Reduction of Chalcones by Complex Metal Hydrides

III.* Chalcone and Chain-deuterated Chalcones with Lithium Aluminium Hydride-Aluminium Chloride

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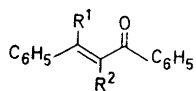
Results with chain-deuterated chalcones indicate that the dimer formed in lithium aluminium hydride-aluminium chloride reduction of chalcone is 1,3,5-triphenyl-4-benzyl-1-pentene (VIII). This is supported by 6-stage synthesis of the aldehyde XII, the ozonisation product of VIII. Deuterium distribution in reduction products from D-containing chalcones supports an allylic carbonium ion mechanism for the overall reaction.

In part II,[1] the reduction of 4- and 4'-methoxychalcone with a 1:2 mixture of lithium aluminium hydride and aluminium chloride was described. The two reactions appeared to follow different mechanisms, the former probably involving a formation of carbon-aluminium bond and the latter proceeding *via* an allylic carbonium ion. In addition to monomeric propenes the reductions also gave dimers, the structures of which were not elucidated because of their inhomogeneity.
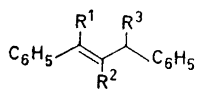
In order to test which mechanism normally operates in mixed-reagent chalcone reductions, and to establish a structure for the dimer, the reaction with chalcone (I) and α- and β-deuterated chalcones (II and III) has been studied.

Chalcone yields, in addition to 40 % of 1,3-diphenylpropene (IV), 27 % of a dimer, $C_{30}H_{28}$ (M^+ 378). This hydrocarbon has a styrene chromophore (λ_{max} (log ε) 254 (4.37), 284 (3.47), 293 (3.22)), benzylic methylene (ν_{max} 1450 cm^{-1}) and a *trans*-disubstituted double bond (ν_{max} 965 cm^{-1}). The infrared spectrum as a whole is very close to that of 1,3-diphenylpropene. The proton magnetic resonance spectrum features a complex 20-proton pattern at τ 2.7—3.1, a two-proton multiplet at τ 3.65, a broad one-proton signal at τ 6.47, and a broad five-proton signal at τ 7.40. Ozonisation followed by reduction gives benzaldehyde and a high molecular weight aldehyde (XII, see below). These
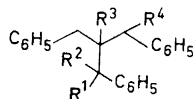
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* Part II, see Ref. 1.

		R¹	R²
	I	H	H
	II	H	D
	III	D	H

	R¹	R²	R³
IV	H	H	H
V	H	D	H
VI	D	H	H
VII	H	H	D

	R^1	R^2	R^3	R^4
VIII	$C_6H_5CH=CH-$	H	H	H
IX	$C_6H_5CH=CD-$	H	D	H
X	$C_6H_5CD=CH-$	H	H	D
XI	$C_6H_5CH=CH-$	D	H	D
XII	$-CHO$	H	H	H
XIII	H	H	OH	H
XV	$=O$		H	H
XVI	$=CH_2$		H	H
XVII	CH_2OH	H	H	H
XVIII	OH	H	H	H

data suggest structure VIII, 1,3,5-triphenyl-4-benzyl-1-pentene as a probable structure for the dimer. A similar dimer, 1,5-diphenyl-4-methyl-1-pentene has been suggested [2] to result, in addition to monomeric olefins, from the action of "dichloroaluminium hydride" (aluminium chloride:lithium aluminium hydride, 3:1) on 1-phenylallyl alcohol.
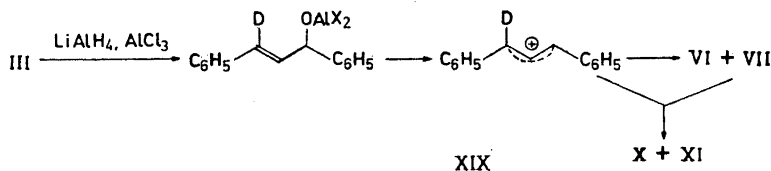
The α-deuterated chalcone (II) yields 1,3-diphenylpropene-2-d (V) [τ 3.66 (1 H, t, $J=1.5$ Hz) and 6.58 (2 H, d, $J=1.5$ Hz)] and a dimer, $C_{30}H_{26}D_2$ (M^+ 380). In accord with structure IX, the proton magnetic resonance spectrum of the dimer consists of a 1:1:4 pattern at τ 3.64, 6.47, and 7.40 in addition to 20 protons in the aromatic region. The first two signals exhibit allylic coupling ($J=1.0$ Hz) whereas the benzylic protons appear as a resolved multiplet instead of a broad envelope (see below). The monomeric fraction from the β-deuterated chalcone (III) consists of a mixture of 1- and 3-deuterated 1,3-diphenylpropenes (VI, VII) at a ratio of 1:1, based on PMR signal intensities [τ 2.86 (20 H), 3.70—3.77 (3 H), 6.50—6.62 (3 H)]. The dimeric fraction ($C_{30}H_{26}D_2$, M^+ 380) consists similarly of a 1:1 mixture of X and XI [τ 2.70—3.15 (40 H), 3.65 (3 H), 6.47 (1 H), and 7.40 (8 H)].

