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Synthesis and Dehydrobromination of 3-Bromomethyl- and 3-Bromo-3-methoxymethylcyclobutane-1-carbonitriles and Methyl 3-Bromomethyl- and 3-Bromo-3-methoxymethylcyclobutane-1-carboxylates

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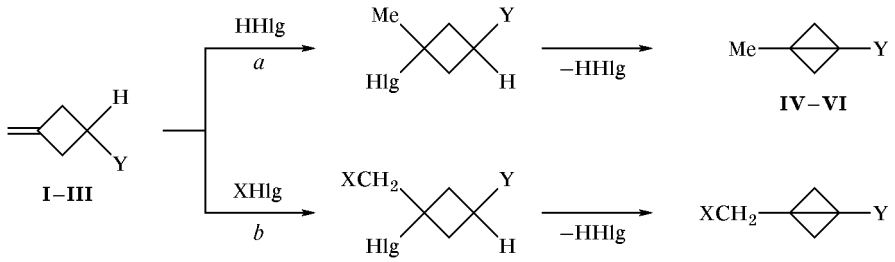
Abstract—The anti-Markownikoff products of bromination and bromomethoxylation of 3-methylenecyclobutane-1-carbonitrile and methyl 3-methylenecyclobutane-1-carboxylate were subjected to dehydrobromination by the action of potassium *tert*-butoxide in THF. The reaction takes two elimination pathways: 1,3-dehydrobromination to give bicyclobutane derivatives and 1,2-dehydrobromination leading to substituted methylenecyclobutane. Structural factors in the substrate were revealed, which are responsible for the ratio of the two concurrent elimination processes.

3-Methylenecyclobutane-1-carbonitrile (**I**) is a cycloadduct formed by thermal reaction of allene with acrylonitrile [1]. As early as 1966, Blanchard and Cairncross [2] successfully converted compound **I** into 3-methylbicyclo[1.1.0]butane-1-carbonitrile (**IV**) via successive hydrohalogenation–dehydrohalogenation. Later on [3, 4], following an analogous approach (pathway *a* in Scheme 1), structurally related bicyclobutane derivatives **V** and **VI** were synthesized from the corresponding methylenecyclobutanes **II** and **III**. We anticipated that the scope of application of the above and analogous methylenecyclobutane derivatives in the synthesis of bicyclobutanes can be extended if the first stage would be addition of XHlg (pathway *b* in Scheme 1). In this case, as in the hydrohalogenation, halogen atom could be introduced into the cyclobutane fragment, providing the possibility for synthesizing 3-(X-methyl)bicyclo[1.1.0]butane-1-carbonitrile and its analogs.

The present communication reports on our attempts to synthesize bicyclobutane derivatives according to pathway *b*. 3-Methylenecyclobutane-1-carbonitrile (**I**) and methyl 3-methylenecyclobutane-1-carboxylate (**II**) were used as starting compounds which were brought into bromination and bromomethoxylation reactions. First, let us consider the results of XHlg addition. The bromination of **I** and **II** was carried out with a solution of bromine in carbon tetrachloride at 20°C. In both cases, the corresponding dibromo derivatives (**VII**, Y = CN, and **VIII**, Y = CO_2Me; Scheme 2) were obtained, each being a mixture of two diastereoisomers. Pure diastereoisomers **VIIa**, **VIIb**, **VIIIa**, and **VIIIb** were isolated by column chromatography. The bromomethoxylation of methylenecyclobutanes **I**

Scheme 1.



I, **IV**, Y = CN; **II**, **V**, Y = CO_2Me; **III**, **VI**, Y = COMe; X = Br, OMe.

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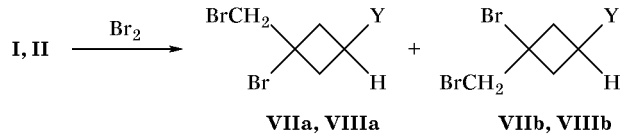
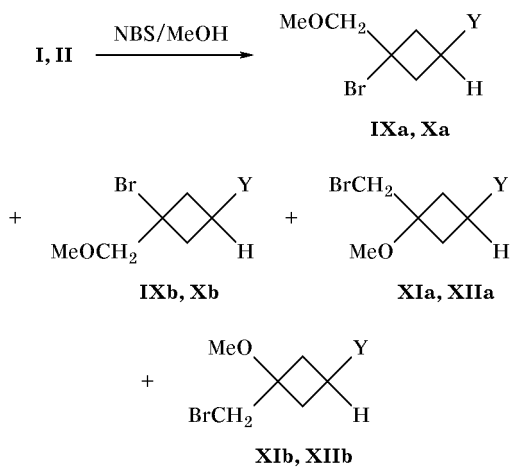
Scheme 2.



VIIa, VIIIa **VIIb, VIIIb**

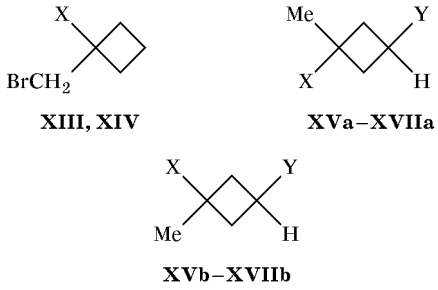
and **II** was effected by the action of *N*-bromosuccinimide (NBS) in methanol at 20°C. Gas chromatographic–mass spectrometric analysis of the reaction mixtures showed the presence in each case of four bromomethoxylation products which were formed according to the Markownikoff rule (**XI**, Y = CN; **XII**, Y = CO_2Me) and contrary to it (**IX**, Y = CN; **X**, Y = CO_2Me); each adduct was a mixture of two diastereoisomers (Scheme 3). For comparison, we also performed bromomethoxylation of unsubstituted methylenecyclobutane. As a result, only the Markownikoff adduct (**XIII**) was obtained.

