and the results are given in Table 1.

Reactions of Triphenylmethyl Tetrafluoroborate with Methyl 1,2-Dialkylcyclohexa-2,5-diene-1-carboxylates.— Triphenylmethyl fluoroborate [16] (3 g, 0·009 mol) was dissolved in acetonitrile (30 ml; distilled from P_2O_5). The ester (0·009 mol) was added and the mixture stirred at room temperature until t.l.c. showed the absence of the original ester. Water (20 ml) was added and the acetonitrile removed. The solid obtained was filtered off and recrystallised from ethanol to give triphenylmethane (*ca.* 1·5 g, 68%), m.p. 92—94° (lit.,[17] 94°). The original filtrate was extracted with ether; distillation of the washed and dried extracts gave the esters; the results are shown in Table 2. Alkaline hydrolysis of methyl 2,3-dimethylbenzoate gave the corresponding acid, m.p. and mixed m.p. with an authentic specimen 144—146° (lit.,[17] 144°).

TABLE 1

Preparation of the cyclohexadiene esters from *o*-toluic acid

Alkyl halide	Product	% Yield	M.p. (°C)	Lit. m.p. (°C) [9]	Ester	% Yield	B.p. (°C) [mmHg]
MeI	(5)	73	72—75	75·5—76·5	(1)	84	90 [15]
EtBr	(6)	66	64—67		(2)	80	92—98 [15]
Pr^iCl	(7) [a]	59	85—96	101—102·5	(3) [a]	78	59—64 [0·1]
$PhCH_2Br$	(8)	51	125—127		(4)	81	130—139 [2]

[a] N.m.r. spectrum shows no trace of resonances at τ 6·5 which would be due to the 1-H of non-alkylated hexadiene.

TABLE 2

Aromatisation of the cyclohexadiene esters

Ester aromatised	Product	% Yield	B.p. (°C) [mmHg]
(1)	(11)	33	48—50 [0·15]
(2)	(12) + (13) *	44	63—70 [0·25]
(3)	Methyl *o*-toluate	25	44—46 [0·3]
(4)	Methyl *o*-toluate	20	44—46 [0·3]

* G.l.c. in methylene chloride on a 15% PEGS column at 145° with a flow rate of 40 ml min^{-1} separated the product into two components (2 : 1). Comparison with authentic samples showed these to be methyl 2-ethyl-3-methylbenzoate (retention time 11 min; major component) and methyl 3-ethyl-2-methylbenzoate (14·2 min; minor component).

3-Ethyl-2-methylbenzoic Acid.—Paraformaldehyde (4 g) was added to the Grignard reagent formed from 1-bromo-2-ethylbenzene (15 g) and magnesium (1·3 g) in dry ether (15 ml); refluxing overnight and work-up in the usual way gave 2-ethylbenzyl alcohol (6·7 g, 61%) as a liquid, b.p. 115° at 6 mmHg, n_D^{19} 1·5329 (lit.,[18] b.p. 117—120° at 16 mmHg, n_D^{20} 1·5355).

This alcohol with thionyl chloride gave [19] 2-ethylbenzyl chloride (81%), which was washed (aq. $NaHCO_3$, H_2O) and dried before distillation; b.p. 88° at 7 mmHg, n_D^{11} 1·5349 (lit.,[19] b.p. 105° at 20 mmHg).

This chloride (5·0 g), by the procedure used for 1-bromo-2-ethylbenzene, gave 3-ethyl-2-methylbenzyl alcohol as an oil (2 g, 44%), b.p. 120—140° at 10 mmHg, containing a small amount of impurity (n.m.r.). This alcohol (2 g), without further purification, was oxidised by dropwise addition of aqueous chromic–sulphuric acid [20] with stirring until the solution acquired an orange tint. Stirring was continued for 1 h; extraction with ether, washing, drying, and evaporation gave crude 3-ethyl-2-methylbenzaldehyde (1 g).

The crude aldehyde (0·7 g) was stirred at 10° while potassium permanganate (1 g) in water (20 ml) was added dropwise.[21] After 1 h, aqueous 5% sodium hydrogen sulphite was added, and addition of hydrochloric acid then precipitated 3-ethyl-2-methylbenzoic acid, obtained as prisms (from light petroleum) (0·22 g), m.p. 99—101°.

Ethyl 5-Oxo-2-propionylhexanoate.—Ethyl propionylacetate [22] (25 g) was added to sodium methoxide [from sodium (0·06 g) in methanol (10 ml)]. Dried [23] methyl vinyl ketone (12·58 g) was then added and the mixture worked up by Begbie and Golding's procedure [24] to give ethyl 5-oxo-2-propionylhexanoate as a pale yellow liquid (17·6 g, 43%), b.p. 108—112° at 0·5 mmHg (lit.,[13] b.p. 117° at 0·5 mmHg).

Ethyl 2-Ethyl-4-oxocyclohex-2-ene-1-carboxylate (14).—Ethyl 5-oxo-2-propionylhexanoate (12 g) was refluxed for 1 h with methanol (18 ml), water (2 ml), acetic acid (0·5 g), and pyrrolidine (0·6 g). The solvent was removed *in vacuo* and the residue, in ether, was washed (1% HCl, aq. $NaHCO_3$, H_2O) and dried. Distillation gave the ester (14) as a pale yellow liquid (8·27 g, 75%), b.p. 83—86° at 0·35 mmHg, n_D^{13} 1·4801.

Ethyl 2-Ethyl-3-methyl-4-oxocyclohexene-1-carboxylate (15).—Sodium (0·7 g) was dissolved in dry ethanol (20 ml) and ethyl 2-ethyl-4-oxocyclohex-2-ene-1-carboxylate (6 g) in dry ethanol (15 ml) was added dropwise. A red colour developed. Methyl iodide (4 g) was added dropwise with stirring, the mixture was refluxed for 3 h, and the bulk of the ethanol was evaporated off. Water was added and distillation of the washed and dried ether extracts gave the *ester* (15) as a pale yellow liquid (4·86 g, 82·5%), b.p. 88—90° at 0·3 mmHg, n_D^{19} 1·4840.

Ethyl 2-Ethyl-4-hydroxy-3-methylcyclohex-2-ene-1-carboxylate (16).—Ethyl 2-ethyl-3-methyl-4-oxocyclohex-2-ene-1-carboxylate (4·86 g) was stirred with sodium borohydride (0·88 g) in ethanol (35 ml) for 21 h. Removal of ethanol and the usual work-up gave the *ester* (16) (4·7 g, 80%) as a liquid, b.p. 94—96° at 0·25 mmHg, n_D^{19} 1·4810.

2-Ethyl-3-methylbenzoic Acid.—Ethyl 2-ethyl-4-hydroxy-3-methylcyclohex-2-ene-1-carboxylate (2·19 g) was heated with palladium–charcoal (0·5 g). Water formed at 170°

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and some gas was given off. Further heating increased the rate of gas evolution (measured by collection over water) and the temperature was maintained (250°) so that this was rapid. After 1½ h temperature increase caused no further gas evolution and the flask was cooled. Extraction of the residue with ether gave an oil which was left overnight with sodium hydroxide (3 g) in aqueous ethanol (15 ml). After removal of ethanol and addition of water a small amount of organic material could be extracted with ether. Acidification of the aqueous layer deposited white crystals of *2-ethyl-3-methylbenzoic acid*, which formed prisms (from light petroleum) (0·45 g, 25%), m.p. 101—103°, converted into the ester with diazomethane.

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