Homolytic addition of bromine-containing addends to cyclohexene

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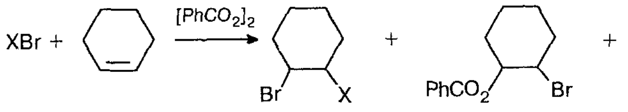
The addition of XBr (X = CCl_3, $CHBr_2$, CH_2CO_2Me, or $PhCH_2$) to cyclohexene in the presence of benzoyl peroxide (BP) or $Fe(CO)_5$ + DMF was studied. In the presence of BP, a product of the addition of the Br and $PhCO_2$ radicals is formed along with the expected adduct. The content of the former increases as the efficiency of XBr as the carrier of the chain reaction decreases.

Key words: radicals; addition; cyclohexene; bromotrichloromethane; bromoform; methyl bromoacetate; benzyl bromide; metallocomplex initiation.

In a continuation of the studies of radical addition involving organobromine compounds,[1] in the present work we studied the reactions of cyclohexene with a series of addends that react with the cleavage of the C—Br bond. It is known that cyclohexene is less reactive in radical addition than α-olefins.[2] However, from the synthetic viewpoint, taking into account possible chemical transformations of adducts, radical addition is the simplest way to incorporate a cyclohexyl moiety in the carbon chain of a molecule. It has been shown that the introduction of a cyclohexane ring into the chain of γ-aminobutyric acid considerably increases its biological activity.[3]

In this work we used CCl_3Br, $CHBr_3$, $BrCH_2CO_2Me$, and $PhCH_2Br$, which differ markedly in reactivity, as the addends in the reaction with cyclohexene. The reactions were carried out using both peroxide and metallocomplex initiation. In the presence of benzoyl peroxide (BP), the usual addition of addends or benzoyloxy radicals[4] is accompanied by competitive addition of the benzoyloxy radical followed by chain transfer to the addend (Scheme 1).

Scheme 1



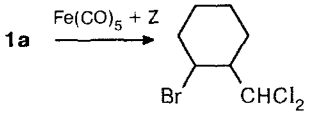
1a—d **2**

+ $PhCO_2C_6H_{11}$-*cyclo*

3

X = CCl_3 (**a**), $CHBr_2$ (**b**), CH_2CO_2Me (**c**), $PhCH_2$ (**d**)

The ratio of adducts **1a—d** and **2** depends considerably on the efficiency of the XBr addends as carriers of the reaction chain. For example, predominantly compound **1a** and only traces of **2** are formed in the case of CCl_3Br. The reaction involving bromoform and methyl bromoacetate produces compounds **1b,c** and **2** in the ratio ≈1.5 (Table 1), whereas the reaction with benzyl bromide, which has very low efficiency, gives compound **2** as the main product. In addition, a considerable amount of cyclohexyl benzoate (**3**) is formed along with adduct **2** due to chain transfer along the C—H bond. Probably, the difference in the polar characteristics of the attacking nucleophile and the olefin is yet another factor that determines this ratio. In the case of polyhalomethanes and methyl bromoacetate, the attacking radicals are rather electrophilic, and they react with nucleophilic cyclohexene faster than the nucleophilic benzyl radical, other conditions being equal. Thus, both factors, the ease of cleavage of the C—Br bond and the polar nature of the radical being added, act in the same direction, whereas addition of the benzoyloxy radicals to cyclohexene can always be regarded as a standard process, which obviously occurs with an invariable rate constant. The selective formation of adducts occurs when the $Fe(CO)_5$+DMF complex system is used as the initiator (see Table 1). Here we should point out how the features of some of the reactions observed depend on the nature of the reactants and the reaction conditions. The addition of CCl_3Br is accompanied by secondary reduction of the CCl_3 group in the adduct.



4

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Table 1. Interaction of cyclohexene with bromine-containing addends*

Addend	In the presence of BP, 2 h, 100 °C			In the presence of $Fe(CO)_5$ + DMF		
	Degree of conversion	Yield of **1**	Yield of **2**	T/°C	Degree of conversion	Yield of **1a—d**
CCl_3Br	32	18.6	0.34	75—80	~100	22
$CHBr_3$	23	14.3	8.8	100	37	30
$BrCH_2CO_2Me$	30	10.6	7.0	140	32	7.0
$PhCH_2Br$	8.0	0.4	3.9	140	40	1.9
		(yield of **3**, 1.3 %)			(yield of **5**, 3.6 %)	

* The conversion and yield are expressed in %.