Scheme 3.



The product mixture obtained by bromomethoxylation of nitrile **I** was subjected to chromatographic separation in a column charged with silica gel. Two fractions containing stereoisomeric mixtures **IXa**/**IXb** and **XIa**/**XIb** were isolated. By crystallization of chromatographically inseparable mixture **XIa**/**XIb** we succeeded in isolating pure isomer **XIb**. The isomer mixture obtained by bromomethoxylation of ester **II** was not subjected to chromatographic separation. Distillation gave a mixture of compounds **XIIa** and **XIIb** containing 6% of **Xa**/**Xb**. All cyclobutane derivatives were characterized by ^1H and ^{13}C NMR and mass spectra.

^{13}C NMR spectroscopy turned out to be very useful for structure determination of compounds **VII**–**IX**, **XI**, and **XII**. First of all, the ^{13}C NMR spectra indicated that these products are 1,1,3-trisubstituted cyclobutane derivatives. Comparison of the chemical shifts of C^3 (which has no protons attached thereto) allowed us to distinguish between bromocyclobutanes **VII**, **VIII**, and **IX** (δ_C 53.4–60.0 ppm) and methoxycyclobutanes **XI** and **XII** (δ_C 73.9–76.6 ppm). The ^{13}C signals were assigned on the basis of known correlations and the data for compounds **XIV**–**XVII** (Tables 1, 2).



XIII, XIV **XVa–XVIIa** **XVb–XVIIb**

XIV, **XV**, X = Br; **XIII**, **XVI**, **XVII**, X = OMe; **XV**, **XVI**, Y = CN; **XVII**, Y = CO_2Me.

The ^1H NMR spectra of **VII**–**IX**, **XI**, and **XII** are fully consistent with the assigned structures. Moreover, following the recommendations formulated in [5], we were able to determine the configuration of each diastereoisomer in accordance with configurations of stereoisomers of **XV**–**XVII**. The 1-H signal in the spectra of *trans* isomers (**a**) is located appreciably downfield relative to the corresponding signal of *cis* isomers (**b**) ($\Delta\delta$ = 0.3 ppm) due to deshielding effect of the *cis*-oriented bromine atom (or methoxy group) on C^3.

A reliable proof for the assigned structure (but not configuration) of compounds **IX**–**XII** is provided by their mass spectra (Table 3). The mass spectra of substituted methoxycyclobutanes **XI** and **XII** characteristically contain the [$M-CH_2Br$] fragment ion peak, while substituted bromocyclobutanes **IX** and **X** show in the spectra a strong peak with *m*/*z* 45; these features allowed us to reliably distinguish the above compounds differing by the relative position of the methoxy group which gives rise to β-decomposition of the molecular ion. Furthermore, the cyclobutane structure of compounds **IX**–**XII** is confirmed by the presence of ion peaks with *m*/*z* 152, 150, 71, and 55 (the latter only for esters **X** and **XII**), which are formed as a result of retro-[2+2]-cycloaddition fragmentation of the molecular or fragment ions [6].

Table 4 contains data characterizing the selectivity of addition to nitrile **I** and ester **II**. The observed violation of regioselectivity in the bromomethoxylation of the terminal double bond in going from unsubstituted methylenecyclobutane to its derivatives **I** and

Table 1. ^{1}H and ^{13}C NMR spectra of substituted bromocyclobutanes **VIIa**, **VIIb**, **VIIIa**, **VIIIb**, **IXa**, **IXb**, **XIV**, **XVa**, and **XVb**

Comp. no.	^{1}H NMR spectrum, δ, ppm (*J*, Hz)					^{13}C NMR spectrum, δ_C, ppm					
	1-H	2-H, 4-H		CH_2X [CH_3]	OCH_3	C^1	C^2, C^4	C^3	CH_2X [CH_3]	OCH_3	CN [CO]
VIIa	3.56 (9) quint	3.02–3.16	2.80–2.93	3.84 s	–	16.7	41.0	58.9	41.0	–	120.0
VIIb		3.09–3.24		3.83 s	–	17.0	41.2	54.2	40.5	–	120.4
VIIIa	3.52 (9) quint	2.83–2.95	2.68–2.80	3.83 s	3.70 s	31.5	40.3	60.0	42.7	51.9	[173.9]
VIIIb	3.04–3.18 (3H)		2.86–3.00	3.88 s	3.73 s	32.8	40.8	55.5	42.0	52.1	[173.4]
IXa	3.45 m	2.90–3.05	2.64–2.79	3.52 s	3.41 s	17.2	39.1	58.6	77.8	59.0	120.3
IXb		2.90–3.05		3.53 s	3.38 s	17.5	40.4	53.4	78.5	58.9	120.6
XVa	3.46 (9) quint	2.87–3.04	2.59–2.75	[1.95 s]	–	17.3	45.0	58.3	[33.6]	–	120.8
XVb	2.90–3.17 (3H)		2.67–2.89	[1.86 s]	–	17.2	44.9	52.6	[31.8]	–	120.3
XIV[a]	1.46–2.46 (2H)	2.56 m (4H)		3.76 s	–	16.0	37.7	62.7	46.0	–	–

[a] The data for compound **XIV** were taken from [7]. For the sake of convenience in comparing the chemical shifts of **XIV** with the data for the other compounds, the atoms in **XIV** were numbered in such a way that its quaternary carbon atom had number 3.

