Cycloaddition of norbornadiene to fluorine-containing heteroaddends

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Cycloaddition reactions of norbornadiene with fluorinated heteroaddends (hexafluoroacetone, dichlorotetrafluoroacetone, trifluoroacetonitrile, and *N*-trifluoroacetylhexafluoropropan-2-imine) were studied. As a rule, the reactions follow the concerted mechanism. The reaction with bis(trifluoromethyl)ketene gave a mixture of tricyclene [2+2]- and [2+2+2]-cycloadducts formed along different pathways.

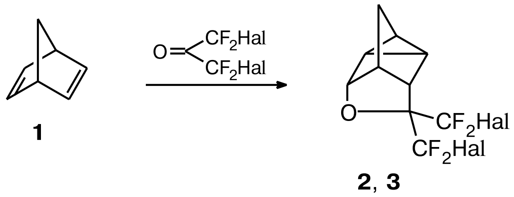
Key words: concerted cycloaddition, norbornadiene, tetracyclononane, heteroaddend.

Thermally allowed, concerted [2+2+2]-cycloaddition reactions of electron-withdrawing dienophiles with norbornadiene (NBD) **1** are known to give tetracyclononanes.[1—3] At the same time, fluorinated alkenes can enter into thermally forbidden [2+2]-cycloaddition reactions[4] through biradical transition states of the triplet type.[5]

We found that the reactions of NBD **1** with fluorinated heteroaddends usually yield [2+2+2]-cycloadducts. For instance, NBD **1** reacted with hexafluoroacetone and *sym*-dichlorotetrafluoroacetone at 80 and 150 °C to give oxatetracyclononanes **2** and **3**, respectively (Scheme 1).

The ^{19}F NMR spectrum of compound **3** revealed the nonequivalence of all the F atoms (four signals form two AB systems). This result can be explained by the diastereotopic effect of the enantiotopic nucleus of fluorine.

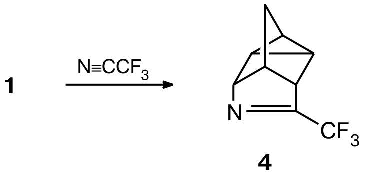
Scheme 1



Hal = F (**2**), Cl (**3**)

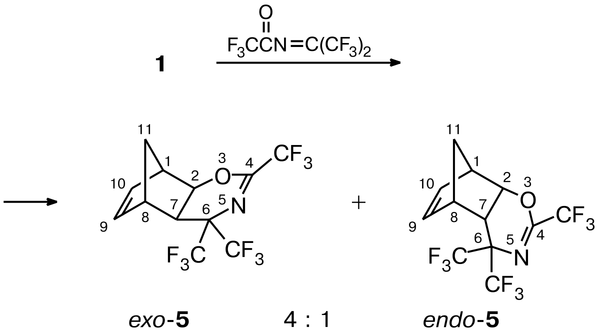
Nitriles are weak dienophiles; only the most electrophilic nitriles enter into concerted cycloaddition.[3] Indeed, NBD **1** reacted with trifluoroacetonitrile only at high temperatures (180—190 °C) and a long reaction time (40 h) was required to obtain azatetracyclononene **4** in 34% yield (Scheme 2).

Scheme 2



Apparently, the reaction of NBD **1** with *N*-trifluoroacetylhexafluoropropan-2-imine proceeds exclusively as [2+4]-cycloaddition. In this case, acylimine served as a diene, while NBD **1** acts as a dienophile. This agrees well with known[6] data on the high reactivities of perfluoroacylimines as electrophilic 1,3-dienes. The [2+4]-cycloaddition gave tricyclic oxazine **5** (Scheme 3) as a mixture of the *endo*- and *exo*-cycloadducts in the 1 : 4 ratio. The *endo*-isomer was assigned by considering the vicinal spin-spin coupling constants of the protons in the dissimilar

Scheme 3



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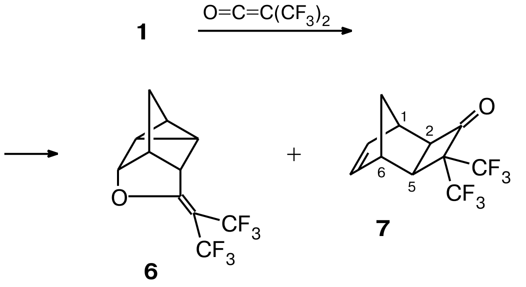
bridgeheads: $J_{H(1),H(2)}$ = 4.0 Hz, $J_{H(7),H(8)}$ = 3.0 Hz, and $J_{H(2),H(7)}$ = 8.4 Hz. The presence of the *exo*-configuration is confirmed by the nondetectable constants $J_{H(1),H(2)}$ and $J_{H(7),H(8)}$ (< 1 Hz) and the constant $J_{H(2),H(7)}$ = 7.0 Hz.[7]

