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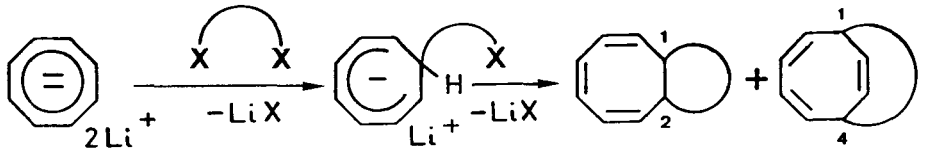
REDUCTIVE TRANSFORMATIONS - 11. STEREOSELECTIVE CYCLOANNELATION AND BRIDGING OF THE CYCLOOCTATETRAENE DIANION.[1]

Günter Krummel and Klaus Müllen*
Department of Organic Chemistry, University of Mainz,
J.J.Becher-Weg 18-20, D-6500 Mainz, FRG

Abstract: Bifunctional electrophiles with C_4-, C_6-, and C_8-chains are reacted with the cyclooctatetraene dianion to selectively give novel cycloannelation and bridging products which possess a surprising stereochemistry and are useful starting compounds for further syntheses.

The alkylation of the cyclooctatetraene dianion (1) with bifunctional electrophiles such as 1,n-dihaloalkanes has been reported to provide cycloannelation products via a 1,2-attack of the reagent.[2-5] Little is known about the controlled synthesis of 1,2(cycloannelation)- and 1,4(bridging)[6,7]-products and the stereochemistry of the quenching processes. With various alkylation reagents we have achieved a regio- and stereoselective reaction of the primary monoanionic product A (see Scheme 1) and succeeded in synthesizing a broad series of bi- and polycyclic hydrocarbons. The easily accessible products transform into novel cyclooctatetraene species and undergo various valence isomerizations.[6,7]

Scheme 1



Reduction of cyclooctatetraene with lithium in mixtures of liquid ammonia and tetrahydrofuran (THF) at -60 °C produced the dianion 1 which was subsequently reacted with the bifunctional dielectrophiles 1 - 10 (see Scheme 2). The following results are typical for the various alkylation agents:
- Even long-chain 1,n-dihaloalkanes with n = 6 and 8 (reagents 2 and 3, steps a and b), provide considerable amounts of cyclization products 11 and 13 (see Scheme 2). The latter compounds are formed via 1,4-attack of the electrophile and involve the formation of 10- and 12-membered rings. This outcome differs

from the behaviour of 1,n-dihaloalkanes with shorter chains (n = 1 - 4) whereby only cycloannelation, i.e. 1,2-attack, is observed;[2-5]