Table 2. ^{1}H and ^{13}C NMR spectra of substituted methoxycyclobutanes **XIa**, **XIb**, **XIIa**, **XIIb**, **XIII**, **XVIa**, **XVIb**, **XVIIa**, and **XVIIb**[a]

Comp. no.	^{1}H NMR spectrum, δ, ppm (*J*, Hz)					^{13}C NMR spectrum, δ_C, ppm					
	1-H	2-H, 4-H		CH_2X [CH_3]	OCH_3	C^1	C^2, C^4	C^3	CH_2X [CH_3]	OCH_3	CN [CO]
XIa	3.12 m	2.47–2.62	2.34–2.45	3.67 s	3.20 s	14.1	34.8	76.6	35.9	49.9	121.9
XIb	2.80 (9) quint	2.48–2.65		3.53 s	3.23 s	13.2	35.3	75.1	35.0	49.9	121.0
XIIa	3.08 m			3.65 s	3.69 s	29.9	34.0	76.2	37.8	50.1	[176.5]
		2.22–2.35			3.20 s					52.6	
XIIb	2.72 (9) quint	2.35–2.55		3.58 s	3.69 s	29.6	34.3	73.9	37.8	50.1	[175.0]
					3.22 s					52.6	
XIII[b]	1.48–1.66	2.09–2.27	1.90–2.05	3.61 s	3.17 s	11.7	30.2	77.8	37.3	49.5	–
	1.70–1.85										
XVIa	3.08 m	2.12–2.37		[1.41 s]	3.12 s	14.5	37.4	76.1	[23.3]	49.7	122.8
XVIb	2.69 (9) quint	2.37–2.58		[1.28 s]	3.14 s	13.2	38.2	73.9	[21.6]	49.7	121.7
XVIIa	2.90–3.17			[1.30 s]	3.14 s	29.9	35.7	75.8	[23.2]	49.6	[176.0]
		2.05–2.20			3.65 s					51.5	
XVIIb	2.67 (9) quint	2.26–2.40		[1.27 s]	3.14 s	28.7	36.7	72.7	[22.4]	49.4	[175.0]
					3.65 s					51.5	

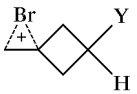
[a] The data for individual diastereoisomers of **XII**, **XVI**, and **XVII** were determined from the spectra of the corresponding two-component mixtures **XIIa**/**XIIb**, **XVIa**/**XVIb**, **XVIIa**/**XVIIb**; the 2-H and 4-H proton signals were not distinguished.

[b] For the sake of convenience in comparing the chemical shifts of **XIII** with the data for the other compounds, the atoms in **XIII** were numbered in such a way that its quaternary carbon atom had number 3.

Table 3. Mass spectra of bromomethoxylation products of nitrile **I** and ester **II** (GC–MS data)

Comp. no.	Retention time, min	*m*/*z* (I_{rel}, %)
IXa	6.7	205 (1) and 203 (1) M^+, 152 (2), 150 (2), 124 (12), 94 (12), 92 (13), 71 (25), 65 (15), 45 (100), 41 (30), 39 (30)
IXb	8.2	205 (0.3) and 203 (0.3) M^+, 152 (4), 150 (4), 124 (25), 92 (5), 71 (20), 65 (6), 45 (100), 41 (14), 39 (12)
XIa	18.1	205 (0.4) and 203 (0.4) M^+, 152 (78), 150 (78), 110 (35), 71 (100), 57 (16), 41 (59), 39 (24)
XIb	22.8	205 (0.4) and 203 (0.4) M^+, 152 (75), 150 (75), 110 (27), 71 (100), 57 (13), 41 (58), 39 (23)
Xa	3.5	238 (0.3) and 236 (0.3) M^+, 207 (4), 205 (4), 157 (7), 156 (4), 152 (6), 150 (6), 125 (27), 97 (100), 93 (10), 87 (12), 72 (25), 71 (20), 67 (12), 65 (10), 59 (15), 55 (37), 53 (16), 45 (89), 41 (41), 39 (25)
Xb	4.5	238 (0.3) and 236 (0.3) M^+, 207 (4), 205 (4), 157 (14), 152 (8), 150 (8), 125 (31), 97 (100), 93 (11), 87 (21), 71 (29), 67 (11), 65 (9), 59 (13), 55 (22), 53 (13), 45 (57), 41 (36), 39 (18)
XIIa	8.9	238 (0.2) and 236 (0.2) M^+, 207 (9), 205 (9), 179 (5), 177 (5), 157 (16), 152 (100), 150 (100), 143 (20), 97 (20), 93 (18), 71 (85), 55 (14), 43 (14), 41 (50), 39 (15)
XIIb	11.1	238 (0.4) and 236 (0.4) M^+, 207 (10), 205 (10), 179 (3), 177 (3), 157 (12), 152 (100), 150 (100), 143 (11), 97 (13), 93 (9), 71 (76), 55 (15), 43 (12), 41 (51), 39 (16)

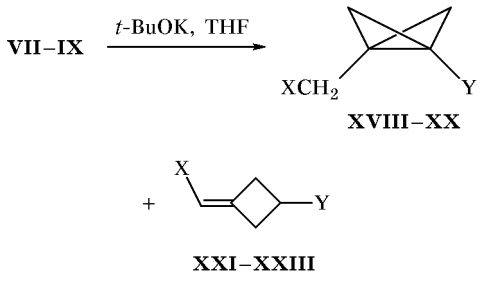
II having an electron-acceptor group in position *3* deserves special comment. Assuming that π-complex **A** is the key intermediate in the reaction under study, strict regioselectivity (according to Markownikoff) in the addition to unsubstituted methylenecyclobutane may be explained in terms of the asymmetric structure of complex **A** (Y = H) due to displacement of the bromine atom from the bridgehead carbon atom, which is caused by positive inductive effect of the cyclobutane methylene groups. Intermediates **A** with Y = CN or CO_2Me are more symmetric due to negative inductive effect of the Y group, so that anti-Markownikoff addition becomes possible. In this case, greater violation of the regioselectivity should be expected for the addition to nitrile **I** [$\sigma_I(CN) = 0.60$] rather than to ester **II** [$\sigma_I(CO_2Me) = 0.32$], as is observed experimentally.



