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Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on Her Jubilee

Nucleophilic Opening of the Aziridine Ring in 1-Alkyl-1-azoniatricyclo[2.2.1.0^{2,6}]heptanes

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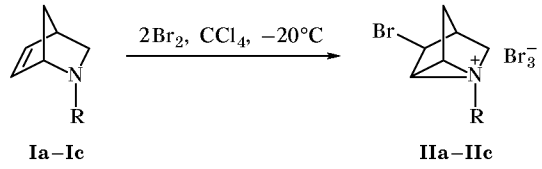
Abstract—Opening of the aziridine ring in 3-bromo-1-alkyl-1-azoniatricyclo[2.2.1.0^{2,6}]heptane bromides by the action of various nucleophiles leads to formation of the corresponding 6-substituted 2-alkyl-2-azabicyclo-[2.2.1]heptanes.

Compounds of the azabicyclo[2.2.1]heptane series exhibit biological activity [1, 2]. For example, the azabicyclic fragment is present in a number of natural moleculs, such as alkaloids anatoxin and epibatidine and drug cocaine. It should also be noted that 2-azabicyclo[2.2.1]heptane is a heterocyclic analog of norbornane which is a classical subject of studies in the field of physical organic chemistry. We previously described properties of polyhalogenides derived from 2-alkyl-2-azabicyclo[2.2.1]hept-5-enes [3]. We found that the aziridine ring in these salts is readily opened by the action of various nucleophiles, affording the corresponding substituted 2-azabicyclo[2.2.1]heptanes. In the present work we performed the above transformations with a wide series of nucleophiles, thus advancing a new approach to functionalization of 2-alkyl-2-azabicyclo[2.2.1]hept-5-enes. The bromination of some 2-alkyl-2-azabicyclo[2.2.1]hept-2-enes **Ia**–**Ic** was reported in [3] (Scheme 1).

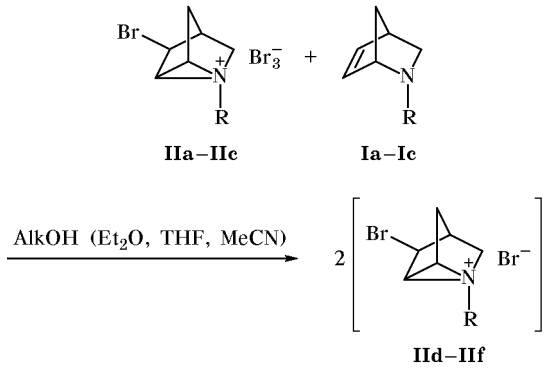
Scheme 1.



Ia–Ic **IIa–IIc**

R = Me (**a**), Et (**b**), $PhCH_2$ (**c**).

Scheme 2.



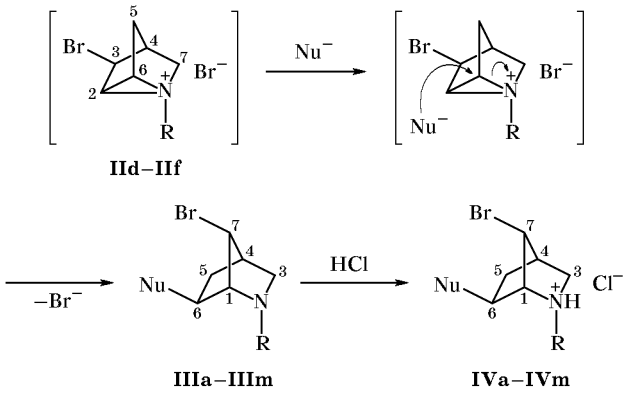
IIa–IIc **Ia–Ic**

IId–IIf

Alk = Me, Et; R = Me (**d**), Et (**e**), $PhCH_2$ (**f**).

The resulting tribromides **IIa**–**IIc** reacted with an equimolar amount of initial azabicycloheptene

Scheme 3.



IId–IIf

IIIa–IIIm **IVa–IVm**

Nu = MeO (**a**–**c**), EtO (**d**), AcO (**e**, **f**), SCH (**g**–**i**), $PhCH_2S$ (**j**), N_3 (**k**, **l**), $CH(COMe)_2$ (**m**); R = Me (**a**, **d**, **e**, **g**, **j**, **k**, **m**), Et (**b**, **f**, **h**, **l**), $PhCH_2$ (**c**, **i**).

