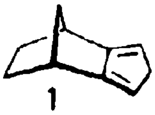
Tetrahedron Letters Vol. 21, pp 3167 - 3170
©Pergamon Press Ltd. 1980. Printed in Great Britain
0040-4039/80/0808-3167$02.00/0

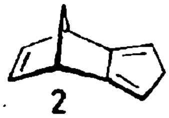
STEREOSELECTIVITY OF THE DIELS-ALDER ADDITIONS OF EXOCYCLIC DIENES GRAFTED ONTO BICYCLO[2.2.n]ALKANES

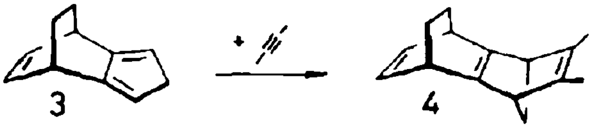
Marco Avenati, Jean-Pierre Hagenbuch, Cyril Mahaim and Pierre Vogel*
Institut de chimie organique de l'Université
2 rue de la Barre, CH 1005 Lausanne/Switzerland

Summary: The stereoselectivity of the Diels-Alder additions of (norborn-2-eno)[c]furan, (E,E)-5,6-bis(chloromethylene)bicyclo[2.2.2]oct-2-ene, (E,E)-5,6-bis(chloromethylene)-exo-2,3-epoxybicyclo[2.2.2]octane, (E)- and (Z)-2-chloromethylene-3-methylene-exo-5,6-bis(chloromethyl)-7-oxanorbornanes is presented.

Paquette et al.[1] have reported recently on the stereoselectivity of the Diels-Alder additions of the cyclopentadienes 1 - 3. The selectivities were attributed to a kinetic stereoelectronic control. We feel that other factors cannot be ruled out yet; e.g.: the stereoselectivity could be governed by the stability of the isomeric adducts (i.e. the Bell-Evans-Polanyi principle would be followed[2]). We report on the cycloaddition of the furan 5 and present a case where the apparent kinetic product is also the most stable isomeric adduct. We show that tetracyanoethylene (TCE) adds to the dichlorodienes 6 and 7 preferentially onto their *endo* face (*syn* to C(2,3)), in apparent contrast with the *"exo"* stereoselectivity reported for the cycloadditions of 3[1]. TCE adds to the chlorodienes 8 and 9 with *"exo"* stereoselectivity (the first case where the stereoselectivity is proven not to be controlled by the stability of the products).

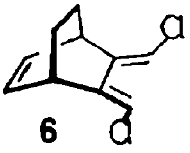

1

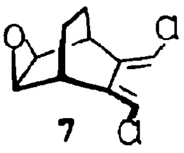

2

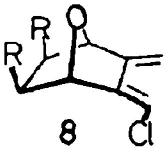

3

4

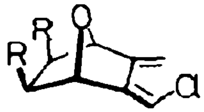

5


6

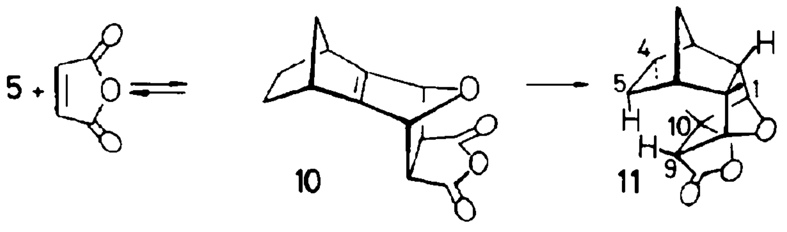

7

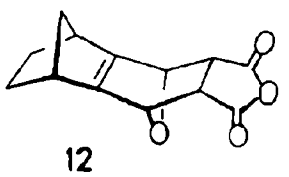

8

R=CH_2Cl


9

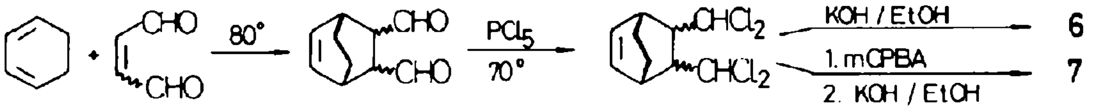
The furan 5[3] added to maleic anhydride at - 60° in acetone and gave the adduct 10[4] as the sole observable product. The same compound was formed at higher temperatures (up to 120° in diphenyl ether). At 21°, 10 equilibrated with the cycloaddends (K = 22 $Lmol^{-1}$). After prolonged heating at 40°, 80° or 120°, no other product could be detected (by ^{1}H-, ^{13}C-NMR, tlc, hplc; < 2 %), thus suggesting that 10 is the product of thermodynamic control. It might also be the