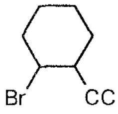
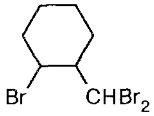
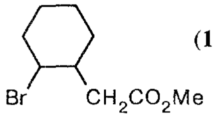
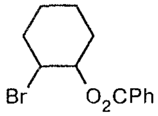
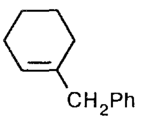
It is interesting that the fraction of compound **4** with respect to adduct **1a** depends largely on the nature of cocatalyst Z: almost no compound **4** is formed in the case of DMF; the yield of **4** reaches 5—10 % when HMPA or triphenylphosphine are used, and is as high as 40 % in the case of 1-benzoyl-2-methoxycarbonylpyrrolidine.

The replacement of BP as the initiator by $Fe(CO)_5$ + DMF in the reaction of bromoform with cyclohexene results in a considerable increase in the yield of adduct **1b**, while the yield of **1c** decreases in the case of methyl bromoacetate (see Table 1).

When $Fe(CO)_5$ is present, adduct **1d** undergoes partial dehydrobromination during the reaction (and complete dehydrobromination during preparative isolation) to give 1-benzylcyclohexene (**5**) as a mixture of isomers.

Adducts **1a—c**, **2**, and **5** were isolated as individual compounds and characterized by physicochemical methods. Their structures were confirmed by ^{13}C spectroscopic (Table 2) and mass-spectral data. The ^{13}C NMR spectrum of each adduct **1a—c** contains two groups of signals similar in intensity, which indicates that *cis-* and *trans-*isomers are present in approximately equal amounts.

Table 2. Physicochemical characteristics of the compounds obtained

Compound		B.p./°C (p/Torr)	n_D^{20}	d_4^{20} /g cm^{-3}	^{13}C NMR (Me_4Si), δ		Found / Calculated (%)			Molecular formula
					CHBr	CHX	C	H	Br	
	(**1a**)	95(1)	1.5472	1.5989	50.3, 51.6	61.0, 61.9	29.80 29.98	3.62 3.60	66.54 66.42	$C_7H_{10}BrCl_3$
	(**1b**)	99(1)	1.5762	1.9716	55.9, 58.3	53.1, 52.3	25.41 25.10	3.46 3.31	70.98 71.59	$C_7H_{11}Br_3$
	(**1c**)	94—96(1)	1.4971	1.3412	58.2, 60.5	38.7, 43.0	46.01 45.97	6.36 6.43	33.91 33.99	$C_9H_{15}BrO_2$
	(**2**)	125(0.1)	1.5500	1.3581	52.5, 54.3	72.5, 75.8	55.70 55.14	5.40 5.34	27.90 28.22	$C_{13}H_{15}BrO_2$
	(**5**)	65(1)	1.5397	0.9638	—	—	90.40 90.60	9.23 9.40	—	$C_{13}H_{16}$

Experimental

Mass spectra were obtained on a VG-7070E chromato-mass spectrometer with a DB-5 column (50 m) using the 30—220 °C (2.5 °C min^{-1}) temperature mode. The *m/z* values for ions refer to the ^{79}Br and ^{35}Cl isotopes. ^{13}C NMR spectra were recorded in $CHCl_3$ on a Bruker WP-200 spectrometer in the IMODECHO mode. GLC analyses were carried out on an LKhM-80 chromatograph equipped with a steel column (1300×3 mm) using 15 % SKTFT-50Kh on Chromaton N-AW, helium (60 mL min^{-1}) as the carrier gas, and a catharometer as the detector; the temperature was programmed in the range 50—250 °C at the rate of 6 °C min^{-1}. Preparative GLC was performed on a 1300×9 mm steel column with 20 % SKTFT-50Kh on the same support using helium (120 mL min^{-1}) as the carrier gas.

Addition of bromine-containing addends to cyclohexene. ***A.*** In the presence of BP. An addend (10 mmol), cyclohexene (10 mmol), and BP (0.5 mmol; 0.1 mmol in the case of CCl_3Br) were placed in a glass tube. The tube was sealed and heated for 2 h at 100 °C in an oil bath. The reaction products formed in four experiments were combined, washed with a Na_2CO_3 solution (to remove the acid) and water and then dried with $CaCl_2$. The unchanged cyclohexene and addend were distilled off and the residue was distilled *in vacuo.* Adducts **1a—c** and **2** were isolated by distillation; preparative GLC was used for additional purification. The physicochemical constants and the data from elemental analyses and ^{13}C NMR spectroscopy are presented in Table 2. Experiments with methyl bromoacetate were carried out with varying amounts of BP (Table 3).

