61. *exo*-Stereoselectivity in *Diels-Alder* Addition of Halogenocyclopropenes to Butadienes and Furans

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The stereochemistry of the *Diels-Alder* reaction of 1,2-dichloro-3,3-difluorocyclopropene (**5a**) to 1,4-diphenyl-1,3-butadiene (**6**) and 1,3-diphenylisobenzofuran (**7**) was unambiguously established by X-ray structure determination. In all cases known so far, tetrahalogenocyclopropenes add *exo* to open-chain dienes and furans. The previously reported *exo*-addition product (**2a**) of 1-bromo-2-chlorocyclopropene (**5b**) to **7** allows assignments of the stereochemistry of other additions of **5b** to furans. *exo*-Addition usually predominates, but in some cases *endo*-adducts are also formed. This contrasts with reports in the literature that **5b** adds preferentially *endo* to open-chain dienes.

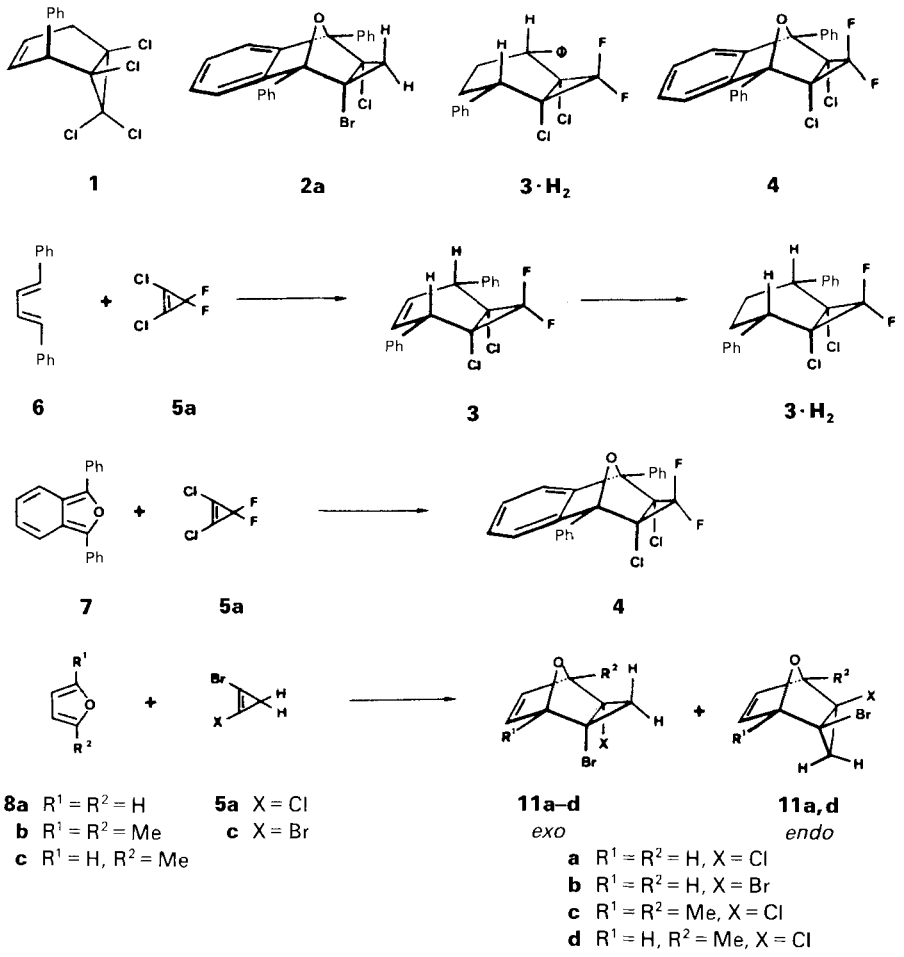
Introduction. – During the past years, we have applied *Diels-Alder* additions to halogenocyclopropenes, followed by aromatization of the adducts, as the principal route for synthesis of cyclopropararenes [1]. Since cyclopropararenes are planar, the relative configuration of the cycloadducts is lost in the subsequent step, and consequently presents only a secondary interest in the context of synthesis, although, in principle, it may have some consequences on the ease of the aromatization step [2]. However, when more and more data on cycloadducts accumulated, we felt it desirable to assign the structures unambiguously, but encountered difficulties due to conflicting evidence in comparison with literature data and to lack of conclusive criteria. Accordingly, we have obtained X-ray crystallographic structures of four cycloadducts which allow us to assign the relative configuration of most of our compounds by combination with NMR data. Our finding is that 1,2-dihalogeno- and tetrahalogenocyclopropenes add with exclusive *exo*-preference[1]) to diphenylisobenzofurans and strong *'exo'*-preference to butadienes and furans.