A

Let us consider the results of dehydrobromination of substituted bromocyclobutanes **VIIa**, **VIIb**, **VIIIa**, **VIIIb**, **IXa**, and **IXb** which are potential precursors of bicyclobutane derivatives (pathway *b* in Scheme 1). As a dehydrobrominating agent we used potassium *tert*-butoxide in tetrahydrofuran. This reagent turned out to be effective in the synthesis of bicyclobutane **IV** [2, 8]. In fact, in all cases, 1,3-dehydrobromination occurred to give bicyclobutane derivatives **XVIII**–**XX** (Scheme 4). However, the main process was accompanied by 1,2-dehydrobromination, leading to formation of substituted methylenecyclobutanes **XXI**–**XXIII**. In none of the cases, the second possible 1,2-dehydrobromination product (cyclobutene derivative) was detected.

Scheme 4.



XVIII, **XIX**, **XXI**, **XXII**, X = Br; **XX**, **XXIII**, X = OMe; **XVIII**, **XX**, **XXI**, **XXIII**, Y = CN; **XIX**, **XXII**, Y = CO_2Me.

The structure of dehydrobromination products **XVIII**–**XXIII** was determined on the basis of their ^1H and ^{13}C NMR spectra. Table 5 contains the data for bicyclobutanes **XVIII**–**XX** and (for comparison) model bicyclobutane **IV**. Noteworthy is that the difference in the chemical shifts of magnetically nonequivalent methylene protons is about 1 ppm, while the corresponding coupling constant $^2J_{HH}$ is close to zero. A characteristic feature of the ^{13}C NMR

Table 4. Regio- and stereoselectivity of bromomethoxylation (BM) and bromination (B) of substituted methylenecyclobutanes **I** and **II**

Comp. no.	Regioselectivity (BM)[a]	Stereoselectivity (*trans* : *cis*)		
		BM[b]	BM[c]	B
I	5.9 : 1	46.5 : 39	6.5 : 8	54 : 46
II	15.7 : 1	48.5 : 45.5	2.5 : 3.5	51 : 49

[a] Ratio of the Markownikoff and anti-Markownikoff adducts.
[b] According to the Markownikoff rule.
[c] Contrary to the Markownikoff rule.

spectra of 1-cyanobicyclobutanes **XVIII**, **XX**, and **IV** is upfield shift of the C^1 signal (up to a negative δ_C value).

The structure of methylenecyclobutane derivative **XXI**, which was isolated in the pure state, unambiguously follows from the NMR spectral data, taking into account the expected similarity with the spectra of **I** (see Experimental). The ^{1}H NMR spectrum of **XXI** characteristically contains a signal at δ ~6 ppm from the olefinic proton, and the C^2 and C^4 atoms give different but closely located signals in the ^{13}C NMR spectrum (δ_C 35–37 ppm). Olefins **XXII** and **XXIII** were detected by NMR spectroscopy among products of dehydrobromination of compounds **VIII** and **IX**, respectively (signals typical of the methylenecyclobutane structure were present).

Below are given the ratios of products formed by the two concurrent dehydrobromination processes (i.e., bicyclobutane and methylenecyclobutane derivatives, BCB : MCB) for the series of substituted bromocyclobutanes **VII**–**IX** differing by the stereochemistry or substitution pattern: **VIIa**, 0.5; **VIIb**, 0.05; **VIIIa**, 4.3; **VIIIb**, 2.2; **IXa**/**IXb**, ~20. It is seen that the BCB : MCB ratio strongly depends on the substrate structure.

Effect of the substrate stereochemistry. The increase in BCB : MCB by an order of magnitude in going from *cis* isomer **VIIb** to *trans* isomer **VIIa** may be interpreted as the result of different rates of 1,3-dehydrobromination, for the effect of orientation of the distant cyano group on the 1,2-dehydrobromination process should be insignificant. It is also important that no substrate stereoisomerization was observed during the dehydrobromination of nitriles **VIIa** and **VIIb**. Thus we conclude that the *syn*-1,3-dehydrobromination in **VII** is preferred. This conclusion is consistent with the data of [9], according to which the rates of 1,3-dehydrobromination of stereoisomeric bromocyclobutanes **XVa** and **XVb** differ by a factor of 30 (the reaction with *trans* isomer **XVa** is faster) while stereoisomerization of the substrate does not occur. According to the results of kinetic study [9], 1,3-dehydrobromination of bromonitrile **XV** follows the $(E1_{cb})_R$ mechanism [$k_{-1} > k_2$] with formation of hydrogen-bonded carbanion **B** as intermediate (Scheme 5). Here, the higher reactivity of the *trans* isomer (with respect to *cis*) should be attributed to the existence of an additional elimination path (k_2'') involving assistance by potassium cation [9]. This scheme can also be applied to interpret the reaction with nitrile **VII**. However, the effect of stereochemical structure of ester **VIII** is much weaker, presumably due to different elimination mechanism (see below).