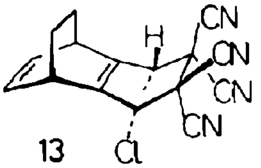


product of kinetic control. The non-observation of the isomeric adduct 12 in the above equilibrium conditions is surprising. It suggests that 12 is at least 2 Kcalmol^{-1} less stable than 10[5]. The structure of 10 was deduced from its spectral data[4] and by catalytic hydrogenation (Pd/C, acetone, - 30°) into 11 whose configuration was given unambiguously by the $^3J_{H,H}$ coupling constants between the bridgehead and vicinal hydrogens[7] and a NOE of ca. 27 % on H(9,10) by irradiating H(4,5).

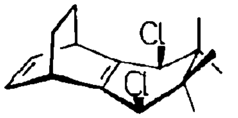
The (E,E)-dichlorodienes 6 and 7 were prepared according to the following scheme[8]:



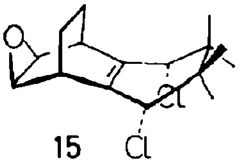
The (E,E) configuration of the chlorine substituents was expected from the mode of formation of 6 and 7. It was confirmed by the shape of the carbon NMR signals of C(5,6) (*cis* $^3J_{C,H}$ < *trans* $^3J_{C,H}$[9]) and by comparison with the spectra of the chlorodienes 8 and 9 (see thereafter).



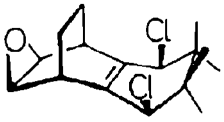
13



14



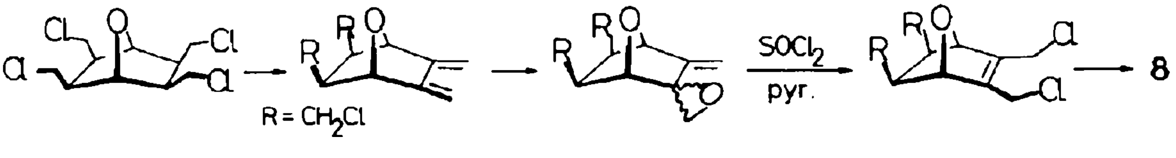
15



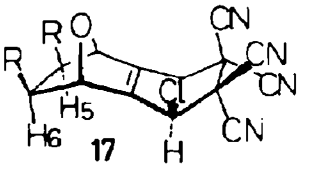
16

The triene 6[10] added to TCE (20°, 24h, C_6H_6) and yielded a 80±2:20±2 mixture (95 %) of the adducts 13/14. Similarly, 7[10] added to TCE (20°, 24 h. C_6H_6) and gave a 75±2:25±2 mixture of 15/16 (95 %). The major adducts 13 and 15 correspond to a dienophile attack onto the *endo* face of the dienes 6 and 7, respectively. 13 and 15 could be purified by fractional crystallization. The configuration of 13 - 16 was given by NOE measured on the chloromethylene hydrogens while irradiating the ethano bridge protons (FT-^{1}H-NMR(360 MHz), by substracting the non-irradiated spectra from the irradiated ones of 1:1 mixtures of 13/14 and 15/16). It is interesting to note that both the endocyclic double bond and the *exo*-epoxide ring have the same orienting effect. One could be tempted to draw a parallelism between this stereochemical effect and the rate retardation effect on the Diels-Alder reactivity introduced by these functions onto homoconjugated exocyclic dienes[11]. The "*endo*" stereoselectivity of 6 + TCE contrasts with the "*exo*" stereoselectivity reported for the cycloadditions of 3[1].

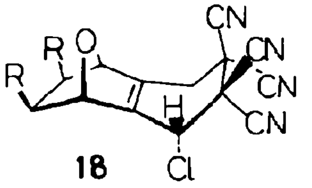
The chlorodienes 8 and 9 were prepared according to the following scheme[8]; they were separated by vapour phase chromatography.