Results. – In [5], we have reported the structures of the adducts **1** (from tetrachlorocyclopropene and 1-phenyl-1,3-butadiene) and **2a** (from 1-bromo-2-chlorocyclopropene (**5b**) and 1,3-diphenylisobenzofuran (**7**)). This series was now completed by X-ray determination of the structures of **3**·H_2 and **4**[2]).

The cycloaddition of 1,2-dichloro-3,3-difluorocyclopropene (**5a**) to 1,4-diphenyl-1,3-butadiene (**6**) has been reported by us several years ago [8] *(Scheme)*. At that time, the *'endo'*-configuration was assigned to the adduct **3** on the grounds of analogy to the

[1]) The *'exo'* and *'endo'* descriptors are used to designate the orientation of the cyclopropane ring in the transition states *and* in the products of the cycloaddition to furans. The use of these descriptors is extended, by analogy, to cycloadditions of cyclopropenes to open-chain dienes [3] [4].

[2]) Data were collected on a *Philips PW-1100* diffractometer (MoK_α). The structure was solved by direct methods (MULTAN 80) [6] and refined by full-matrix least-squares analysis (XRAY 76) [7]. Crystallographic data have been deposited with the *Cambridge Data Center*, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.



proposed structure of the adduct of perchlorocyclopropene to **6** [9]. Since no suitable crystals of **3** could be obtained for X-ray analysis (presumably owing to twining), the compound was subjected to catalytic hydrogenation to yield **3**·H_2 (m.p. 136–138° (from EtOH); *Fig. 1*).

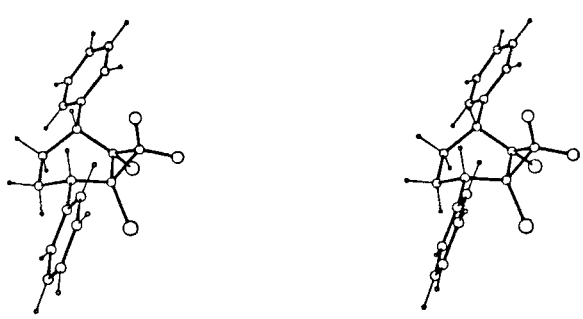


Fig. 1. *Stereoscopic view of* r-*1*,c-*6*-*dichloro*-*7*,*7*-*difluoro*-c-*2*,c-*5*-*diphenylbicyclo*[*4.1.0*]*heptane* (**3**·H_2)

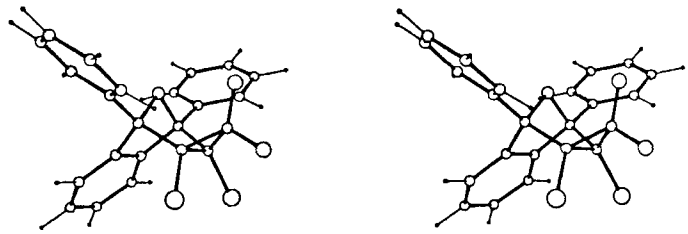


Fig. 2. *Stereoscopic view of* r-*1a*,c-*7a-dichloro-2,7-epoxy-1,1-difluoro-1a,2,7,7a-tetrahydro*-c-*2*,c-*7-diphenyl-1*H-*cyclopropa*[b]*naphthalene* (**4**)

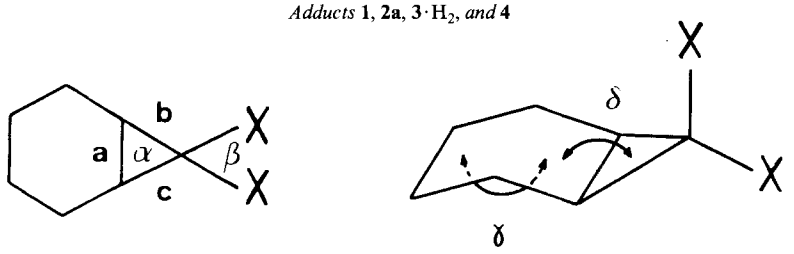
Table 1. *Crystal Data, Intensity Measurement and Structure Refinement for Cyclopropene Adducts* **1**, **2a**, **3**·H_2, *and* **4**