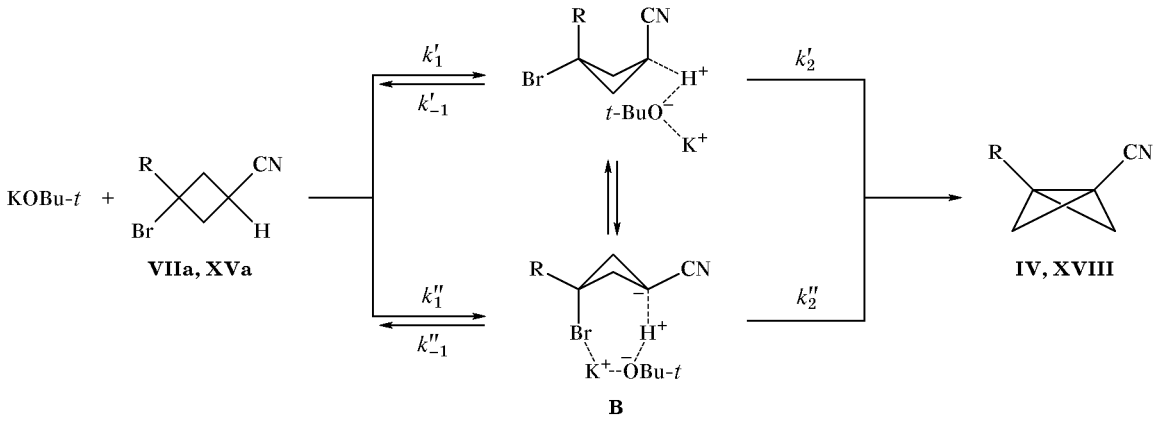
Effect of the activating group. In going from nitrile **VII** to ester **VIII**, the fraction of the bicyclobutane derivative in the dehydrobromination product considerably increases. Assuming that the effect of ester or cyano group on the 1,2-elimination process is insignificant (for that group is remote from the reaction center), the observed increase in BCB : MCB should be treated in terms of a greater efficiency of 1,3-dehydrobromination in ester **VIII** as compared to

Table 5. ^{1}H and ^{13}C NMR spectra of substituted bicyclobutanes **IV** and **XVIII**–**XX**

Comp. no.	^{1}H NMR spectrum,[a] δ, ppm				^{13}C NMR spectrum, δ_C, ppm					
	endo-2-H, *endo*-4-H	*exo*-2-H, *exo*-4-H	CH_2X [CH_3]	OCH_3	C^1	C^2, C^4	C^3	CH_2X [CH_3]	OCH_3	CN [CO]
IV	1.28	1.98	[1.72 s]	–	–3.6	40.2	22.8	[12.4]	–	120.0
XVIII	1.50	2.34	4.05 s	–	0.4	39.4	29.4	28.9	–	121.3
XIX	1.40	2.45	3.87 s	3.70 s	17.2	37.6	27.9	30.9	51.9	[170.0]
XX	1.38	2.21	3.95 s	3.42 s	–3.9	38.7	23.7	69.2	58.7	118.9

[a] The signals from 2-H and 4-H appear as broadened singlets.

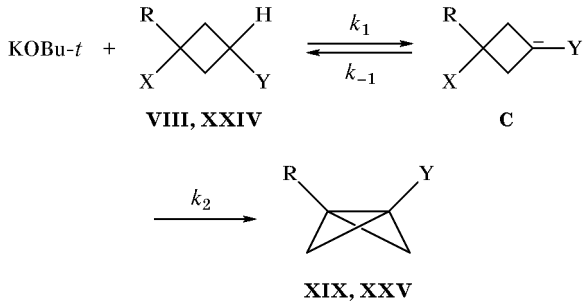
Scheme 5.



VIIa, **XVIII**, R = CH_2Br; **XVa**, **IV**, X = Me.

nitrile **VII**. We also found that, unlike nitriles **VIIa** and **VIIb**, the dehydrobromination of esters **VIIIa** and **VIIIb** is accompanied by stereoisomerization. This fact, as well as the weak effect of steric structure of **VIII** on the BCB : MCB ratio, indicates change of the mechanism of elimination in going from nitrile **VII** to ester **VIII**. Presumably, the reaction with ester **VIII** follows the $(E1_{cb})_I$ mechanism [$k_2 > k_{-1}$] with participation of carbanion **C** as intermediate (Scheme 6). An analogous mechanism was proposed in [9] for the 1,3-dehydrohalogenation of ketone **XXIV**.

Scheme 6.



VIII, **XIX**, R = CH_2Br; **XXIV**, **XXV**, R = H; **VIII**, **XIX**, Y = CO_2Me; **XXIV**, **XXV**, Y = COPh; **VIII**, X = Br; **XXIV**, X = Cl.

We believe that the difference in electronic effects of the activating groups (cyano and methoxycarbonyl) is responsible for formation of different intermediates in the reactions with nitrile **VII** and eester **VIII**. Taking into account that the relative contribution of resonance stabilization (with respect to stabilization due to inductive effect) of carbanionic center by the ester group is considerably greater than the corresponding contribution for the cyano group.* Therefore, charge delocalization (and formation of free carbanion **C**) should be expected for ester **VIII**, and charge localization on the carbon atom (and formation of hydrogen-bonded carbanion **B**) should be expected for nitrile **VII**. Furthermore, free carbanion is assumed to be more reactive than the anionic center in hydrogen-bonded ion in intramolecular nucleophilic attack leading to formation of the bicyclobutane product.

Effect of substituent in the CH_2X fragment. The contributions of 1,3-elimination in the reactions with nitriles **VII** and **IX**, differing by the substituent in the CH_2X fragment, may be regarded as approximately similar. Then, considerable increase in the BCB : MCB ratio in going from methoxymethyl derivative **IX** to bromomethyl analog **VII** originates from sharp increase in the efficiency of 1,2-dehydrobromination for the latter. Presumably, the stronger electron-acceptor power of bromine (σ_I 0.48) as compared to methoxy group (σ_I 0.30) is the main factor responsible for the greater contribution of 1,2-dehydrobromination in the case of dibromide **VII**. This assumption is consistent with the fact that nitrile **XV** undergoes exclusively 1,3-elimination to give the corresponding bicyclobutane derivative **IV** as the only product [2, 8].

To conclude, it should be noted that the above interpretation of the observed relations between the chemoselectivity of dehydrobromination in the series of substituted bromocyclobutanes **VII**–**IX** and substrate structure is a matter of discussion.

