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ON INTRAMOLECULAR DYOTROPY: STRUCTURAL EFFECTS ON REACTION RATES AND X-RAY CRYSTAL STRUCTURE - MOLECULAR MECHANICS CORRELATIONS

Judith A.K. Howard, Kenneth Mackenzie and Robert E. Johnson

School of Chemistry, The University, Bristol, BS8 1TS

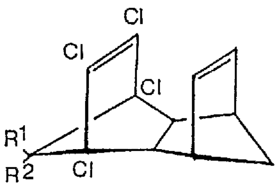
K. Brian Astin

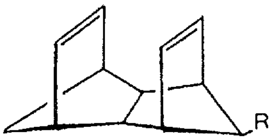
Chemistry Department, University of Bahrain, P.O. Box 32038, Bahrain.

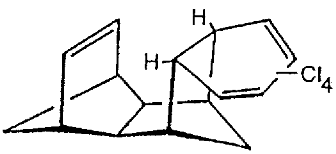
Summary: Differential kinetic behaviour in thermal dyotropic rearrangement of compounds containing a cyclohexa-1,3-diene ring as 2H donor held proximate to a variously-substituted norbornene element as acceptor is discussed in terms of parameters derived by single crystal X-ray structure analysis and Molecular Mechanics calculations.

Contemporary interest[1,2] in the stereospecific intra-molecular group-transfer of two hydrogen atoms to a proximate π-bond in a non-catalysed thermal dyotropic rearrangement[3] prompts us to report further examples of this process in appropriate model compounds [7, 8 and 9 below] and to comment on structural effects on rearrangement rates for these and analogous compounds we have previously described.[3]

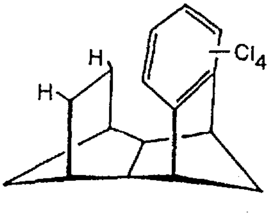
Zn/Cu-couple reduction of isodrin 1 (Et_2O, 36°) gives convenient high-yield access to syn and anti-monodechloroisodrin analogues 2 and 3[4], whilst as previously reported[5] bisdechloroisodrin 4 results from Zn-HOAc reduction of 1, accompanied by significant amounts of anti-dechloro-compound 3.[4] Unlike hexadechloroisodrin 5, which reacts rapidly with tetrachlorothiophenedioxide ("TCTD")[6] at 36°, concomitant 2H group-transfer giving aromatic







1 $R^1 = R^2 = Cl$ 3 $R^1 = Cl$ $R^2 = H$ 5 R = H   T
2 $R^1 = H$ $R^2 = Cl$ 4 $R^1 = R^2 = H$



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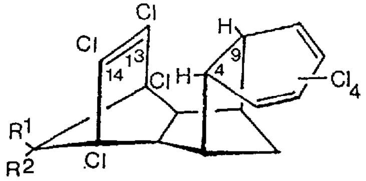
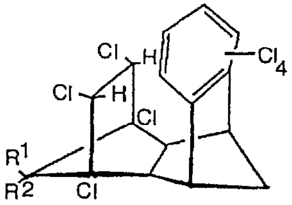


7 $R^1 = H$ $R^2 = Cl$
8 $R^1 = Cl$ $R^2 = H$
9 $R^1 = R^2 = H$
13 $R^1 = R^2 = Cl$



10 $R^1 = H$ $R^2 = Cl$
11 $R^1 = Cl$ $R^2 = H$
12 $R^1 = R^2 = H$
14 $R^1 = R^2 = Cl$

compound 6 and not the anticipated triene T[3,7], chlorinated analogues 2, 3 and 4 react only very slowly with TCTD at this temperature.[8] However, heating dienophiles 2, 3 and 4 (1 mmol) with TCTD (1.05 mmol, $CHCl_3$ 2 ml, 60° ~72 h) with adventitious solvent evaporation and slow cooling yields crystals of trienes 7 - 9[10] suitable for X-ray crystallographic analysis. Each of these trienes cleanly rearranges at the "m.p." (>180°) into their respective isomers 10, 11 and 12[11] (more slowly in C_6H_5Me, 48 - 72 h, 110°), and previous methodology[3] furnishes unimolecular rate constants, k_1, for their rearrangement at 100 - 120° and activation parameters similar to those previously obtained for compound 13; relative rates at 100° for 9:8:7:13 are 1.0:2.1:2.4:20 - small kinetic differentials compared to that observed for triene T, (k_1 T:k_1 13 ~2 x 10^5 at 36°).

