The Attempted Preparation of Optically Active βγ-Dideuterobutyrophenone.

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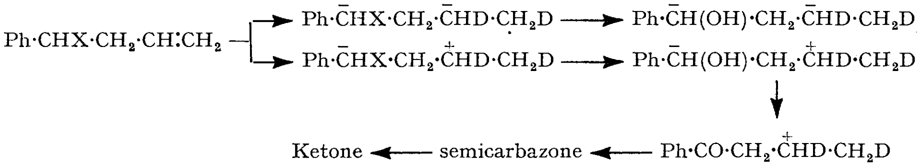
(—)-α-Allylbenzyl hydrogen 3-nitrophthalate was reduced with deuterium in the presence of platinum. Crystallisation of the resulting dideutero-compound, followed by hydrolysis and oxidation, gave βγ-dideuterobutyrophenone, which after purification through the semicarbazone, was optically inactive within the limits of visual accuracy.

Coppock, Kenyon, and Partridge (*J.*, 1938, 1069) attempted to obtain optically active αβ-dideuteropropiophenone by reducing (—)-α-phenylallyl alcohol with deuterium to (+)-2 : 3-dideutero-1-phenylpropanol, but the purified ketone eventually obtained after oxidation was optically inactive. Later, Eliel (*J. Amer. Chem. Soc.*, 1949, **71**, 3970) obtained (—)-1′-deuteroethylbenzene by the reduction of (—)-1′-chloroethylbenzene with lithium aluminium deuteride, and optically active 2 : 3-dideutero-*trans*-menthane (Alexander and Pinkus, *ibid.*, p. 1786) and 3-deutero-*trans*-*p*-menthane (Alexander, *ibid.*, 1950, **72**, 3796) have also been prepared. The following reactions, similar to those of Coppock, Kenyon, and Partridge (*loc. cit.*), were therefore attempted with a compound not containing a keto-group adjacent to the asymmetric centre:



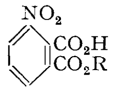
$$\mathrm{Ph{\cdot}CHX{\cdot}CH_2{\cdot}CH{:}CH_2} \begin{cases} \longrightarrow \mathrm{Ph{\cdot}\overset{-}{C}HX{\cdot}CH_2{\cdot}\overset{-}{C}HD{\cdot}CH_2D} \longrightarrow \mathrm{Ph{\cdot}\overset{-}{C}H(OH){\cdot}CH_2{\cdot}\overset{-}{C}HD{\cdot}CH_2D} \\ \longrightarrow \mathrm{Ph{\cdot}\overset{-}{C}HX{\cdot}CH_2{\cdot}\overset{+}{C}HD{\cdot}CH_2D} \longrightarrow \mathrm{Ph{\cdot}\overset{-}{C}H(OH){\cdot}CH_2{\cdot}\overset{+}{C}HD{\cdot}CH_2D} \end{cases}$$

$$\downarrow$$

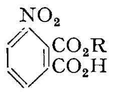
$$\text{Ketone} \longleftarrow \text{semicarbazone} \longleftarrow \mathrm{Ph{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{C}HD{\cdot}CH_2D}$$

[X = $NO_2{\cdot}C_6H_3(CO_2H){\cdot}CO{\cdot}O{\cdot}$]

α-Allylbenzyl alcohol (Klimenko, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 212) was converted into the hydrogen 3-nitrophthalate, separable by chloroform into isomeric forms. Dissociation-constant measurements showed the higher-melting isomer to be the stronger acid, from which the annexed structures (R = $CH_2{:}CH{\cdot}CH_2{\cdot}CHPh{\cdot}$) may be inferred (cf. Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons Ltd., London, 1953, p. 739 *et seq.*). The (—)-hydrogen 3-nitrophthalate was reduced by deuterium in the presence of platinum, and the product recrystallised fourteen times from benzene–light petroleum, the last crop having $[\alpha]_D^{20}$ —54·1° and m. p. 131—132° (the analogous dihydro-compound had $[\alpha]_D^{18}$ —53·2° and m. p. 131—132°). The ester was hydrolysed by alkali, and the alcohol oxidised to βγ-dideuterobutyrophenone which was purified by conversion into the semicarbazone. After recrystallisation, the semicarbazone and resulting ketone were optically inactive within the limits of experimental error.



M. p. 166—167°



M. p. 155—156°

This failure may be due to similarity in the solubilities of the diastereoisomeric esters, or to an undetectable rotation in the product, the former seeming the more likely, since the system CHDRR′ has been known to exhibit measurable optical activity (see above); a resolution of this type by fractional crystallisation has not yet been reported.

