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Chlorinated Polycyclic Compounds. VIII. A New Approach to 2-Functionalized 3,6-Dibenzobicyclo[3.3.0]octadiene Derivatives

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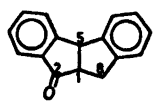
The reaction of chlorosubstituted dibenzobicyclo[3.2.1]octadiene-4-ones with zinc and ethanol gave a rearranged reduction product, 3,6-dibenzobicyclo[3.3.0]octadiene-2-one, when the starting material had an *anti*-8-chlorine atom. The yields of the rearranged product depended on the substitution pattern of the starting ketone and the best yields were obtained from 8,8-dichloro or 8-iodo ketones.

With some exceptions,[1,2] derivatives of 3,6-dibenzobicyclo[3.3.0]octadiene (ring system in *1*) have so far been synthetized by cleavage of the cyclopropane ring in 3,6-dibenzotricyclo-[3.3.0.0^{2,8}]octadiene derivatives (ring system *2*).[3–9] The latter are prepared by photoisomerization of dibenzobicyclo[2.2.2]octatrienes (ring system *3*)[10–12] or by dehydrohalogenation of properly substituted dibenzobicyclo[3.2.1]octadienes (ring system in *4*).[13–15] In the present paper, a novel approach to the ring system *1* is reported. This synthesis, based on the reaction of halogen-substituted dibenzobicyclo-[3.2.1]octadiene-4-ones (*4*) with zinc and ethanol, seems to present the first direct conversion of this ring structure to the system *1*.



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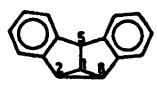

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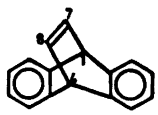

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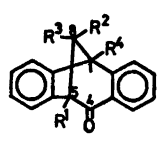

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In connection with other studies[16] it was found that the reduction of the ketone *4l* with zinc and ethanol, in addition to *4d*, gave a number of other compounds. Later, the most important of the side products was identified as the known[17] ketone *1*.

To study the influence of the substitution pattern of the starting compound on the formation of *1*, the chloro ketones *4b*–*4p* were reacted under similar conditions. The results (Table 1) reveal that the crucial feature in the formation of *1* is the presence of an 8-chlorine atom. Moreover, under these reaction conditions only the *anti*-8-chlorine (R_3=Cl) reacted to give observable amounts of *1*. The greater activity of the *anti*-8-chlorine compared with the epimeric *syn*-8-chlorine atom has been already noted in another type of reduction.[18] The 8-chlorines seem to be somewhat activated by a chlorine atom at an adjacent carbon (*4d* and *4k* compared with *4c*) but a very marked enhancement is observed with 8,8-dichloro compounds (*4g*, *4h*, *4o* and *4p*). An iodine atom at the 8-position is so much more active than chlorine that even the *syn*-8-iodo ketones *4q*–*4s* gave high yields of *1*. Although the best yields were obtained with the 8,8-dichloro ketone *4g*, the iodo compounds are superior for preparative purposes because of their availability.

The carbonyl function was shown to be essential for the rearrangement; experiments with various 4-substituted alcohols and chlorides caused dehalogenations at the 5-, 8- and 4-positions, but no skeletal rearrangement. Thus, the formation of *1* may proceed by an intramolecular reaction of the Grignard type

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Table 1. Products from the reactions of the ketones *4b*–*4s* with zinc and ethanol.

Starting material					Reaction products
No.	R^1	R^2	R^3	R^4	
4a	H	H	H	H	
4b	H	H	H	Cl	No reaction
4c	H	H	Cl	H	No reaction
4d	H	H	Cl	Cl	70 % *4d*, 20 % *1*
4e	H	Cl	H	H	No reaction
4f	H	Cl	H	Cl	No reaction
4g	H	Cl	Cl	H	95 % *1*
4h	H	Cl	Cl	Cl	85 % *1*
4i	Cl	H	H	H	100 % *4a*
4j	Cl	H	H	Cl	100 % *4b*
4k	Cl	H	Cl	H	80 % *4c*, 20 % *1*
4l	Cl	H	Cl	Cl	80 % *4d*, 15 % *1*
4m	Cl	Cl	H	H	100 % *4e*
4n	Cl	Cl	H	Cl	100 % *4f*
4o	Cl	Cl	Cl	H	60 % *1*, 30 % *4e*
4p	Cl	Cl	Cl	Cl	80 % *1*
4q	H	I	H	H	75 % *1*, 25 % *4a*
4r	H	I	H	Cl	80 % *1*, 20 % *4b*
4s	Cl	I	H	H	70 % *1*, 30 % *4a*

followed by isomerization of the resulting cyclopropanol to the more stable ketone. As, however, the reaction under normal Grignard reaction conditions occurred sluggishly and did not give clear results, this point was not investigated further.