To obtain undisputable proof of the structure of the dimers, the aldehyde XII, formed by ozone-triphenylphosphine treatment of VIII, was synthetised *via* the route given below. A number of unsuccessful approaches are briefly
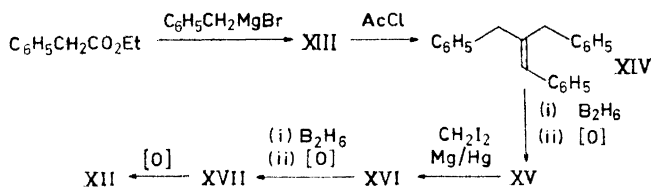
mentioned. Carbonylation with carbon monoxide at atmospheric pressure [3] of diborane-treated XIV, followed by hydrogen peroxide oxidation, failed to produce any XII, the product being simply XVIII, easily oxidisable to XV. In the Darzens mono- and dichloroacetate syntheses (XV→ XII) with soda-mide or potassium t-butoxide base no reaction took place, starting material being recovered in each case. Condensation of 2-bromo-1,3-diphenylpropane with phenylacetonitrile yielded only untractable tars.

The formation of dimers, and the mode of distribution of deuterium in products from D-containing chalcones is in accord with the allylic carbonium ion mechanism proposed by Brewster and Bayer [2] in analogous reactions.

$$III \xrightarrow{LiAlH_4, AlCl_3} \underset{XIX}{C_6H_5 \overset{D}{\diagup}\diagdown\overset{OAlX_2}{\diagup}C_6H_5} \longrightarrow C_6H_5 \overset{D}{\diagup}\overset{\oplus}{\diagdown}\diagup C_6H_5 \longrightarrow VI + VII$$

$$\downarrow$$

$$X + XI$$

In the dimer VIII, the 4-H signal evidently coincides with those of the four benzylic protons, its low position being explained by the threefold β-phenyl substituent effect. The crowding of the molecule with resulting steric hindrance to free rotation causes nonequivalence of the benzylic protons. In compound IX, deuteration at C-4 has removed the vicinal coupling, and the resulting spectrum of IX consists of an AB-quartet (τ 7.37, $J=14$ Hz) of one benzylic group and a singlet (τ 7.41) of the other. Another case of steric hindrance to free rotation, causing nonequivalence of the benzylic protons is encountered in the well-resolved A_2B_2X-type spectrum of XV, with two overlapping quartets of A_2- and B_2-protons (each benzyl carbon carries one A- and one B-proton) and an unsymmetrical sextet of the X-proton ($J_{AB}=13.2$ Hz). The spectra of XII and XVI—XVIII approach the A_2B_2C-type with additional splitting of the C-proton signal.

EXPERIMENTAL

UV spectra were recorded on a Beckman DK-2 spectrophotometer using ethanol solutions, and IR spectra on a Perkin-Elmer 125 spectrophotometer using KBr pellet and liquid film techniques for solids and liquids, respectively. NMR spectra were recorded on a Varian A-60 spectrometer using CCl_4 solutions with TMS as the internal standard. The symbols s, d, t, q, and m denote singlets, doublets, triplets, quartets, and multiplets, respectively. Mass spectra were recorded on an AEI MS 702 spectrometer. Preparative TLC was performed on silica gel plates (2 mm thickness), made from Merck's $PF_{254+366}$ silica gel.

Petroleum ether refers to the fraction boiling at 40—60°C. All melting points are uncorrected. Elementary analyses were carried out on an F & M CHN Analyzer Model 185.

Preparation of deuterated chalcones. Chalcone-α-d [4] (II) was prepared from aceto-phenone-α-d_3 and benzaldehyde. It had m.p. 57°C; M^+ 209; IR spectrum as reported;[4] τ 2.05 (2 H, q with fine structure, 2′,6′-H_2), 2.40—2.86 (9 H, m).