* The alkoxycarbonyl and cyano groups are characterized by similar resonance substituent constants, σ_R 0.10 and σ_R^- 0.23, but different inductive constants σ_I (see above).

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of solutions in $CDCl_3$ were recorded on a Bruker AM-200 spectrometer. GLC analyses were performed on a Tsvet-101 instrument equipped with a flame ionization detector; carrier gas nitrogen, flow rate 40 ml/min; glass column, 3000 × 2 mm; stationary phase 10% of OV-17 on Chromosorb W-HMDS (60–100 mesh). GC–MS data were obtained using an LKB-2091 mass spectrometer; carrier gas helium; glass column, 2000 × 3 mm; stationary phase 3% of XE-60 on Inerton Super (0.16–0.20 mm); energy of ionizing electrons 70 eV, emission current 25 mA; accelerating voltage 3.5 kV. Silufol UV-254 plates were used for analytical thin-layer chromatography; eluent hexane–ether, 1 : 1; development with UV light or iodine vapor. Column chromatography was performed on silica gel L (40/100 μm).

3-Methylenecyclobutane-1-carbonitrile (**I**) was synthesized by the procedure described in [1]. bp 65–66°C (21 mm), n_D^{20} 1.4615; published data [1]: bp 64–65°C (21 mm), n_D^{25} 1.4595. ^{1}H NMR spectrum, δ, ppm: 4.78–4.86 (2H, CH_2=C), 3.02–3.08 (5H, 1-H, 2-H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 17.1 (C^1), 36.6 (C^2, C^4), 141.4 (C^3), 108.4 (CH_2=), 121.9 (CN).

Methyl 3-methylenecyclobutane-1-carboxylate (**II**) was prepared according to [10]. bp 57–60°C (20 mm), n_D^{20} 1.4490; published data [10]: bp 60–61°C (20 mm), n_D^{25} 1.4469. Bromo nitriles **XVa** and **XVb** [9], methoxy nitriles **XVIa** and **XVIb** [11], methoxy esters **XVIIa** and **XVIIb** [11], and bicyclobutane **IV** [8] were synthesized by known methods. *N*-Bromosuccinimide (pure grade) was recrystallized from water prior to use. Potassium *tert*-butoxide was prepared as described in [12]. The substituent constants σ were taken from [13].

Bromination of 3-methylenecyclobutane-1-carbonitrile (I). A solution of 3.2 g (20 mmol) of bromine in 15 ml of carbon tetrachloride was added over a period of 1 h to a solution of 1.86 g (20 mmol) of nitrile **I** in 15 ml of CCl_4 while stirring at 20°C. The mixture was stirred for 0.5 h, and the solvent was removed under reduced pressure. The product, 4.80 g (95%), was a mixture of dibromo derivatives **VIIa** and **VIIb** at a ratio of 54 : 46 (according to the GLC data, 150°C; retention time 20.7 and 27.2 min, respectively). The mixture was subjected to chromatographic separation in a column charged with silica gel.

***trans*-3-Bromo-3-bromomethylcyclobutane-1-carbonitrile (VIIa).** R_f 0.60, mp 36–37°C (from hexane). Found, %: C 28.24, 28.51; H 2.86, 2.92; Br 63.02, 62.89; N 5.59, 5.68. $C_6H_7Br_2N$. Calculated, %: C 28.49; H 2.79; Br 63.18; N 5.54.

***cis*-3-Bromo-3-bromomethylcyclobutane-1-carbonitrile (VIIb).** R_f 0.52, mp 55–56°C (from hexane). Found, %: C 28.30, 28.56; H 2.87, 2.63; Br 63.08, 62.87; N 5.61, 5.48. $C_6H_7Br_2N$. Calculated, %: C 28.49; H 2.79; Br 63.18; N 5.54.

Bromination of methyl 3-methylenecyclobutane-1-carboxylate (II). Following the above procedure, from 1.89 g (15 mmol) of ester **II** and 2.4 g (15 mmol) of bromine in 25 ml of CCl_4, we obtained 4.0 g (93%) of a mixture of dibromo derivatives **VIIIa** and **VIIIb** at a ratio of 51 : 49 (GLC, 150°C; retention time 10.2 and 13.4 min, respectively). The isomers were separated by column chromatography on silica gel.

Methyl *trans*-3-bromo-3-bromomethylcyclobutane-1-carboxylate (VIIIa). R_f 0.65, oily liquid. Found, %: C 29.35, 29.48; H 3.59, 3.41. $C_7H_{10}Br_2O_2$. Calculated, %: C 29.40; H 3.52.

Methyl *cis*-3-bromo-3-bromomethylcyclobutane-1-carboxylate (VIIIb). R_f 0.60, mp 45–47°C. Found, %: C 29.27, 29.22; H 3.39, 3.42. $C_7H_{10}Br_2O_2$. Calculated, %: C 29.40; H 3.52.

The ^{1}H and ^{13}C NMR spectra of compounds **VIIa**, **VIIb**, **VIIIa**, and **VIIIb** are given in Table 1.