The configuration of the chlorodienes was deduced from the spectral data[12] (sum of $^3J_{C,H}$ and $^2J_{C,H}$ of C(3) was larger in 9 than in 8[9]) and by radical induced isomerization (I_2, C_6H_5C 130°) of the (Z)-chlorodiene 9 into its more stable (E)-isomer 8. The latter added slowly to TCE at 65° in C_6H_5Cl and gave a 85±2:15±2 mixture of the adducts 17/18 (90 %). The less stabl diene 9 was ca. 650 times less reactive than 8 toward TCE (probably because of deformations o the diene due to the C-H...Cl-C repulsive interactions; cf. UV spectra of 8 and 9[12] and cf.[13] At 130° (C_6H_5Cl) 9 yielded a 20±2:80±2 mixture of 17/18. These products were stable under the conditions of their formation. Their structure was given by their spectral data[12]. A NOE of c 20 % was recorded on the chloromethylene hydrogens of 17 while irradiating the H(5,6) protons (no such effect for 18). Thus, in contrast with the *"endo"* stereoselectivity observed for the cycloadditions of 1[1,14], the TCE prefers to attack onto the *exo* face of 8 and 9[15]. The two latter reactions represent the first case of a Diels-Alder addition of exocyclic dienes graft onto a bicyclic skeleton whose stereoselectivity is shown not to be controlled by the stabili of the isomeric adducts.



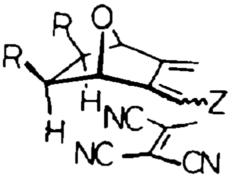
17

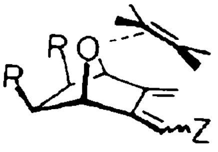


18

R = CH$_2$Cl

Among several possible explanations, one can invoke a steric hindrance between the cycloa dends in the transition state that retards the *"endo"* attack (such an hypothesis does not ho for 7 + TCE) or/and formation of a charge-transfer complex implying the participation of the n(O) electrons of the oxygen bridge, thus favoring the *"exo"* attack. More data must be collec before adventuring into a general theory[1] of the observed stereoselectivities[16].





Acknowledgments. We are grateful to Hoffmann-La Roche and Co., Basel, to the "Swiss National Science Foundation" (FN 2.891.0.77) and to "Fonds Herbette", Lausanne, for generous support.

References and Notes

1. L.A. Paquette, R.V.C. Carr, M.C. Böhm & R.Gleiter, *J.Amer.Chem. Soc.* 102, *1186 (1980)*.
2. M.J.S. Dewar & R.C. Dougherty, "*The PMO Theory of Organic Chemistry*", Plenum Press, New York, 1975, p. 212.
3. J.P.Hagenbuch & P. Vogel, *Tetrahedron Lett.* 1979, *561*.
4. Characteristics of 10 : m.p. 115-7^0; $\delta_H(CDCl_3)$: 0.73 (*ddd*, 12.0, 5.0 & 2.4 Hz, 2H), 1.31 (*md*, 9.0 & 1.6 Hz, 1H), 1.58 - 1.97 (*m*, 3H), 2.89 (*s*, 2H), 3.2 (*m*, 2H), 5.37 (*s*, 2H); IR(KBr) : 3000, 1870, 1830, 1790, cm^{-1}; m/z : 232(2), 187(3), 135(11), 134(100);

   11 : m.p. 157-8^0, $\delta_H(CDCl_3)$: 1.57 - 1.87 (*m*, 6H), 2.47 (*m*, 2H), 2.67 (*m*,2H), 3.9 (*s*, 2H), 4.85 (*dd*, 2.2 & 2.7 Hz, 2H); IR(KBr) : 2980, 1870, 1835, 1785 cm^{-1}; m/z : 234(1), 206(5), 133(21), 66(100).
5. The cause of the enhanced stability of 10 relative to that of 12 is not clear yet. It might be due to the π-polarization of the endocyclic double bond toward the exo faces of the 2-norbornene and 7-oxanorbornene systems[6] or/and to electrostatic binding interactions between the H_2C and oxygen bridges.
6. A.A. Pinkerton, P.A. Carrupt, P. Vogel, T. Boschi, N.H. Thuy & R. Roulet, *Inorg. Chim. Acta* 28, *123 (1978)*; S. Inagaki, H. Fujimoto & K. Fukui, *J. Amer. Chem. Soc.* 98, *4054 (1976)*.
7. A. Chollet, J.P. Hagenbuch & P. Vogel, *Helv. Chim. Acta* 62, *511 (1979)* and ref. therein; H. Joela, *Org. Magn. Reson.* 9, *338 (1977)*.
8. Details on these reactions and products will be given in a full paper.
9. A.W. Douglas, *Org. Magn. Reson.* 9, *69 (1977)*; U. Vögeli & W. von Philipsborn, *ibid.* 7, *617 (1975)*.
10. Characteristics of 6 : $\delta_H(CDCl_3)$: 1.0 - 2.0 (*m*, 4H), 4.0(*m*, 2H), 6.1 (*s*, 2H), 6.3(*m*, 2H); $\delta_C(CDCl_3)$: 23.7(*t*, 134), 34.9(*d*, 141), 107.1(*d*, 194), 133.0(*d*, 170), 140.2(br.*s*); IR(film) : 3070, 2940, 2880, 1630, 780, 750 cm^{-1}; m/z : 204(3), 202(18), 200(27), 176(10), 174(70), 172(100); λ_{max}(EtOH) : 261 nm(ε, 11 000).