Chalcone-β-d (III) was prepared from acetophenone and benzaldehyde-d.[5] It had m.p. 56.5°C; M^+ 209; ν_{max} (bands not exhibited by undeuterated chalcone) 1580, 1235,

1025, 806, and 750 cm^{-1}; τ 2.06 (2 H, q with fine structure, 2′,6′-H$_2$), 2.43—2.87 (9 H, m). In the PMR spectra of II and III two sharp signals at τ 2.34 and 2.43, displayed by I, are absent.

Reduction of chalcones. The procedure described earlier [1] was followed.

chalcone	products		
I	IV, 40 %	VIII, 27 %, m.p. 99°C	
II	V, 40 %	IX, 26 %, m.p. 99°C	
III	VI+VII, 38 %	X+XI, 24 %, m.p. 98°C.	

IV ν_{max} 963 cm^{-1}; τ 2.89 (10 H, s), 3.48—4.13 (2 H, m), 6.64 (2 H, d, $J=5$ Hz).
V M$^+$ 195; ν_{max} 920 and 760 cm^{-1}.
VI+VII M$^+$ 195.
VIII Found: C 92.76; H 7.29. C$_{30}$H$_{28}$ requires C 92.74; H 7.26.
IX ν_{max} 920, 783, 771, and 729 cm^{-1} (bands not exhibited by VIII).
X+XI M$^+$ 380.

Ozonisation of VIII. O$_3$—O$_2$ (2 %) mixture was passed to a solution of VIII (0.37 g) in 30 ml of CHCl$_3$:CH$_3$OH (1:1) at −77°C, until TLC indicated no starting material left. Excess triphenylphosphine was then added and the stirred solution was allowed to reach room temperature. After 15 h part of the solvent was removed and the residue chromatographed (preparative TLC, elution 3 times with cyclohexane:chloroform 1:1). Benzaldehyde (0.06 g) and 0.16 g of another aldehyde (XII, see below) was collected from the plates.

Tribenzylcarbinol (XIII) [6] had ν_{max} 3550 and 1085 cm^{-1}; τ 2.80 (15 H, s, phenyl), 7.26 (6 H, s, methylene) and 8.52 (1 H, s, hydroxyl).

1,3-Diphenyl-2-benzylpropene (XIV) [7] had λ_{max} nm (log ε) 246 (3.89), 266sh (3.54), and 270sh (3.39); ν_{max} 1650 and 910 cm^{-1}; τ 2.80—3.16 (15 H, m, phenyl), 3.50 (1 H, broad, olefinic), 6.51 (2 H, broad, benzyl), 6.72 (2 H, broad, benzyl).

1,3-Diphenyl-2-benzyl-1-propanone (XV) was prepared using the general procedure of Brown and Garg.[8] 7.5 g of BF$_3$-etherate in 10 ml of anhydrous ether was added to a stirred mixture of 6.7 g of the preceding propene (XIV) and 0.85 g LiBH$_4$ in 50 ml of ether. After 2 h water (10 ml) and 50 ml of aqueous chromic acid (from 7.5 g Na$_2$Cr$_2$O$_7$·2H$_2$O and 5.8 ml of conc. H$_2$SO$_4$) was added with stirring. After 30 min work-up and column chromatography (silica gel, benzene) gave 6.1 g (86 %) of XV, m.p. 70°C (petroleum ether); λ_{max} nm (log ε) 245 (4.20), 285sh (3.10) and 320 (2.09); ν_{max} 1675 cm^{-1}; τ 2.24—2.49 (2 H, m, benzoyl-2,6-H$_2$), 2.78—3.11 (13 H, m, aromatic), 6.05 (center of sextuplet, 1 H, −COCH−), 7.03 and 7.16 (centers of q, 2+ 2 H, $J=13.2$ Hz, benzyl). (Found: C 88.00; H 6.67. C$_{22}$H$_{20}$O requires C (87.96; H 6.71). The same ketone was produced in 74 % yield by CrO$_3$-pyridine oxidation of XVIII.

2,4-Diphenyl-3-benzyl-1-butene (XVI). The method of Cainelli et al.[9] was used. 1.4 g of the preceding ketone (XV) and 5 g of methylene iodide in 50 ml of anhydrous ether were refluxed with a large excess of magnesium amalgam. Work-up with dil. H$_2$SO$_4$ and column chromatography (alumina grade I, benzene) gave 0.8 g (60 %) of XVI, λ_{max} nm (log ε) 237 (3.74) and 269 (3.21); ν_{max} 895 cm^{-1}; τ 2.92 (15 H, s, phenyl), 4.79 and 4.96 (1+1 H, broad s, =CH$_2$), and 6.48—7.45 (5 H, m). (Found: C 92.66; H 7.48. C$_{23}$H$_{22}$ requires C 92.57; H 7.43).