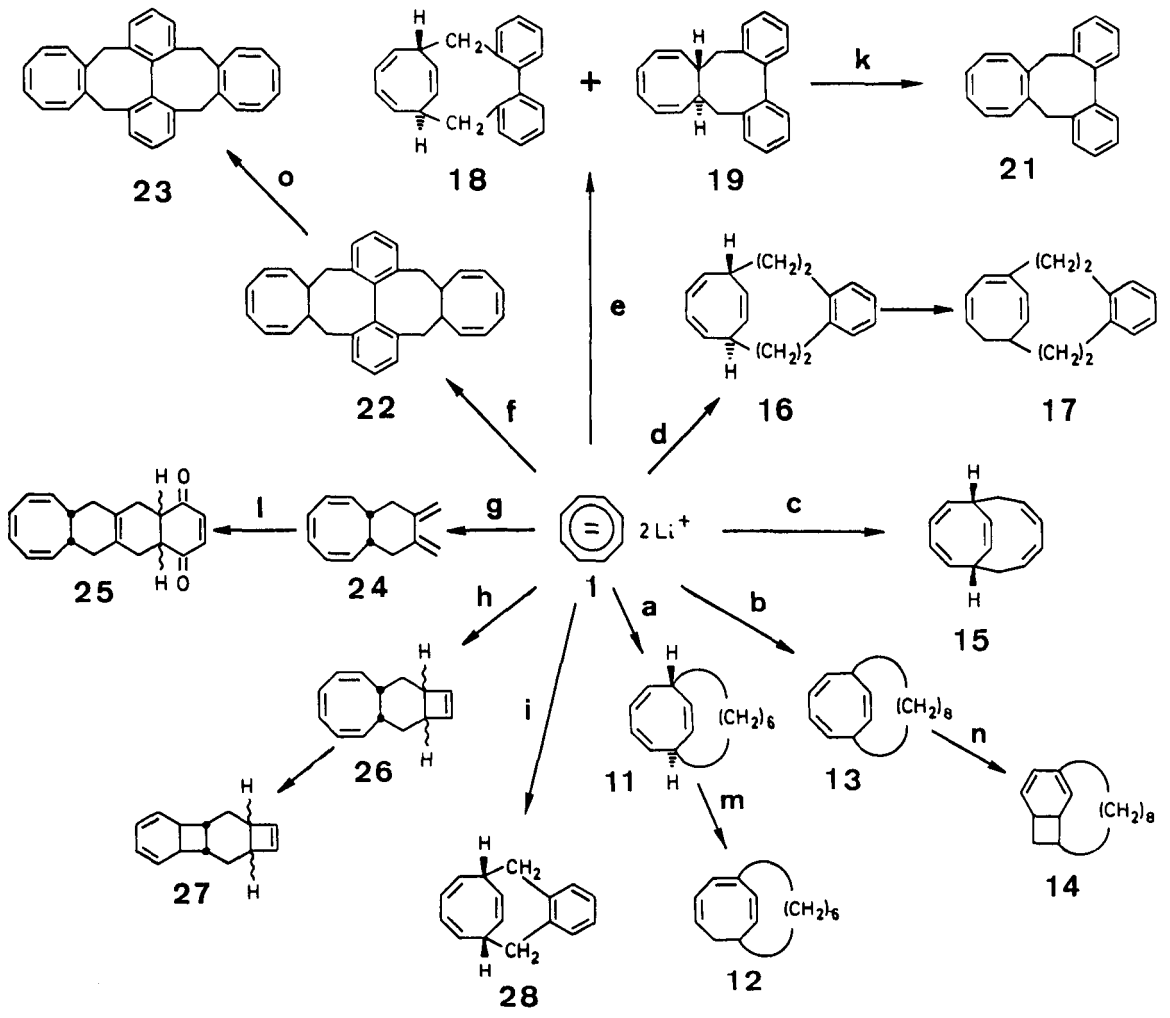
- The conformational mobility of the long-chain dielectrophiles and thus the average distance of the electrophilic groups should influence the competitive formation of 1,2- and 1,4-products. However, exclusive formation of the 1,4-products 15 and 16 is even observed if 1 is reacted with the dimesylate 4, derived from cis,cis-hexa-2,4-diene-1,6-diol, and with 1,2-bis(2-bromoethyl) benzene (5) (steps c and d);
- The 2,2'-bis(halomethyl)biphenyl species 6 appear to play a special role as C_6-dielectrophiles since both the 1,2-adduct 19 and the 1,4-adduct 18 are formed (step e). Thus, 2,2'-bis(chloromethyl)biphenyl gives 19 (27%) and 18 (16%) in addition to 9,10-dihydrophenanthrene (20) (7%);
- As in the case of the parent compound 1,4-dibromobutane, C_4-dielectrophiles of lower conformational mobility such as tetrakis(bromomethyl)ethylene (8) and the ditosylate (9) derived from cis-3,4-bis(hydroxymethyl)cyclobutene (9) afford the 1,2-products 24 and 26, respectively (steps g and h). In contrast, reaction of 1 with 1,2-bis(bromomethyl)benzene (10) only produces the 1,4-compound 28 (step i).

The tendency of the primary monoanionic quenching product A to undergo a subsequent intramolecular alkylation is great enough that ring formation can compete with polymerization reactions by intermolecular S_N-processes.[8] Increasing chain length (note e.g. the exclusive formation of 13) favours 1,4- over 1,2-attack. It appears, however, (see the formation of 24, 26 and 28) that the regioselectivity of the ring closure of A depends sensitively upon the structure of the alkylating reagent.

Ring formation in A can give rise to a cis- or trans-configuration of the 1,2-product while the 1,4-attack can produce an outward, outward ("cis") or outward, inward ("trans") pyramidalization of the bridgehead CH-groups. It appears that the 1,2- and 1,4-products 24 and 28 (formed with C_4-dielectrophiles) both possess a cis-configuration. On the other hand, the 1,4-product 18 as well as the 1,2-product 19 (formed with C_6-dielectrophiles) have a trans-configuration. An assignment of configuration is possible by NMR spectroscopy: the number of ^{13}C-NMR signals reflects the symmetry (e.g. C_1 in 11 and C_s in 28), and the bridgehead protons exhibit characteristic ^{1}H-NMR chemical shifts: cis-1,4: δ 3.5 - 3.2, trans-1,4: 4.3 - 4.0 (endo), 3.4 - 3.1 (exo); cis-1,2: 2.9 - 2.8; trans-1,2: 2.9 - 2.8.[9] The cis-configuration of 24 is proven via the C_s symmetry of its Diels-Alder adduct 25.