	1	**2a**	**3**·H_2	**4**
Formula	$C_{13}H_{10}Cl_4$	$C_{23}H_{16}BrClO$	$C_{16}H_{19}Cl_2F_2$	$C_{23}H_{14}Cl_2F_2O$
Molecular weight	308.0	423.7	353.2	415.3
Crystal system	orthorhombic	monoclinic	triclinic	monoclinic
Space group	*Pbca*	$P2_1/c$	*P*-1	$P2_1/n$
Crystal size (mm)	0.08 × 0.21 × 0.25 × 0.25	0.15 × 0.15 × 0.28	0.15 × 0.18 × 0.19	0.20 × 0.25
a [Å]	7.2286 (13)	10.232 (3)	7.631 (2)	13.448 (3)
b [Å]	15.986 (4)	8.907 (2)	9.844 (1)	10.408 (2)
c [Å]	22.750 (7)	20.638 (9)	11.569 (2)	14.017 (3)
α [°]	90.0	90.0	106.80 (1)	90.0
β [°]	90.0	101.78 (1)	93.89 (1)	100.03 (1)
γ [°]	90.0	90.0	94.26 (2)	90.0
Z	8	4	2	4
D_c [g·cm^{-3}]	1.56	1.53	1.42	1.43
F_{000}	1248	856	364	848
μ [mm^{-1}]	0.878	2.364	0.408	0.370
$(\sin\theta/\lambda)_{max}$ [Å^{-1}]	0.528	0.482	0.595	0.528
No. of measured reflections	1901	1935	2902	2664
No. of observed reflections	1042	1269	1912	1636
Criterion for observed reflections	$\|F_o\| > 4\sigma(F_o)$ and $\|F_o > 8$	$\|F_o\| > 4\sigma(F_o)$ and $\|F_o > 8$	$\|F_o\| > 4\sigma(F_o)$ and $\|F_o > 8$	$\|F_o\| > 4\sigma(F_o)$ and $\|F_o > 8$
No. of parameters	154	234	208	254
Refinement (on *F*)	full-matrix	2 blocks	full-matrix	2 blocks
Weighting scheme	$w = 1$	$w = 1$	$w = 1/\sigma^2(F)$	$w = 1$
H-atoms	calculated	calculated	calculated	calculated
Max. and average Δ/σ	0.0010, 0.0002	0.347, 0.064	0.0036, 0.0008	0.672, 0.024
Max. and min. $\Delta\rho$ (eÅ^{-3})	0.43, −0.46	0.63, −1.05	0.32, −0.35	0.24,−0.28
S	1.94	3.08	2.49	2.31
R, R_w (%)	5.2, –	6.2, –	5.7, 3.0	4.8, –

The cycloadduct **4** *(Fig. 2)* was obtained upon mixing equimolar amounts of **5a** and 1,3-diphenylisobenzofuran (**7**) in CH_2Cl_2 at −20° and allowing the mixture to warm up to r.t. Recrystallization from EtOH afforded transparent prisms (m.p. 113°). *Table 1* summarizes crystallographic data, and *Table 2* shows relevant structural parameters of compounds **1**, **2a**, **3**·H_2, and **4**.

Discussion. – a) *Adducts of 1,2-Dichloro-3,3-difluorocyclopropene* (**5a**). As demonstrated by the structures of **3**·H_2 and **4** in *Fig. 1* and *Fig. 2*, the cycloaddition of **5a** proceeds with both substrates in the *exo*-fashion. In the case of the addition to diphenyl-

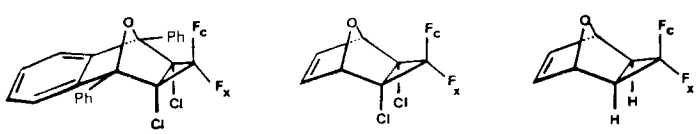
Table 2. *Selected Bond Distances* [Å], *Bond Angles* [°], *and Angles between Best Fitted Planes* [°] *for Cyclopropene Adducts* **1**, **2a**, **3**·H_2, *and* **4**