Bromomethoxylation of nitrile I. A solution of 4.65 g (50 mmol) of nitrile **I** in 10 ml of methanol was added over a period of 2 h to a suspension of 9.25 g (52 mmol) of *N*-bromosuccinimide in 20 ml of methanol on stirring at 20°C. The mixture was stirred at 35°C until initial nitrile **I** disappeared (~3 h, GLC monitoring). The solvent was distilled off on a rotary evaporator, and 150 ml of carbon tetrachloride was added to the residue which was a mixture of crystals and viscous liquid. The precipitate (succinimide) was filtered off, and the filtrate was washed with a solution of sodium chloride (3 × 30 ml), dried over $MgSO_4$, and evaporated under reduced pressure. The yield of the crude product was 9.65 g (95%); according to the GLC data (150°C), it was a mixture of four compounds; **IXa**, **IXb**, **XIa**, and **XIb**. Below are given their retention times (min) and fractions (%) in the mixture: **IXa**, 6.7, 6.5; **IXb**, 8.2, 8.0; **XIa**, 18.1, 46.5; **XIb**, 22.8, 39.0. The product mixture was subjected to chromatographic separation on silica gel to obtain two fractions. The first fraction, R_f 0.62, was a mixture of *trans*- and *cis*-3-bromo-3-methoxymethylcyclobutane-1-carbonitriles **IXa** and **IXb** (GLC data), bp 90°C (1 mm). Yield 1.05 g (10.3%). Found, %: C 40.93, 40.71; H 4.93, 4.82; Br 38.98, 38.77; N 6.90, 6.95. $C_7H_{10}BrNO$. Calculated, %: C 41.20; H 4.94; Br 39,15; N 6.87.

The second fraction, R_f 0.55, was a mixture of *trans*- and *cis*-3-bromomethyl-3-methoxycyclobutan-1-carbonitriles **XIa** and **XIb**. Yield 6.95 g (68%). It was a mixture of crystals and a viscous liquid. By dissolution in a warm hexane–ether mixture (1:1) and subsequent cooling of the solution to –25°C we isolated crystalline product **XIb**. The procedure was repeated for several times to obtain an additional amount of compound **XIb**. mp 52°C. Found, %: C 41.11, 40.99; H 4.97, 4.95; Br 38.80, 38.75; N 6.94, 6.98. $C_7H_{10}BrNO$. Calculated, %: C 41.20; H 4.94; Br 39.15; N 6.87. From the mother liquor we isolated by distillation compound **XIa** as a viscous liquid containing (GLC) about 20% of isomer **XIb**. bp 88–92°C (1 mm). Found, %: C 41.08, 40.97; H 4.88, 4.96; N 6.88, 7.03. $C_7H_{10}BrNO$. Calculated, %: C 41.20; H 4.94; N 6.87.

The ^1H and ^{13}C NMR spectra of compounds **IXa** and **IXb** are given in Table 1, and of **XIa** and **XIb**, in Table 2.

Bromomethoxylation of ester II. A solution of 3.15 g (25 mmol) of ester **II** in 10 ml of methanol was added over a period of 2 h to a suspension of 4.65 g (26 mmol) of *N*-bromosuccinimide in 20 ml of methanol on stirring at 0°C. The mixture was stirred at room temperature, and the disappearance of initial ester **II** was monitored by GLC. When the reaction was complete, the solvent was removed under reduced pressure, and the residue (which was a mixture of crystals and a viscous liquid) was diluted with 50 ml of ether. The undissolved crystals (succinimide) were separated, and the ether solution was washed with water (2×20 ml) and dried over $MgSO_4$. The solvent was evaporated, and the residue was distilled under reduced pressure to obtain 5.2 g (88%) of a crude product which was a mixture of four compounds: methyl *trans*- and *cis*-3-bromo-3-methoxymethylcyclobutane-1-carboxylates **Xa** and **Xb** and methyl *trans*- and *cis*-3-bromomethyl-3-methoxycyclobutane-1-carboxylates **XIIa** and **XIIb**. bp 82–86°C (3 mm), n_D^{20} 1.4872. Found, %: C 40.81, 40.65; H 5.57, 5.47; Br 33.36, 33.43. $C_8H_{13}BrO_3$. Calculated, %: C 40.53; H 5.53; Br 33.70. Below are given compound no., retention time (min, 150°C), and fraction in the crude product (%): **Xa**, 3.5, 2.5; **Xb**, 4.5, 3.5; **XIIa**, 8.9, 48.5; **XIIb**, 11.1, 45.5. The structure of esters **Xa** and **Xb** was established on the basis of their mass spectra (Table 3), and the configuration was assigned on the basis of their retention times, by analogy with the behavior of the corresponding nitriles **IXa** and **IXb**. The ^1H and ^{13}C NMR spectra of esters **XIIa** and **XIIb** are given in Table 2.

1-Bromomethyl-1-methoxycyclobutane (XIII) [14]. Methylenecyclobutane, 1.30 g (19 mmol), was added at 0°C to a suspension of 2.65 g (15 mmol) of *N*-bromosuccinimide in 20 ml of methanol, and the mixture was stirred for 2 h. Most part of the solvent was distilled off under atmospheric pressure, 50 ml of ether was added to the residue, the precipitate of succinimide was filtered off, and the filtrate was washed with water and dried over magnesium sulfate. Removal of the solvent gave 2.45 g (91%) of compound **XIII** containing more than 99% of the main substance (GLC). bp 79–81°C (6 mm); published data [14]: bp 77–80°C (5 mm). The ^1H and ^{13}C NMR spectra are given in Table 2.

Determination of regio- and stereoselectivity of addition to alkenes I and II. *a. Bromination.* Alkene **I** or **II**, 0.3 mmol, was mixed with an equimolar amount of bromine in 1 ml of carbon tetrachloride at 20°C; after 0.5 h, the mixture was analyzed by GLC.

b. Bromomethoxylation. An equimolar amount of alkene **I** or **II** was added to a suspension of 53 mg (0.3 mmol) of *N*-bromosuccinimide in 2 ml of MeOH, and the mixture was stirred for 5 h at 20°C. Most part of the solvent was evaporated under reduced pressure, 15 ml of ether was added to the residue, and the ether solution was washed with water and dried over $MgSO_4$. The solution was analyzed by GLC and GC–MS. The mass spectra of the bromomethoxylation products are given in Table 3. Table 4 contains the data on the selectivity of bromination and bromomethoxylation (each value is an average from three parallel runs).