EXPERIMENTAL

(±)-α-*Allylbenzyl Alcohol.*—Klimenko's method (*loc. cit.*) gave the alcohol (87%), b. p. 88—90°/3 mm., $n_D^{21\cdot5}$ 1·5289 (Found: C, 81·1; H, 8·2. Calc. for $C_{10}H_{12}O$: C, 81·0; H, 8·2%). Its 3 : 5-*dinitrobenzoate* separated from aqueous ethanol as pale yellow plates, m. p. 90—91° (Found: C, 60·1; H, 4·2; N, 8·4. $C_{17}H_{14}O_6N_2$ requires C, 59·6; H, 4·1; N, 8·2%). Reduction afforded 1-phenylbutanol [hydrogen phthalate, m. p. 90—91° (lit., 90—91°)].

(±)-α-*Allylbenzyl Hydrogen* 3-*Nitrophthalate.*—A mixture of the foregoing alcohol (133 g.) and 3-nitrophthalic anhydride (173·5 g.) in pyridine (70 g.) was heated for 2 hr. at 110—115°. Next day, the product, diluted with an equal volume of acetone, was decomposed with hydrochloric acid and ice. The crude mixture (290 g., 94%) was partly separated into isomeric esters by chloroform extraction. The chloroform-insoluble (±)-α-*allylbenzyl hydrogen* 3-*nitrophthalate* (about 33% of the mixture) crystallised from benzene as a pale yellow granular solid, m. p. 155—156° after recrystallisation from the same solvent (Found: C, 63·8; H, 4·7; N, 4·3%; equiv., 343. $C_{18}H_{15}O_6N$ requires C, 63·3; H, 4·6; N, 4·2%; equiv., 341). The chloroform-soluble *ester* (about 66% of the mixture) separated from benzene as colourless needles, m. p. 166—167° after recrystallisation from the same solvent (Found: C, 63·8; H, 4·6; N, 4·2%; equiv., 341). A mixture began to melt at 140°. The dissociation constants were determined in 50% (by weight) aqueous ethanol having κ 0·45 gemmho, ρ_{25} 0·9107. Specific conductances were determined at 25° ±0·005 in a bottle-type cell having greyed platinum electrodes of constant $1/A$ 0·09146. Resistances were measured on a 1 : 1 ratio bridge employing a Wagner earth compensator and supplied with a sine-wave current. The total R.M.S. bridge voltage was less than 0·1 v and the signal was amplified. The ratio (2·24) of the dissociation constants $[(6\cdot01 \times 10^{-5})/(2\cdot68 \times 10^{-5})]$ was independent of the Λ_0 value, obtained by the application of Walden's rule to comparable data in aqueous ethanol and aqueous acetone.

(−)-α-*Allylbenzyl Hydrogen* 3-*Nitrophthalate.*—To a solution of the (±)-phthalate (92 g.) (from which much of the higher-melting form had been removed by chloroform) in methanol–chloroform (5 : 1; 2000 c.c.) was added strychnine (88 g.), and the mixture was heated under reflux until dissolution was complete. When the solution was concentrated (1250 c.c.) and set aside, the strychnine salt (70·4 g.) separated as pale yellow prisms. Three recrystallisations gave the pure salt (53 g.), m. p. 199—200°, $[\alpha]_D^{23}$ −1·73° (*l*, 4; *c*, 7·80 in $CHCl_3$), from which the (−)-ester (26·8 g.), pale yellow prisms (from benzene–light petroleum), m. p. 126—127°, $[\alpha]_D^{20}$ −17·3° (*l*, 4; *c*, 5·74 in $CHCl_3$), was obtained by decomposition with ammonia and extraction.

(+)-α-*Allylbenzyl Hydrogen* 3-*Nitrophthalate.*—The mother-liquors from the above crystallisation were decomposed, and the recovered ester (60 g.) crystallised from benzene–light petroleum. This ester (56 g.) was dissolved in methanol (650 c.c.), cinchonine (48 g.) was added, and the mixture heated under reflux until dissolution was complete. On cooling, the cinchonine salt separated as needles, m. p. 175—182°, $[\alpha]_D^{23}$ +128° (*l*, 4; *c*, 7·28 in $CHCl_3$). After five recrystallisations from methanol, the salt (23·4 g.), m. p. 192—193°, $[\alpha]_D^{18}$ +178·5° (*l*, 4; *c*, 5·80 in $CHCl_3$), was decomposed, to give the (+)-ester (12·7 g.), separating from benzene–light petroleum as plates, m. p. 126—127°, $[\alpha]_D^{18}$ +17·9° (*l*, 4; *c*, 5·76 in $CHCl_3$).