Molecular mechanics calculations are useful in clarifying the relative importance of steric effects and π-energy differences[1] which may be responsible for the observed substitutent effects and relevent data[12] are illustrated in Table 1:

Table 1: Heats of Formation, ΔH_f Strain E_s- and π-Energies, E_π (k cal mol^{-1})

	ΔH_f	E_s	E_π		ΔH_f	E_s	E_π	$\Delta\Delta H_f$	ΔE_π
7	46.725	98.18	-273.06	→ 10	7.386	102.28	-315.25	-39.339	-42.19
8	45.900	97.37	-273.10	→ 11	10.040	104.89	-315.22	-35.860	-42.12
9	45.323	86.49	-273.21	→ 12	6.978	91.48	-315.25	-38.345	-42.04
13	49.965	109.74	-272.94	→ 14	14.407	117.68	-315.28	-35.558	-42.34
T	61.060	70.22	-268.82	→ 6	27.108	66.74	-315.38	-33.952	-46.56

The data show that trienes 7 - 9 and 13 are less stable by 37.448 ± 1.89 k cal mol^{-1} in ΔH_f and more stable by 4 - 8 k cal mol^{-1} in E_s than their aromatic isomers, a fairly obvious result. The data correctly predicts the rate-order 7 > 9 but not the relative reactivity of trienes 8 and particularly 13, possibly due to π-perturbation effects at the receptor π-bond concomitant on polarization changes with substituent pattern at the adjacent methylene bridge. Triene T, exceptionally, is less stable than its isomer 6 both with respect to E_s (by 3.48 k cal mol^{-1}) and as expected with respect to ΔH_f, and here further important insight derives from the E_π data; E_π is closely similar for all of the trienes 7 - 9 and 13 but for triene T the absence of Cl substitutents at the 2H acceptor π-element raises the π energy by ~4 k cal , and contributes to the greater exothermicity for rearrangement to the also less strained isomer 6, i.e. ΔE_s and ΔE_π conspire in contributing to an impressive rate acceleration compared to all the acceptor π-bond substituted analogues.

Prinzbach *et. al.*[7] have suggested that enhanced reaction zone π-orbital occupation underlies the kinetic reactivity of triene T, but Chow *et. al.*[2] emphasise the importance of π-orbital alignment with the transferring H's; given the pyramidalised geometry at sp^{2}C in norbornene derivatives[13,14], we have carried out X-ray crystal structure determinations for trienes 7 and 9[15] to investigate these hypotheses and for comparison of calculated and actual geometries. The main molecular features for compounds 7 and 9 are shown in Figure 1 and 2, confirming the expected overall stereochemistry.

However in triene 7, Cl atoms at C-13, C-14 tilt very slightly away from the H atoms at C-4, C-9 with an interplanar angle of 1.6° whilst for triene 9 the corresponding Cl atoms tilt in the opposite direction (1.8°). Sp^2 carbon pyramidalisation is in the expected exo direction[13,14] for triene 9, attenuating electron density in the reaction zone, and perhaps correlating with its slightly reduced reactivity compared to triene 7; here endo pyramidalisation increases electron density in this region and probably aligns the π-orbital more favourably with respect to H-4, H-9. The relevent H-4/C-14 and H-9/C-13 distances (d_{CH}) are 2.46 and 2.48 Å in triene 9, and slightly larger, 2.49 and 2.59 Å for 7, in excellent agreement with the MM calculated d_{CH} values of 2.45 Å in 7, and 2.46 Å in 9 (and in 13). The slightly larger d_{CH} values in 7 compared to 9 could be one reason why the more favourable π-bond geometry here is not more conspicuously reflected in the relative rates, $k_1$7:$k_1$9. For triene T, the calculated d_{CH} value is significantly shorter at 2.38 Å; thus all quantified data for triene T correlate with the exceptional relative reactivity of this compound.