Since the ion pairing situation and the prevailing steric effects in A are unknown, the in,out-arrangement of the bridgehead hydrogens in e.g. 11, 16 or 18 cannot be readily explained. It should be noted that force field calculations predict the in,out-structures to be more stable in the case of larger bicycloalkanes.[10] Consequently, it is not clear whether the above stereochemistry results from kinetic or thermodynamic control.

Scheme 2



Reductive alkylation[11] of 1 (steps a-i): NH_3/THF (5:1), Li (2 eq.), -60°C; a) 1,6-Dibromohexane (2): 44% 11; b) 1,8-Dibromooctane (3): 18% 13; c) 1,6-Bis (mesyloxy)-cis,cis-hexa-2,4-diene (4): 38% 15; d) 1,2-Bis(2-bromoethyl)benzene (5): 59% 16;e) 2,2'-Bis(halomethyl)biphenyl (6): X = Br, 8% 18, 14% 19, 27% 20; X = Cl, 16% 18, 27% 19, 7% 20; f) 2,2',6,6'-Tetrakis(halomethyl)biphenyl (7): X = Br 11% 22, X = Cl 24% 22;g) Tetrakis(bromomethyl)ethylene (8): 54% 24;h) cis-3,4-Bis(tosyloxymethyl)cyclobutene (9): 35 % 27 (two diastereomers, differing by the (syn/anti-)arrangement of the two four-membered rings which are both cis-fused with the cyclohexane); i) 1,2-Bis(bromomethyl)benzene (10): 24%, 28.

Further transformations of the alkylation products: k) NH_3/THF (4:1), -40 °C, 1. KNH_2 2.$CdCl_2$ 58% 21; l) $CHCl_3$, p-benzoquinone, 20 °C, 1 h, 87% 25 (only one diastereomer); m) 60°C, 1/2 h; n) 80 °C, 3 h; o) NH_3/THF (4:1), -40 °C, 1. KNH_2 2. $CdCl_2$ 92% 23.

Certain 1,2(cycloannelation)-products are not isolated as 1,3,5-cyclooctatriene, but as bicyclo[4.2.0]octadiene systems. Thus, one obtains 27, and not the isomer 26; in contrast, 19 only exists as the cyclooctatriene isomer. The 1,4-products with trans-configuration characteristically undergo a 1,5-hydride shift under rather mild conditions to produce 1,3,5-cyclooctatriene systems such as 12. In the case of 13, the hydride shift leading to the formation of a 1,3,5-cyclooctatriene species is followed by an electrocyclic reaction to afford the tricycle 14.

1,2-Cycloannelation of two cyclooctatetraene units can be achieved by the use of tetrafunctional electrophiles. Thus, 2,2',6,6'-tetrakis(halomethyl)biphenyl (7) affords compound 22 with four condensed eight-membered rings (step f). The syntheses of 19 and 22 constitute the first cyclooctannelations of cyclooctatetraene. Via deprotonation and subsequent oxidation (see Scheme 2, steps k and o) 19 can be transformed into the dihydrooctalene species 21, while 22 gives rise to the analogous product 23 with two separate cyclooctatetraene units.[12]

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11. The structure proof of all products rests upon elemental analyses and (^{1}H, ^{13}C) NMR spectroscopy. Some typical NMR-spectroscopic data; 11: δ_H = 5.9-5.6 (m,5H, olef.), 5.35 (t,1H,olef.), 4.22 (m,1H,endo bridgehead), 3.07 (m,1H,exo bridgehead), 2.01-1.1 (m,12H,-$(CH_2)_6$-),; δ_C = 140.8, 140.4, 140.2, 126.0, 124.5, 124.1 (C, olef.), 41.1, 38.0 (bridgehead carbons), 33.1, 32.6, 28.1,25.3, 24.8, 22.3 (-$[CH_2]_6$-); 18: δ_H = 7.4-7.25 (m,8H,H-arom.), 5.85-5.2 (m,6H,H-olef.), 4.33 (m,1H,endo bridgehead), 3.37 (m,1H, exo bridgehead), 3.2-2.9 (m,3H), 2.42 (t,1H,CH_2); δ_C = 147.9, 142.5, 140.5, 139.6, 138.6, 138.1, 137.6, 133.2, 130.4, 130.1, 129.4, 127.8, 126.9, 126.7, 126.3, 125.8, 125.4, 124.5, 41.6, 40.3, 38.9, 36.5; 19: δ_H = 7.4-7.25 (m,8H,H-arom.), 5.93-5.71 (m, 6H,H-olef.), 2.83 (m,2H,bridgehead), 2.56, 2.37 (m,4H,CH_2); δ_C = 141.6, 140.8, 140.5, 129.4, 128.6, 127.8, 127.4, 126.1, 123.9, 44.9, 39.9.
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