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STEREOSELECTIVITY AND STEREOSPECIFICITY IN CYCLOADDITIONS WITH NORBORNADIENE DERIVATIVES

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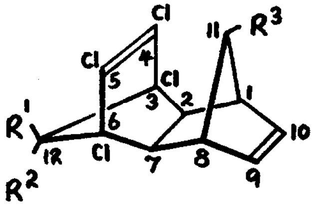
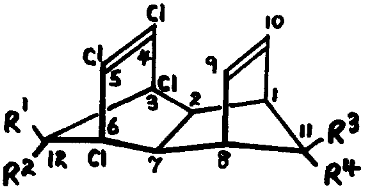
It is generally believed that Diels-Alder cycloaddition of hexachlorocyclopentadiene to norbornadiene gives stereospecifically the endo-exo adduct (1) (aldrin).[1] In contrast - presumably due to the steric effect of the dichloromethano bridge - addition of cyclopentadiene to 1,2,3,4,7,7-hexachloronorbornadiene[2] and its simple derivatives[3] exhibits endo-endo stereospecificity, giving analogues of adduct (2) (isodrin).[4] However, little is known about the effect of a single, norbornadiene bridge methylene substituent either in respect of rate, or of stereochemical effect[5] in diene additions, variation in the diene component having received rather more attention.[6,7] As might be expected for example halogenated cyclopentadienone acetals e.g. (3) and (4)[7] and cyclopentadienones[6] parallel the behaviour of hexachlorocyclopentadiene in giving apparently exclusively endo-exo adducts with norbornadiene [whilst endo-endo adducts result from addition of tetrachloronorbornadien-7-one acetals with cyclopentadiene[8,9] or dienone acetal (4)[9]].

In preliminary work directed to the possible synthesis and fragmentation of endo-cis-tetrachlorotricyclo[6,2,1,$0^{2,7}$]undeca-3,5,9-triene for comparison with the known exo-cis isomer,[7,10] we investigated additions of dienone acetal (3) with 7-t-butoxynorbornadiene (5).[11] In sealed tube reactions [120-130°, 48 hr., excess (3)] good overall yields of endo-exo adduct (6) m.p. 196-197°, and the isomeric endo-endo adducts (7) (syn-O^{t}Bu) m.p. 124-125° and (8) (anti-O^{t}Bu) m.p. 116-117° (lit.[10] 116.5°) are formed in the approximate ratios[*†] 1.0:1.8:3.2 respectively and are readily separated by silicagel column chromatography.[12] The stereoisomers may be distinguished from the expectation that due to a perpendicular dihedral, ^{1}H nmr ^{3}J H1/H2 coupling will be small or zero in the endo-exo adducts,[7] H2/H7 appearing as a sharp singlet. By contrast, this signal appears as a 'triplet' or 'quartet' in the various endo-endo adducts[13] and in addition is deshielded 0.2-0.3τ by proximate chlorine or alkoxy groups;[14] when taken with evidence for H9,10/anti-H11 ^4J coupling, bridge methylene substituent stereochemistry may thus also be deduced. On the other hand the bridgehead H1/H8 resonance invariably appears as a complex multiplut in all stereoisomers. Relevant ^1H nmr chemical shifts are summarised in Table 1.

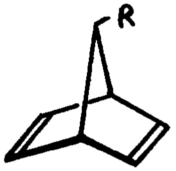
Similar endo-endo adducts (9) (a-O^{t}Bu) m.p. 134.5-135.5° and (10) (s-O^{t}Bu) m.p. 143-144°, and an endo-exo adduct (11), roughly in the ratio 3.4:2.4:1.0 are isolated from the complex



	$R^{1,2}$	R^3
(1)	Cl	H
(6)	OMe	O^{t}Bu
(11)	OCH_2CH_2O	O^{t}Bu
(15)	OMe	O_2CPh
(16)	Cl	O^{t}Bu
(21)	OMe	H
(22)	OCH_2CH_2O	H

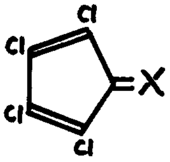


	$R^{1,2}$	R^3	R^4
(2)	Cl	H	H
(7)	OMe	O^{t}Bu	H (i.e. syn)
(8)	OMe	H	O^{t}Bu (i.e. anti)
(9)	OCH_2CH_2O	H	O^{t}Bu
(10)	"" ""	O^{t}Bu	H
(14)	OMe	H	O_2CPh
(17)	Cl	O^{t}Bu	H
(18)	Cl	H	O^{t}Bu
(19)	OMe	H	H
(20)	OCH_2CH_2O	H	H



(5) R = O^{t}Bu

(13) R = O_2CPh



(3) X = $(OMe)_2$

(4) X = OCH_2CH_2O

product mixture which results from heating the cyclic dienone acetal (4) with norbornadiene (5), considerable dimer $[4]_2$ and a bis-adduct m.p. 286° (decomp.) - probably (12), from the reaction of (3) with (9) - also appearing and complicating analysis. In the similar addition of dienone acetal (3) to 7-benzoyloxynorbornadiene (13)[15] only one significant endo-endo adduct, probably (14) m.p. 154-155° is apparently formed, with essentially the same amount of the endo-exo isomer (15) m.p. 185-186°; but adduction of hexachlorocyclopentadiene and t-butoxynorbornadiene (5) runs more nearly parallel to the similar reaction with dienone acetal (3), giving endo-exo adduct

(16), and the endo-endo isomers (17) (s-O^{t}Bu) m.p. 131.5-133°, and (18) (a-O^{t}Bu) m.p. 108-109°, in the ratio 1.0:1.4:3.8.