EXPERIMENTAL

For general experimental conditions, see Ref. 16.

The ketones *4a*,[19] *4b*,[20] *4c*,[19] *4d*,[16] *4e*,[21] *4f*,[16] *4g*,[22] *4h*,[23] *4i*[23,24] *4j*[20], *4k*,[22] *4l*,[16] *4m*,[22] *4n*,[16] *4o*[22] and *4p*[25] have been reported earlier.

5-Chloro-syn-8-iododibenzobicyclo[3.2.1]octadien-4-one (4s). A mixture of 4.76 g (0.02 mol) of 7-chlorodibenzobicyclo[2.2.2]octatriene,[26] 6.68 g (0.04 mol) of AgOAc and 5.08 g (0.02 mol) of iodine in 100 ml of glacial acetic acid was stirred for 24 h at room temperature. The silver iodide was filtered off, the acetic acid removed under reduced pressure and the residue dissolved in 20 ml of acetone. The solution was filtered to remove remaining silver acetate and the filtrate evaporated. According to ^{1}H NMR, the product consisted of two epimeric acetates, the approximate yields being 50 % for the *endo* and 35 % for the *exo* epimer. Because chromatographic separation of the acetates proved difficult, the mixture was hydrolyzed with 100 ml of 10 % ethanolic KOH for 40 min at room temperature and the alcohols were separated by TLC (several elutions with chloroform–light petroleum 1:3) and crystallized from 80 % aqueous EtOH to give 5-chloro-*syn*-8-iododibenzobicyclo[3.2.1]-octadien-*endo*-4-ol, m.p. 130 °C, $\bar{\nu}_{max}$ 3440 cm^{-1}, δ 4.07 (1-H), 5.03 (*exo*-4-H), 4.91 (*anti*-8-H), 1.97 (OH)+8 Ar-H, $J_{1,8}$=4.5 Hz, and the *exo* epimer, m.p. 174 °C, $\bar{\nu}_{max}$ 3560 cm^{-1}, δ 4.16 (1-H), 4.44 (*endo*-4-H), 4.88 (*anti*-8-H), 2.67 (OH)+8 Ar-H, $J_{1,8}$=4.3 Hz.

The *endo* alcohol (0.2 g) refluxed for 80 min with 10 ml of Ac_2O and 1 ml of pyridine, gave the *endo* acetate, m.p. 186 °C. $\bar{\nu}_{max}$ 1748 cm^{-1}, δ 4.18 (1-H), 6.53 (*exo*-4-H), 4.95 (*anti*-8-H), 2.13 (OAc)+8 Ar-H, $J_{1,8}$=4.0 Hz. The *exo* acetate was similarly prepared, m.p. 188 °C, $\bar{\nu}_{max}$ 1740 cm^{-1}, δ 4.24 (1-H), 6.04 (*endo*-4-H), 4.90 (*anti*-8-H), 2.22 (OAc)+8 Ar-H, $J_{1,8}$= 4.0 Hz.

Oxidation of the epimeric alcohol mixture with Jones reagent gave the ketone *4s*, m.p. 186 °C, $\bar{\nu}_{max}$ 1714 cm^{-1}, δ ($CDCl_3$) 4.47 (1-H). 5.29 (*anti*-8-H)+8 Ar-H, $J_{1,8}$=4.6 Hz.

1-Chloro-syn-8-iododibenzobicyclo[3.2.1]octadien-4-one (4r). The Prévost reaction was performed and the mixture worked up as above. Starting from 1,4-dichlorodibenzobicyclo[2.2.2]-octatriene [23] gave directly an 85 % yield of the ketone *4r*, m.p. 159 °C, $\bar{\nu}_{max}$ 1705 cm^{-1}, δ 4.19 (5-H), 5.22 (*anti*-8-H)+8 Ar-H, $J_{5,8}$=4.5 Hz, *m/e* 253 (M-127, 100), 218(77), 189(76).