2,4-Diphenyl-3-benzyl-1-butanol (XVII). 0.8 g of the preceding butene (XVI) in 25 ml of anhydrous ether was stirred with 0.3 g of LiBH$_4$ and 2.8 g of BF$_3$-etherate. After 2 h acetone (20 ml), aqueous conc. Na$_2$SO$_4$, and solid Na$_2$SO$_4$ were added, filtered, evaporated, and 0.8 g of NaOH in 30 ml of ethanol added followed by 1.5 ml of 30 % H$_2$O$_2$. Work-up and column chromatography (silica gel, benzene) gave 0.45 g (53 %) of XVII, m.p. 88°C (petroleum ether); ν_{max} 3420, 1315 and 1037 cm^{-1}; τ 2.80—3.15 (15 H, m, phenyl), 6.22 (2 H, broad d, $J=7$ Hz, −CH$_2$−O−), 7.11—8.16 (6 H, m), 8.00 (1 H, broad s, hydroxyl). (Found: C 87.41; H 7.71. C$_{23}$H$_{24}$O requires C 87.30; H 7.65).

2,4-Diphenyl-3-benzylbutyraldehyde (XII). The dipyridine-chromium(VI) oxide method of Collins et al.[10] was used. 0.35 g of the preceding alcohol (XVII) in 50 ml of methylene chloride was mixed with a 5 % solution of 1.75 g of the complex [10] in methylene chloride.

After stirring for 30 min, the mixture was worked up and chromatographed (preparative TLC, chloroform:cyclohexane 1:1) to give 0.31 g (89 %) of XII, m.p. 75.5°C (petroleum ether); ν_{max} 1727 cm^{-1}; τ 0.41 (1 H, d, $J = 1$ Hz, $-$CHO), 2.73$-$3.09 (15 H, m, phenyl),

6.56 (1 H, d+d, $J_1 = 5$ Hz, $J_2 = 1$ Hz, $=$CH$-$C⟨^{O}) and 6.93$-$8.15 (6 H, m). (Found: C 87.81; H 7.08. $C_{23}H_{22}O$ requires C 87.86; H 7.05). This compound was identical in every respect, including mixed m.p. and TLC behaviour, with the aldehyde obtained by ozonisation of VIII.

1,3-Diphenyl-2-benzyl-1-propanol (XVIII). In an attempted carbonylation of di-borane-treated XIV in the presence of $LiAlH(OCH_3)_3$, the directions of Brown et al.[3] were closely followed. 1.2 g of XIV yielded 0.81 g of XVIII, m.p. 64°C (petroleum ether); ν_{max} 3550, 3400, 1300 and 1021 cm^{-1}; τ 2.82$-$3.09 (15 H, m, phenyl), 5.42 (1 H, broad d, $J = 3$ Hz, $-$CH$-$O$-$), 7.10$-$7.98 (5 H, m) and 8.10 (1 H, broad s, exchanged with D_2O). (Found: C 87.26; H 7.40. $C_{22}H_{22}O$ requires C 87.37; H 7.33).

Darzens reaction with XV. In attempted Darzens reactions with ethyl chloroacetate or dichloroacetate and with sodamide or potassium *t*-butoxide base the directions of Newman and Magerlein [11] were closely followed. 30$-$70 % of starting material (XV) was recovered in different runs, and TLC indicated no significant amounts of new compounds being formed. Further treatment [11] of the reaction mixture gave no XII.

1,3-Diphenyl-2-propanol [12] had ν_{max} 3550, 3420, 1075, and 1025 cm^{-1}; τ 2.90 (10 H, s, phenyl), 6.18 (1 H, center of septuplet, $-$CH$-$O$-$), 7.21$-$7.49 (4 H, m, methylene), 8.01 (1 H, broad s, exchanged with D_2O).

1,3-Diphenyl-2-bromopropene,[12] prepared from 1,3-diphenyl-2-propanol, had τ 2.88 (10 H, s, phenyl), 5.71 (1 H, center of septuplet, $-$CHBr), and 6.95 (4 H, center of d, methylene). Attempted condensation with phenylacetonitrile in the presence of soda-mide [13] yielded much tar and no major reaction product (TLC).

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