Table 1: ^{1}H Nmr Chemical Shifts (τ) for Stereoisomeric Adducts (CDCl$_3$/TMS)

	9,10 vinyl	1,8 brhd.	2,7 ring j.	11 or CHO	12 (OR)$_2$	O^{t}Bu
(1)	3.68 t	7.11 t	7.28 s	8.41,8.69 dd	-- --	--
(2)	3.93 t	6.97 sext.	6.61 t	8.21,8.47 dd	-- --	--
(6)	3.91 pent.	7.23 q	7.54 s	5.84 brd.s	6.54,6.56 s	8.91 s
(7)	4.06 brd.s	7.06 hept.	6.92 q	6.18 brd.s	6.38,6.50 s	8.88 s
(8)	4.10 t	7.34 sext.	6.63 t	6.56 t	6.35,6.48 s	8.84 s
(9)	4.14 t	7.34 mult.	6.68 t	6.59 t	5.81 complx.	8.86 s
(10)	4.07 brd.s	7.04 mult.	6.92 t	6.20 brd.s	5.80 complx.	8.88 s
(11)	3.83 mult.	7.11 t	7.47 s	obscured	5.8 complx.	8.86 s
(14)	4.00 t	6.89 sext.	6.58 t	5.29 t	6.37,6.49 s	2-2.5 (Ph)
(15)	4.12 brd.s	6.73 s	6.69 mult.	5.11 brd.s	6.38,6.50 s	2-2.6 (Ph)
(16)	3.79 brd.s	7.07 mult.	7.30 s	5.73 brd.s	-- --	8.86 s
(17)	4.00 pent.	6.98 sext.	6.71 t	6.16 brd.s	-- --	8.86 s
(18)	4.06 t	7.25 sext.	6.45 t	6.4 (obsc.)	-- --	8.85 s
(19)[a]	4.07 t	7.10 mult.	6.81 t	obscured	6.36,6.47 s	--
(20)[8,9]	4.04 t	7.05 mult.	6.84 t	8.26,8.45 dd	5.83 complx.	--
(21)	3.69 t	7.16 pent.	7.43 s	8.44,8.75 dd	6.42,6.46 s	--
(22)	3.75 t	7.17 pent.	7.47 s	8.48,8.78 dd	5.83 complx.	--

[a] at 10% conc. in mixture with (21)

Table 2: ^{13}C Nmr Chemical Shifts[b] for Selected Stereoisomers

	1,8/2,7	3,6	4,5	9,10	11	12	MeO, MeO	13	14
(6)	54.60, 46.17	80.33	115.1	135.6	75.78	130.6	51.45, 52.42	73.59	28.51
(7)	48.35, 48.84	91.80	115.6	126.6	76.69	127.5	51.45, 52.54	73.65	28.09
(8)	46.53, 51.21	88.76	116.9	128.3	76.57	128.3	51.45, 52.42	74.02	28.15

[b] ppm downfield from TMS in CDCl$_3$

The non-stereospecificity in these (4+2)π cycloadditions clearly implies a fine balance of combined steric and electronic factors as between alternative transition states for endo-exo, and endo-endo modes of adduction. For comparison we studied the actual stereospecificity in the addition of dienone acetals (3) and (4) to norbornadiene; only 1-1.5%, and up to 6% of endo-endo adducts (19), and (20)[8,9] were formed, respectively, in addition to the expected endo-exo adducts (21) m.p. 117-118.5°[7] and (22) m.p. 105-106°.

The results of dienone acetal cycloaddition with norbornadiene (5) indicate a notable preference for faster *endo* addition at the dienophilic site *syn* to the O^tBu group - quite the reverse of steric expectation based on e.g. incipient ring-junction hydrogen/O^tBu opposition. A simplified explanation might be that since the dominating orbital interaction in the transition state for $(4+2)\pi$ inverse electron demand cycloaddition is HOMO(dienophile)-LUMO(diene),[16a] $O(S)\sigma$ lone pair-$\pi(S)$ mixing may raise the relative energy level of HOMO(dienophile) increasing its interaction with LUMO(diene) and stabilising the transition state. Similarly, increased *secondary* LUMO(diene)-HOMO(dienophile) interaction during addition at the olefinic site *anti* to the O^tBu group could favour *endo-endo* addition over the *endo-exo* mode - as is observed. Interestingly, addition of phenyl azide to *t*-butoxynorbornadiene (5) also exhibits *endo-syn* selectivity[17] consistent with the proposed raising of the dipolarophile HOMO energy; however relevant HOMO/LUMO orbital energy separations for phenyl azide additions are such as to allow both raising and lowering of the dipolarophile MO's to result in a nett transition state stabilisation.[16b] A more refined M.O. treatment of our data will appear in the full paper.

*Product compositions determined by ^1H nmr integration and product separation.

†Traces of a compound $C_{20}H_{16}Cl_8O_4$ arise by an *exo-exo* addition-elimination sequence involving acetal (3) and adduct (6) (W.P.Lay and K.Mackenzie, unpublished observations).

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