Reduction of the ketone 4r *with sodium borohydride and acetylation of the resulting alcohols.* The ketone *4r* was reduced considerably slower than its chloro analogue.[16] Thus a mixture of 3.80 g (10 mmol) of *4r*, 0.38 g (10 mmol) of $NaBH_4$ and 100 ml of EtOH was refluxed for 4 h and the reduction products were isolated by ether extraction. The alcohol mixture contained 35 % of 1-chloro-*syn*-8-iododibenzobicyclo[3.2.1]octadien-*endo*-4-ol, m.p. 163 °C, $\bar{\nu}_{max}$ 3270 cm^{-1}, δ 5.13 (*exo*-4-H), 3.63 (5-H), 5.03 (*anti*-8-H), 1.26 (OH)+8 Ar-H, $J_{4,5}$=5.0 Hz, $J_{5,8}$=5.0 Hz, and 65 % of the *exo* epimer, m.p. 199 °C, $\bar{\nu}_{max}$ 3540 cm^{-1}, δ 4.45 (*endo*-4-H), 3.73 (5-H), 4.92 (*anti*-8-H), 2.85 (OH)+8 Ar-H, $J_{5,8}$=4.5 Hz. The alcohols were separated by TLC (several elutions with chloroform–light petroleum 1:3) and crystallized from 80 % aqueous EtOH.

Acetylation as above gave the *endo* acetate, m.p. 173 °C, $\bar{\nu}_{max}$ 1730 cm^{-1}, δ 6.33 (*exo*-4-H), 3.91 (5-H), 4.98 (*anti*-8-H), 2.07 (OAc)+8 Ar-H, $J_{4,5}$=4.8 Hz, $J_{5,8}$=5.2 Hz and the *exo* epimer, m.p. 219 °C, $\bar{\nu}_{max}$ 1725 cm^{-1}, δ 5.72 (*endo*-4-H), 3.87 (5-H), 4.99 (*anti*-8-H), 2.24 (OAc)+8 Ar-H, $J_{5,8}$=4.6 Hz. A 40:60 mixture of these acetates was obtained when 1-chlorodibenzobicyclo[2.2.2]octatriene [23] was used as starting material in the Prévost reaction.

syn-8-Iododibenzobicyclo[3.2.1]octadien-4-one (4q). 1-Chloro-*syn*-8-iododibenzobicyclo[3.2.1]-octadien-4-ol (an epimeric mixture, 5.0 g) was refluxed for 40 min with a mixture of 15 g of H_2SO_4 and 35 g of HOAc. The reaction mixture

was poured into water and the product isolated by ether extraction. TLC and ^{1}H NMR showed the presence of only one compound which was identified as the iodo ketone *4q* by comparison with a sample obtained by a different synthesis.[19]

Reactions of the ketones 4b–4s *with zinc and ethanol.* General method: A mixture of 1.0 g of the ketone, 5.0 g of zinc dust and 50 ml of EtOH was refluxed for 24 h. The mixture was filtered, the filtrate evaporated and the residue dissolved in ether. The ethereal solution was washed with HCl and water, dried and evaporated. The product mixture was analyzed by TLC and ^{1}H NMR (Table 1). The pure sample of *1* was obtained by TLC separation (chloroform–light petroleum 1:3) and crystallization from EtOH and had m.p. 132 °C (lit.[17] m.p. 123–124 °C), $\bar{\nu}_{max}$ 1700 cm^{-1}, δ 3.29 (3 H, br. s), 4.77 (1 H, d, J = 5.2 Hz) + 8 Ar-H.

Preparation of the dithioketal of 1 *and desulfurization with Raney nickel.* A mixture of 0.5 g of *1*, 2.0 ml of 1,2-ethanedithiol and 1.0 ml of BF_3-etherate was stirred for 24 h at room temperature. The reaction mixture was added to 50 ml of ether and the solution thoroughly washed with 10 % aqueous KOH, washed with water, dried and evaporated.

The dithioketal was desulfurized by refluxing with 5.0 g of Raney nickel in 50 ml of EtOH for 8 h. The solution was filtered, evaporated and the product purified by TLC (light petroleum) and crystallization from light petroleum to give 0.30 g (64 % from *1*) of 3,6-dibenzobicyclo[3.3.0[octadiene, m.p. 94–95 °C (lit.[14] m.p. 95 °C), ^{1}H NMR spectrum is similar to that reported.[6]

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