Table 3. Results of experiments in the presence of BP

[BP]	Degree of conversion	Yield (%)	
(mol. %)	of methyl bromoacetate (%)	**1c**	**2**
2	19.5	4.5	2.2
5	30.0	10.6	7.0
10	~75.0	15.0	10.0

B. In the presence of $Fe(CO)_5$ + DMF. An addend (10 mmol), cyclohexene (10 mmol), $Fe(CO)_5$ (1 mmol), and DMF (3 mmol) were placed in a glass tube (*V* = 25 mL). The tube was sealed and heated for 2 h at a specified temperature (see Table 1). The reaction products formed in 10 experiments were combined, dissolved in chloroform, washed three times with HCl (1 : 1) and three times with water, and then dried with $CaCl_2$. The chloroform and cyclohexene were distilled off, and the residue was distilled *in vacuo*. Experiments with $BrCCl_3$ were carried out in the presence of $Fe(CO)_5$ and various cocatalysts; the yields of compounds **1a** and **4** were determined by GLC using an internal standard (Table 4).

Table 4. Results of experiments in the presence of cocatalysts

Cocatalyst	C_{cocat} (mol. %)	Yield (%)	
		1a	**4**
DMF	30	22	<1
HMPA	30	20	1.6
Ph_3P	10	40	4.2
1-Benzyl-2-methoxycarbonylpyrrolidine	10	18	13

Mass spectra of the compounds formed, *m/z* (I_{rel}(%)), number of halogen atoms: **1a** (one of the diastereomers): 278 $[M]^{+\cdot}$ (15.2), 1 Br, 3 Cl; 243 $[M-Cl]^+$ (4.3), 1 Br, 2 Cl; 207 $[M-Cl-HCl]^+$ (37.0), 1 Br, 1 Cl; 199 $[M-Br]^+$ (32.6), 3 Cl; 163 $[M-Cl-HBr]^+$ (89.1), 2 Cl; 127 $[M-Cl-HCl-HBr]^+$ (100.0), 1 Cl; 91 $[C_7H_7]^+$ (65.2); 81 $[C_6H_9]^+$ (52.2). **1b** (one of the diastereomers): 332 $[M]^{+\cdot}$ (1.8), 3 Br; 253 $[M-Br]^+$ (1.2), 2 Br; 173 $[M-Br-HBr]^+$ (100.0), 1 Br; 93 $[M-Br-2\ HBr]^+$ (71.4); 91 $[C_7H_7]^+$ (53.3); 81 $[C_6H_9]^+$ (49.7). **1c** (one of the diastereomers) 234 $[M]^{+\cdot}$ (<1), 1 Br, 203 $[M-OMe]^+$ (4.7), 1 Br; 155 $[M-Br]^+$ (34.9); 154 $[M-HBr]^+$ (4.7); 123 $[M-HBr-OMe]^+$ (32.6); 95 $[M-HBr-CO_2Me]^+$ (46.5); 81 $[M-Me-CO_2H]^{+\cdot}$ (76.7); **1d** (one of the diastereomers): 252 $[M]^{+\cdot}$ (13.1); 173 $[M-Br]^+$ (21.4); 172 $[M-HBr]^{+\cdot}$ (7.0); 105 $[Ph(CH_2)_2]^+$ (10.7); 104 $[PhCH{=}CH_2]^+$ (7.5); 91 $[PhCH_2]^+$ (100); 81 $[C_6H_9]^+$ (42.9). **2** (one of the diastereomers): 282 $[M]^{+\cdot}$; 203 $[M-Br]^+$ (0.5); 202 $[M-HBr]^{+\cdot}$ (0.5); 160 $[M-PhCO_2H]^{+\cdot}$ (17.0), 1 Br; 123 $[PhC(OH)_2]^+$ (45); 105 $[PhCO]^+$ (100); 81 $[M-PhCO_2H-Br]$ (48); 77 $[Ph]^+$ (32); **3**: 204 $[M]^{+\cdot}$ (<1); 123 $[PhC(OH)_2]^+$ (100); 105 $[PhCO]^+$ (95); 77 $[Ph]^+$ (51.0). **4** (one of the diastereomers): 244 $[M]^{+\cdot}$ (6.5), 1 Br, 2 Cl; 165 $[M-Br]^+$ (28.3), 2 Cl; 164 $[M-HBr]^+$ (21.7), 2 Cl; 129 $[M-Br-HCl]^+$ (100), 1 Cl; 93 $[M-Br-2\ HCl]^+$ (37.0); 81 $[C_6H_9]^+$ (19.6). **5**: 172 $[M]^{+\cdot}$ (47.6); 143 $[M-Et]^+$ (4.8); 129 $[M-C_3H_7]^+$ (17.9); 115 $[M-C_4H_9]^+$ (11.9); 104 $[PhCH{=}CH_2]^{+\cdot}$ (19.0); 91 $[PhCH_2]^+$ (50.0); 81 $[C_6H_9]^+$ (100); 80 $[C_6H_8]^+$ (52.4).

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