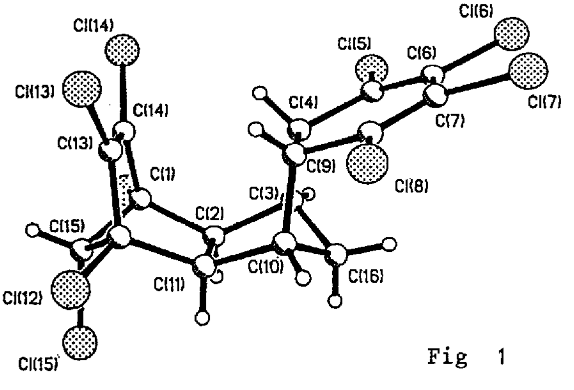


Fig 1

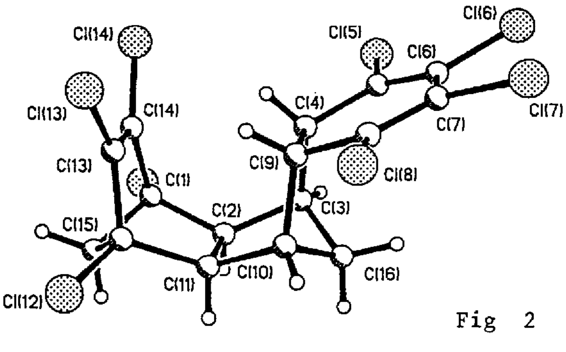


Fig 2

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11. 10; m.p. 304 - 305°. 11: m.p. 347 - 350° decomp. 12: m.p. 243 - 244°.
12. Calculations performed using the Allinger MM2 and MMPI methods, e.g. U. Burket and N.L. Allinger, Molecular Mechanics, Am. Chem. Society, Washington D.C., 1982 implemented by the MMX programme of J.J. Gajewski and K.E. Gilbert available from Serena Software, 489 Serena Lane, Bloomington, Indiana, IN 47401, U.S.A.
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15. Crystal data: 7 $C_{16}H_9Cl_9$ M = 520.3 a = 13.779(6) b = 8.220(3) c = 16.889(7) Å, β = 93.00(3)° Space group $P2_1/c$ (no 14) U = 1910(1) $Å^3$ z = 4 D_c = 1.82 g cm^{-3}, F(000) = 1032 $\mu(Mo\ K_\alpha)$ = 13.3 cm^{-1} 9 $C_{16}H_{10}Cl_8$ M = 485.9 a = 30.842(10) b = 8.588(5) c = 14.296(6) Å β = 97.17° Space group C2/c (No 15) U = 3757 $Å^3$ z = 8 D_c 1.72 g cm^{-3} F(000) = 1936 $\mu(Mo\ K_\alpha)$ = 12.2 cm^{-1} Mo K_α X-Radiation (graphite monochromator) λ = 0.71073 Å. 7 R(R′) 0.0028 (0.031) [1337 data] 9 R(R′) 0.044 (0.044) [1597 data]. No exactly analogous structures have been reported but for two compounds containing the isodrin skeletal element e.g. 5 (R = $O.COC_6H_4COOH$) d_{cc} is 2.921 Å (O. Ermer, C-D. Bodecker and H. Pruet, Angew. Chem. Int. Ed. Engl., 1984, 23 55) and for the 4,5:9,10-bis-benzo annulated analogue of 5 d_{cc} is 3.04 Å.[7] To achieve greater certainty in the location of hydrogen atoms H-4/9, a neutron diffraction study is in progress with triene 9.

Footnote: Neutron diffraction data in the preliminary stages of refinement have confirmed the geometry shown for 9. Full details will appear later with the X-ray results for 10.

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