(+)- *and* (−)-α-*Allylbenzyl Alcohol.*—(+)-α-Allylbenzyl hydrogen 3-nitrophthalate (3 g.) was steam-distilled in an excess of aqueous sodium hydroxide (16 g. in 50 c.c.). Extraction of the distillate gave the (+)-alcohol (1·2 g.) as a colourless liquid, $[\alpha]_D^{18}$ +48·3° (*l*, 4; *c*, 6·74 in C_6H_6), $n_D^{22\cdot5}$ 1·5253. The (−)-alcohol (1·2 g.) obtained similarly from the (−)-ester (3·1 g.) had $[\alpha]_D^{18}$ −48·7° (*l*, 4; *c*, 6·92 in C_6H_6), $n_D^{22\cdot5}$ 1·5250. A second resolution gave the (−)-alcohol of $[\alpha]_D^{20}$ −50·0° (*l*, 4; *c*, 5·50 in C_6H_6). The (−)-ester (3·3 g.) was reduced with hydrogen in the presence of platinum to (−)-1-phenylbutyl hydrogen 3-nitrophthalate (3·0 g.), m. p. 131—132°, colourless needles (from benzene–light petroleum), $[\alpha]_D^{18}$ −53·2° (*l*, 4; *c*, 6·81 in $CHCl_3$), $[\alpha]_D^{20}$ −24·3° (*l*, 4; *c*, 6·81 in Et_2O). Hydrogenolysis of the ester (3·0 g.) with lithium aluminium hydride (1·8 g.) gave, after distillation (b. p. 90—92°/2 mm.), (−)-1-phenylbutanol (0·7 g.) as long colourless needles, m. p. 46—47°, $[\alpha]_D^{20}$ −44·7° (*l*, 4; *c*, 5·13 in C_6H_6). A sample of (+)-1-phenylbutanol, kindly supplied by Dr. J. Kenyon, had $[\alpha]_D^{20}$ +45·1° (*l*, 2; *c*, 4·79 in C_6H_6).

(−)-3 : 4-*Dideutero*-1-*phenylbutyl Hydrogen* 3-*Nitrophthalate.*—Deuterium was obtained by the electrolysis between platinum electrodes of "Norsk Hydro" heavy water (D_2O 99·7%)

acidified with a little sulphur trioxide. The gas was collected in an evacuated rubber bladder and admitted to the evacuated deuteration apparatus until the internal pressure was just below atmospheric. (–)-α-Allylbenzyl hydrogen 3-nitrophthalate (11·6 g.) with the platinum catalyst in ethyl acetate (80 c.c.) was drawn into the deuteration apparatus from a separating funnel. Deuteration proceeded smoothly during 2 hr. at 40—45°, the initially colourless solution becoming pale yellow. Removal of the catalyst and solvent gave (–)-3 : 4-dideutero-1-phenylbutyl hydrogen 3-nitrophthalate (11 g.), m. p. 128—129°, $[\alpha]_D^{18}$ –52·6° (*l*, 4; *c*, 5·84 in $CHCl_3$), as pale yellow needles from benzene–light petroleum. Deuteration of more ester (11·6 g.) in ether at room temperature, gave the same product (11·6 g.), m. p. 128—129°, $[\alpha]_D^{18}$ –53·0° (*l*, 4; *c*, 5·93 in $CHCl_3$). The combined products were recrystallised fourteen times from benzene–light petroleum, the last crop (6·6 g.) having m. p. 131—132°, $[\alpha]_D^{20}$ –54·1° (*l*, 4; *c*, 5·82 in $CHCl_3$).

βγ-Dideuterobutyrophenone.—The ester (6·6 g.) was hydrolysed by steam-distillation with aqueous sodium hydroxide as described above, the 3 : 4-dideutero-1-phenylbutanol (2·7 g.), m. p. 45—46°, having $[\alpha]_D^{20}$ –44·7° (*l*, 4; *c*, 5·17 in C_6H_6), $[\alpha]_D^{20}$ –49·3° (*l*, 4; *c*, 5·13 in $CHCl_3$). To this (2·7 g.) in acetic acid (15 c.c.) was added chromic oxide (1·8 g.) in aqueous acetic acid (17 c.c. of 88%) at 40—45°. The product was stirred for a further 0·5 hr., the excess of chromic oxide decomposed with a few drops of sulphurous acid, and the mixture neutralised with sodium carbonate solution, and then distilled in steam. Extraction of the distillate gave βγ-dideuterobutyrophenone (2·3 g.) as a very pale yellow liquid. The semicarbazone (3·1 g.) separated from aqueous ethanol as colourless plates, m. p. 188—190°, α_D^{20} ±0·02° (*l*, 4; *c*, 25·0 in AcOH), and it (3·0 g.) was reconverted into the ketone (2·0 g.) by steam-distillation from sulphuric acid, the product having α_D^{20} ±0·02° (*l*, 0·5; homogeneous), $n_D^{18\cdot5}$ 1·5162. The oxidation was repeated with the alcohol (1·0 g.) from the hydrogen 3-nitrophthalate obtained from a fraction of the mother-liquors during crystallisation. Hydrolysis of the semicarbazone gave a ketone showing α_D^{20} ±0·02° (*l*, 0·5; homogeneous), $n_D^{17\cdot5}$ 1·5166.

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