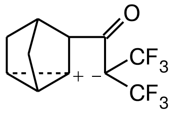
Among the heteroaddends studied, only bis(trifluoromethyl)ketene behaved ambiguously in the cycloaddition reaction with NBD **1**: under mild conditions, this reaction yielded a mixture of cycloadducts **6** and **7** (Scheme 4), which are well separated off by fractionation. Unsaturated tricyclic adduct **7** was obtained stereospecifically as the *exo*-isomer, as evident from the absence of significant vicinal spin-spin coupling constants of the protons in the dissimilar bridgeheads (H(1)—H(2), H(5)—H(6)) and the presence of the vicinal spin-spin coupling constant of the protons in the *endo*-positions ($J_{H(2),H(5)}$ = 6.0 Hz).[7]

Scheme 4



Apparently, the formation of adduct **7** follows the zwitterionic mechanism. Intermediate species **8** is highly stabilized by the electronic effects of the substituents.

Thus, we found that the reactions of NBD **1** with fluorinated heteroaddends predominantly occur as thermally allowed [2+2+2]- and [2+4]-cycloaddition.



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Partial [2+2]-cycloaddition, along with [2+2+2]-cycloaddition, in the reaction of NBD **1** with bis(trifluoromethyl)ketene is probably due to the high stabilization of the dipolar intermediate.

Experimental

^1H NMR spectra were recorded on a Bruker AC-300 spectrometer (300.13 MHz). ^{19}F NMR spectra were recorded using a Bruker DRX-500 spectrometer (470 MHz). Chemical shifts (δ) are referenced to Me_4Si (^1H) and CF_3COOH (^{19}F) as the external standards. IR spectra were recorded on a UR-20 spectrometer (thin film). The purity of the compounds obtained was checked by GLC on an HP 5890 II Series chromatograph fitted with an HP 5972A MSD mass-selective detector (column length 30 m, SE-30 as the mobile phase). The physicochemical characteristics, the elemental analysis data, the yields of the products, and the reaction conditions are given in Table 1. ^1H and ^{19}F NMR and IR spectra are presented in Table 2. Commercial reagents and solvents were prepared according to known procedures.[7]

Reactions of norbornadiene 1 with unsaturated polyfluorinated heteroaddends (general procedure). A mixture of an unsaturated addend (25 mmol) and NBD **1** (27.5 mmol) in dry ether (5 mL) was heated in a closed tube at a specified temperature (see Table 1). Volatile components were removed at a residual pressure of ~20 Torr and 20 °C and the residue was fractionated *in vacuo*. Compounds **6** and **7** were fractionated twice.

Table 1. Physicochemical characteristics of products **2**—**7**

Product	Reaction conditions		Yield (%)	B.p. /°C (*p*/Torr)	n_D^{20}	Found / Calculated (%)			Molecular formula
	T/°C	τ/h				C	H	N	
5,5-Bis(trifluoromethyl)-4-oxatetracyclo[4.2.1.0^{3,7}]nonane (**2**)	80	20	48	80 (24)	1.400	46.86 46.52	3.42 3.12	—	$C_{10}H_8F_6O$
5,5-Bis(chlorodifluoromethyl)-4-oxatetracyclo[4.2.1.0^{3,7}]nonane (**3**)	150	10	36	95 (5)	1.4595	41.65 41.26	2.90 2.77	—	$C_{10}H_8Cl_2F_4O$
5-Trifluoromethyl-4-azatetracyclo[4.2.1.0^{3,7}]non-4-ene (**4**)	180—190	40	34	30 (2)	1.4342	57.95 57.76	4.45 4.31	7.81 7.48	$C_9H_8F_3N$
4,4,6-Tris(trifluoromethyl)-3-oxa-5-azatricyclo[6.2.1.0^{2,7}]undeca-4,9-diene (**5**)	20	100	70	120 (20)	1.3960	40.58 40.81	2.42 2.28	4.12 3.97	$C_{12}H_8F_9NO$
5-[2,2,2-Trifluoro-1-(trifluoromethyl)ethylidene]-4-oxatetracyclo[4.3.0.0^{2,9}.0^{3,7}]nonane (**6**)	20	40	42	120 (10)	1.4300	48.66 48.90	2.57 2.98	—	$C_{11}H_8F_6O$
4,4-Bis(trifluoromethyl)tricyclo[4.2.1.0^{2,5}]non-7-en-3-one (**7**)	20	40	31	81 (10)	1.4145	48.56 48.54	3.55 3.70	—	$C_{11}H_{10}F_6O$