Dehydrobromination of dibromonitriles VIIa and VIIb. *a.* A solution of 0.63 g (2.5 mmol) of dibromide **VIIa** in 5 ml of THF was added at 0°C to a solution of 0.39 g (3.5 mmol) of potassium *tert*-butoxide in 10 ml of THF. The mixture was stirred for 5 h and was allowed to gradually warm up to room temperature. Water, 30 ml, and ether, 30 ml, were added, the organic phase was separated, and the aqueous phase was extracted with ether. The extract was combined with the organic phase, washed with water, and dried over magnesium sulfate. Removal of the solvent left 0.35 g (83%) of a viscous liquid which (according to the GLC data, 150°C, and ^1H NMR spectrum) was a mixture of compounds **XVIII** and **XXI** (retention time 10.3 and 7.2 min, respectively) at a ratio of 1:2. bp 70°C (1 mm). Found, %: C 41.71, 41.60; H 3.25, 3.31; N 7.89, 7.80. C_6H_6BrN. Calculated, %: C 41.89; H 3.52; N 8.14.

3-Bromomethylbicyclobutane-1-carbonitrile (XVIII). Mass spectrum, *m*/*z* (I_{rel}, %): 173 and 171 (65, M^+), 92 (100), 65 (94), 39 (65).

b. Following an analogous procedure, from 0.35 g of compound **VIIb** we obtained 0.19 g (80%) of

a product which (according to the GLC and ^{1}H NMR data) was a mixture of compounds **XVIII** and **XXI** at a ratio of 1:20. bp 71°C (1 mm). Found, %: C 41.74, 41.80; H 3.35, 3.31; N 7.80, 7.98. C_6H_6BrN. Calculated, %: C 41.89; H 3.52; N 8.14.

3-Bromomethylenecyclobutane-1-carbonitrile (XXI). Mass spectrum, *m*/*z* (I_{rel}, %): 173 and 171 (28, M^+), 120 (30), 118 (30), 92 (100), 65 (65), 54 (18), 41 (23), 39 (93). ^{1}H NMR spectrum, δ, ppm: 5.95–6.01 (1H, CHBr), 2.95–3.30 (5H, 1-H, 2-H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 16.6 (C^1), 35.7 and 36.4 (C^2, C^4), 137.8 (C^3), 99.8 (CHBr), 121.3 (CN).

GLC monitoring of the dehydrobromination of compounds **VIIa** and **VIIb** (according to *a* and *b*) showed that the ratio of products **XVIII** and **XXI** did not change with time and that no epimerization of initial dibromo nitrile **VIIa** or **VIIb** occurred.

Dehydrobromination of dibromo esters VIIIa and VIIIb. *a.* A solution of 0.35 g (1.2 mmol) of compound **VIIIa** in 3 ml of THF was added dropwise with stirring at 0°C to a solution of 0.19 g (1.7 mmol) of potassium *tert*-butoxide in 5 ml of THF. The cooling bath was removed, and the mixture was stirred for 5 h. It was then diluted with 20 ml of water and extracted with ether (3 × 15 ml). The extracts were washed with water and dried over magnesium sulfate. Removal of the solvent under reduced pressure left 0.20 g (80%) of a viscous oily substance which (according to the ^{1}H NMR data) was a mixture of methyl 3-bromomethylbicyclobutane-1-carboxylate (**XIX**) and methyl 3-bromomethylenecyclobutane-1-carboxylate (**XXII**) at a ratio of 4.3:1. bp 45°C (1 mm). Found, %: C 40.81, 40.75; H 4.35, 4.29. $C_7H_9BrO_2$. Calculated, %: C 41.00; H 4.42.

b. Following an analogous procedure, from 0.30 g of compound **VIIIb** we obtained 0.16 g (75%) of a mixture of products **XIX** and **XXII** at a ratio of 2.2:1. Ester **XXII**: ^{1}H NMR spectrum, δ, ppm: 5.82–5.90 (1H, CHBr), 2.82–2.97 (5H, 1-H, 2-H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 31.8 (C^1), 34.1 and 34.8 (C^2, C^4), 51.9 (OCH_3), 97.9 (CHBr), 136.9 (C^3), 170.0 (C=O). GLC monitoring of the dehydrobromination of **VIIIa** and **VIIIb** (methods *a* and *b*) showed that in both cases epimerization of initial dibromo esters **VIIIa** and **VIIIb** occurred.

3-Methoxymethylbicyclobutane-1-carbonitrile (XX). A solution of 0.2 g (1 mmol) of mixture **IXa**/**IXb** (1.2:1) in 1 ml of THF was added at 0°C to a solution of 0.16 g (1.4 mmol) of potassium *tert*-butoxide in 5 ml of THF. The mixture was stirred for 3 h at 20°C, and the progress of the reaction was monitored by GLC (150°C). When the reaction was complete, the mixture was diluted with 20 ml of water and extracted with ether (3 × 15 ml). The extracts were washed with water and dried over magnesium sulfate. Distillation gave 102 mg of bicyclobutane **XX**. Yield 84%. bp 60–62°C (7 mm). Mass spectrum, *m*/*z* (I_{rel}, %): 123 (4, M^+), 92 (18), 71 (100), 65 (34), 53 (37), 52 (15), 51 (11), 45 (85). Found, %: C 68.41, 68.03; H 7.38, 7.31; N 11.57, 11.33. C_7H_9NO. Calculated, %: C 68.27; H 7.37; N 11.37. According to the ^{1}H NMR data, the product contained ~5% of compound **XXIII** which was identified by the following weak signals, δ, ppm: 5.9–6.0 (CH=C), 2.95–3.15 (1-H, 2-H, 4-H), 4.0 s (OCH_3).

The ^{1}H and ^{13}C NMR spectra of bicyclobutanes **XVIII**–**XX** are given in Table 5.

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