	1 X = Cl	**2a** X = H	**3**·H_2 X = F	**4** X = F
a	1.499 (11)	1.474 (13)	1.557 (6)	1.539 (8)
b	1.523 (11)	1.517 (15)	1.488 (6)	1.486 (8)
c	1.511 (11)	1.518 (14)	1.488 (6)	1.487 (7)
α	59.2 (5)	58.1 (6)	63.1 (3)	62.3 (4)
β	110.3 (4)	–	109.1 (3)	108.0 (4)
γ	166.9	110.4	124.0	108.8
δ	250.2	114.6	115.4	118.0

isobenzofuran **7** it was shown that the *exo*-adduct **4** is the result of kinetic control of the reaction. When **5a** and **7** were mixed at −70° in $CDCl_3$ and the ^{19}F-NMR spectra was recorded at low temperature (−70° to −20°), only the lines corresponding to the simultaneous presence of **4** and **5a** were observed. Although the absence of detectable amounts of the *endo*-isomers of **4** does not entirely rule out its occurrence as an intermediate in the reaction, it supports the hypothesis that the cycloaddition is not reversible, and that there is not stereomutation [10] occurring, which would interconvert an initially formed *endo*-adduct into the *exo*-isomer **4**. Analogous evidence could, however, not be obtained for **3**, because in this case the cycloaddition is carried out at elevated temperature (120°), and the desired product is obtained only in low yield [6] together with decomposition products.

The preference for *exo*-addition to open-chain dienes and furans appears to be general for tetrahalogenated cyclopropenes. While this work was in progress, we were informed by *Apeloig et al.* [3] that perchlorocyclopropene adds *exo* to **6** and also to furan (**8a**), and not *endo*, as previously assumed [2] [11]. It is very likely, therefore, that the adduct **9** of **8a** to 1,2-dichloro-3,3-difluorocyclopropene (**5a**) also has *exo*- rather than the proposed *endo*-configuration [11]. This follows from comparison of the ^{19}F-NMR spectra of **4**, **9**, and **10**. For **10**, the *exo*-configuration of the cyclopropane ring has been established [12]. In **4**, **9**, and **10**, the F-substituent *syn* to the O-bridge (F_c) is strongly deshielded and resonates at 55.6 (**4**), 49.3 (**9**), and 56.9 ppm (**10**), while F_x appears at 32.0, 26.3, and 17.6 ppm. In contrast, cycloadducts of **5a** to open-chain dienes exhibit resonance lines in the range of 18 to 25 ppm (F_c) and 31 to 36 ppm (F_x) [1] [8] [13]. The deshielding by the



4 **9** **10**

O-bridge is also effective in the ^{1}H-NMR spectra of adducts of furans to **5b** and **5c** (see below) and provides a criterion for configurational assignment.

Comparison of the structural data in *Table 2* illustrates, in addition, the expected weakening of the central cyclopropane bond upon replacement of the H-atoms by F-atoms [14], which increases from 1.47 in **2a** to 1.54 Å in **3**·H_2 and **4**, while the lateral cyclopropane bonds are slightly shortened by 0.03 Å.

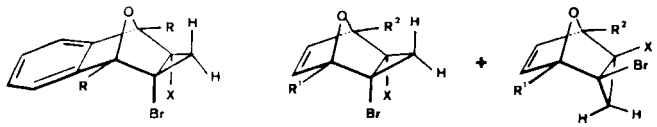
b) *Adducts of 1,2-Bromochlorocyclopropene* (**5b**). The structure of the adduct **2a** was originally assigned *exo* on the grounds that one of the geminal cyclopropane H-atoms appears at very low field in the ^{1}H-NMR (3.20 ppm) which was attributed to shielding by the O-bridge [4]. The H-atom *'anti'* to the O-bridge resonates in the normal range (2.18 ppm). Since the *exo*-structure of **2a** is now definitely established [5], this argument may be applied with confidence to other adducts of **5b** to isobenzofurans and furans. *Table 3* lists NMR data of compounds prepared in this and other laboratories, to which *exo*-configuration may be attributed on these grounds. All additions to isobenzofurans are stereoselective *exo*, which is not the case with furans, where in two cases the *endo*-isomers were also obtained. As expected [4], the cylcopropane protons of the *endo*-adducts resonate in a narrow range at *ca.* 2 ppm.