    7 : liq.; $\delta_H(CDCl_3)$: 1.25 (*m*, 2H), 1.9(*m*, 2H), 3.25(*m*, 2H), 3.7(*m*, 2H), 6.45(*s*, 2H); $\delta_C(CDCl_3)$: 21.9(*t*, 134), 33.3(*d*, 141), 51.7(*d*, 188), 110.9(*d*, 194), 138.7(br.*s*); IR(film) : 3080, 3020, 2980, 2950, 2910, 2870, 1670, 1950, 1460, 1405, 850, 790, 750; m/z : 220(9), 218(37), 216(58), 183(4), 181(15), 115(100); λ_{max}(EtOH) : 260 nm(ε,10100).

    13 : m.p. 182-3^o; $\delta_H(CDCl_3)$: 1.45(*m*, 2H), 1.55(*m*, 2H), 3.8(*m*, 2H), 5.2(*s*, 2H), 6.5(*m*, 2H); IR(KBr) : 3080, 3000, 2960, 2940, 2900, 2880, 2260, 1660, 1610, 1470, 810, 765 cm^{-1}.

    15 : m.p. 246-7^o(dec.); $\delta_H(CDCl_3)$: 1.0 - 1.5(*m*, 2H), 2.0 - 2.25(*m*, 2H), 3.5(*m*, 4H), 5.25(*s*, 2H); IR(KBr) : 3050, 3000, 2960, 2940, 2920, 2880, 2260, 1470, 1415, 1290, 855, 800 cm^{-1}.
11. O. Pilet, A. Chollet & P. Vogel, *Helv. Chim. Acta* 62, *2341 (1979)*; M. Hardy, P.A. Carrupt & P. Vogel, *ibid.* 59, *1685 (1976)*.
12. Characteristics of 8 : m.p. 62-3^0; $\delta_H(CD_3COCD_3)$: 2.5(*m*, 2H), 3.75(*m*, 4H), 4.95(br.*s*, 1H), 5.18(*s*, 1H), 5.25(br.*s*, 1H), 5.4(*s*, 1H), 6.7( ); λ_{max}(hexane) : 250 nm(ε, 10000).
    9 : m.p. 83-4^0; $\delta_H(CD_3COCD_3)$: 2.55(*m*, 2H), 3.75(*m*, 4H), 4.9(br.*s*, 1H), 4.95(br.*s*, 1H), 5.48(*s*, 1H), 6.0(*s*, 1H), 6.6(*s*, 1H); λ_{max}(hexane) : 245 nm(ε, 9000).
    17 : m.p. : 212-2^0; $\delta_H(CDCl_3)$: 2.18(*m*, 2H), 3.25(*m*, 1H), 3.24(*m*, 1H), 3.55(*m*, 1H), 3.58(*m*, 1H), 3.5 & 3.7(2*m*, 4H), 5.09(br.*s*, 1H), 5.14(*dd*, 1H), 5.17(br.*s*, 1H).
    18 : $\delta_H(CDCl_3)$: 2.26(*m*, 1H), 2.52(*m*, 1H), 3.4 & 3.7(2*m*, 4H), 5.03(br.*s*, 1H), 5.22(br.*s*, 1H), 5.42(*m*, 1H).
13. C. Rücker, D. Lang, J. Sauer, H. Friege & R. Sustmann, *Chem. Ber.* 113, *1663 (1980)*.
14. T. Sugimoto, Y. Kobuke & J. Furukawa, *J. Org. Chemistry*, 41, *1457 (1976)*.
15. The stereoselectivity of 9 + TCE was not exactly the reverse of that of 8 + TCE because of the different temperatures at which these reactions were carried out.
16. All the new compounds presented here gave satisfactory elemental analysis.

(Received in Germany 2 June 1980)