Table 2. Spectroscopic data for compounds **2**—**7**

Compound	NMR ($CDCl_3$, δ, *J*/Hz)		IR, ν/cm^{-1}
	^{1}H	^{19}F	
2	1.45 (m, 2 H, CH); 1.55 (m, 1 H, CH); 1.70 (br.s, 2 H, CH); 2.53, 2.80, 4.60 (all s, 1 H each, CH)	−7.41, −1.13 (both q, 3 F each, CF_3, J_{CF_3,CF_3} = 10.3)	2995 (C—H)
3	1.45 (m, 1 H, CH); 1.58 (m, 2 H, CH); 1.70 (s, 2 H, CH); 2.55, 2.92, 4.62 (all s, 1 H each, CH)	−24.2$_{B'}$ (d, 1 F, CF_2Cl, $J_{A'B'}$ = 173.0); −22.5$_{A'}$ (br.d, 1 F, CF_2Cl, $J_{A'B'}$ = 173.0); −19.2$_B$, −17.0$_A$ (both dm, 1 F each, CF_2Cl, J_{AB} = 177.2)	2991 (C—H)
4	1.60, 1.80 (both m, 2 H each, CH_2); 1.90 (m, 1 H, CH); 2.40, 3.10 (both br.s, 1 H each, CH); 4.50 (s, 1 H, CH)	−6.4 (s, 3 F, CF_3)	2992 (C—H); 1713 (C=N)
exo-**5**	1.48$_B$, 1.76$_A$ (both d, 1 H each, CH, J_{AB} = 10.0); 2.40 (d, 1 H, CH, $J_{H(7),H(2)}$ = 7.0); 3.25 (br.s, 2 H, CH); 4.55 (d, 1 H, CH, $J_{H(2),H(7)}$ = 7.0); 6.20, 6.50 (both br.s, 1 H each, =CH)	−3.49 (br.q, 3 F, CF_3, J_{CF_3,CF_3} = 10.8); −1.68 (q, 3 F, CF_3, J_{CF_3,CF_3} = 10.8); −1.21 (s, 3 F, CF_3)	2992 (C—H); 1713 (C=N)
endo-**5**	1.52$_B$, 1.60$_A$ (both dd, 1 H each, CH, J_{AB} = 10.0); 2.85 (dd, 1 H, CH, $J_{H(7),H(2)}$ = 8.4, $J_{H(7),H(8)}$ = 3.0); 3.20, 3.40 (both m, 1 H each, CH); 5.17 (dd, 1 H, CH, $J_{H(2),H(7)}$ = 8.4, $J_{H(2),H(1)}$ = 4.0); 6.10, 6.20 (both br.s, 1 H each, =CH)	−3.02, −2.54 (both q, 3 F each, CF_3, J_{CF_3,CF_3} = 10.3); −1.26 (s, 3F, CF_3)	2992 (C—H); 1713 (C=N)
6	1.65, 1.68, 1.72 (all m, 1 H each, CH); 1.80$_B$, 1.95$_A$ (both d, 1 H each, CH, J_{AB} = 12.0); 2.40, 3.45, 4.90 (all s, 1 H each, CH)	−20.82, −18.71 (both q, 3 F each, CF_3, J_{CF_3,CF_3} = 8.5)	2950 (C—H); 1662 (C=C)
7	1.55$_B$, 1.80$_A$ (both d, 1 H each, CH, J_{AB} = 9.7); 2.65 (d, 1 H, CH, $J_{H(5),H(2)}$ = 6.0); 3.38, 3.45 (both s, 1 H each, CH); 3.55 (dm, 1 H, CH, $J_{H(2),H(5)}$ = 6.0); 6.24, 6.38 (both m, 1 H each, =CH)	−14.0, −8.93 (both q, 3 F each, CF_3, J_{CF_3,CF_3} = 9.9)	2998 (C—H); 1803 (C=O); 1663 (C=C)

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