Table 3. *^{1}H-NMR Data of Addition Products of 1,2-Disubstituted Cyclopropenes to Isobenzofurans and Furans*[a])

Compound		δ [ppm]		$H(H_{syn}, H_{anti})$ [Hz]	Ref.
		H_{syn}	H_{anti}		
2a	R = Ph, X = Cl	3.20	2.18	7.0	[5]
2b	R = Ph, X = Br	3.22	2.13	7.3	[4]
2c	R = H, X = Cl	2.79	1.82	7.3	[16]
2d	R = Ph, X = $SiMe_3$	2.96	1.98	5.5	[4]
2e	R = H, $SiMe_3$[b]) X = Cl	2.68	1.81	8.0	[17]
11a *exo*	$R^1 = R^2$ = H, X = Cl	2.70	1.70	7.0	[16]
11b *exo*	$R^1 = R^2$ = H, X = Br	2.73	1.67	7.3	[4]
11c *exo*	$R^1 = R^2$ = Me, X = Cl	2.58	1.51	7.0	[16]
11d *exo*	R^1 = H, R^2 = Me, X = Cl	2.65	1.60	7.0	[16]
11a *endo*	$R^1 = R^2$ = H, X = Cl	2.25	1.96	7.8	[16]
11b *endo*	$R^1 = R^2$ = H, X = Br	2.27	1.96	7.5	[4]

[a]) Details on the synthesis of these compounds will be reported elsewhere [16].
[b]) Regioselectivity of addition undetermined.

Addition of **5b** to furan (**8a**) at −20° leads to a *ca.* 9:1 mixture of *exo*/*endo*-isomers of **14a**. The composition remains unchanged upon heating of the mixture to 60° for several hours. The isomers could be separated by preparative TLC, and a ^{1}H-NMR of the pure *endo*-**14a** was obtained at room temperature. Separation of *exo*/*endo*-isomers has also been achieved by *Halton* and coworkers [4] in the case of **14b**. This implies that the product composition is kinetically controlled as in the case of **4**. The observation of



2a–e **11a–d** *exo* + **11a,b** *endo*

a $R^1 = R^2 = H$, X = Cl
b $R^1 = R^2 = H$, X = Br
c $R^1 = R^2 = Me$, X = Cl
d $R^1 = H$, $R^2 = Me$, X = Cl

endo-adducts is, however, restricted to the unsubstituted furan itself. The methyl- (**8b**) and dimethyl-substituted (**8c**) furan afford exclusively *exo*-adducts with **5b**.

In contrast to these results, *Apeloig et al.* [3] recently presented conclusive evidence based on X-ray structures and NOE experiments for preferred *'endo'*-addition of 1-bromo-2-chlorocyclopropene (**5b**) to open-chain dienes.

c) exo/endo-*Preference for Cycloaddition of Halogenated Cyclopropenes.* In all cases where the structures are unambiguously established, it is obvious that tetrahalogenocyclopropenes add exclusively *exo* to 1,3-dienes and furans. In the light of this finding, the structures assigned to such adducts [11] [18] may need revision. Addition of 1-bromo-2-chlorocyclopropene to furans is preferentially *'exo'*, but *'endo'*-addition predominates in reactions with open-chain 1,3-dienes. The parent cyclopropene has an intrinsic preference for *endo*-addition to cyclopentadiene [19] and to open-chain dienes [3], but addition to **7** is exclusively *exo*, and 3,3-disubstituted cyclopropenes add preferentially *exo* to furans [15]. The presence of bulky substituents at C(3) may overrule the *endo*-preference and make *'exo'*-addition more favorable even for acyclic dienes [3] [20]. In addition, the influence of the vinylic halogen atoms of the cyclopropene must be taken into consideration: halogen substituents at dienophiles cause a strong preference for *endo*-addition [21] and may even compete with carboxyl groups for the *endo*-orientation [22]. Obviously, there must be a subtle balance between the intrinsic *endo*-preference of the cyclopropene *vs.* that of the halogen atoms, and this is further complicated by the steric effect due to the C(3) substituents of the cyclopropene and the preference of furans to react with cyclopropenes preferentially in an *'exo'*-mode. In our view, the various theoretical models dealing with *'exo'*/*'endo'*-preferences in *Diels-Alder* reactions [23] are not sufficiently developed to allow sound predictions in such complicated situations.

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