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Table 1. Reaction of compounds **IId**–**IIf** with various nucleophiles

Nucleophile	Product (yield, %)		
	R = Me	R = Et	R = $PhCH_2$
MeONa	**IIIa** (30)	**IIIb** (54)	**IIIc** (61)
	IVa (57)	–	–
EtONa	**IIId** (34)	–	–
AcONa	**IIIe** (54)	**IVf** (82)	–
	IVe (63)	–	–
KSCN	**IVg** (49)	**IVh** (34)	**IVi** (96)
$PhCH_2SNa$	**IVj** (55)	–	–
NaN_3	**IVk** (52)	**IVl** (52)	–
$NaCH(COMe)_2$	**IVm** (71)	–	–

Ia–**Ic** in various solvents to give unstable monobromides **IId**–**IIf** (Scheme 2). The present communication reports on the reactions of compounds **IId**–**IIf** (which were obtained by one-pot procedure) with various nucleophiles. We have found that nucleophile attacks the aziridinium ring at the C^6 atom. Cleavage of the C^6–N bond results in formation of *exo*-6-substituted 2-alkyl-*syn*-7-bromo-2-azabicyclo[2.2.1]heptanes **IIIa**–**IIIm** (Scheme 3).

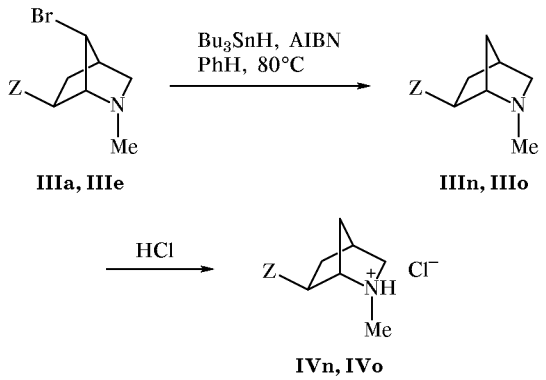
The following compounds were used as nucleophiles: sodium methoxide, sodium ethoxide, and sodium acetate (C–O bond formation); potassium thiocyanate and sodium phenylmethanethiolate (C–S bond formation); sodium azide (C–N bond formation); and sodium acetylacetonate (C–C bond formation). The *syn*,*exo*-orientation of substituents in the products was assigned on the basis of our previous data for compound **IIIa** [3]. Irradiation at a frequency corresponding to resonance of the 7-H proton revealed *W*-coupling with 6-H and *endo*-5-H (J = 1.3 Hz). Taking into account that the ^{1}H NMR spectra of the other compounds contain analogous set of signals (except to those corresponding to the substituents), they were assigned the same structure as **IIIa**.

Compounds **IIIa**–**IIIm** were converted (without isolation from the reaction mixture) into hydrochlorides **IVa**–**IVm**. In some cases, the corresponding free bases (compounds **IIIa**–**IIIe**) were isolated. The yields of the products are given in Table 1.

Using compounds **IIIa** and **IIIe** as examples, we have shown that the bromine atom in position *7* of the azanorbornane skeleton can be reduced with tributylstannane (Scheme 4; cf. [4]).

Thus nucleophilic opening of the aziridine ring in 1-alkyl-3-bromo-1-azoniatricyclo[2.2.1.$0^{2,6}$]heptane bromides gives various substituted 2-alkyl-2-azabicyclo[2.2.1]heptanes. The reaction involves formation of a new C–O, C–S, C–N, or C–C bond.

Scheme 4.



Z = MeO (**a**, **n**), AcO (**e**, **o**).

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra (400 and 100 MHz, respectively) were recorded on a Varian VXR-400 spectrometer at 28°C using TMS as internal reference. The proton signals were assigned on the basis of ^{1}H–{^{1}H} double-resonance experiments and published data [5]. In some cases, APT pulse sequence (which allows edition of spectra) was applied to assign ^{13}C signals. The ^{1}H NMR spectral parameters of compounds **III** and **IV** are given in Table 2, and Table 3 contains the yields, melting points, IR spectra, and analytical data of hydrochlorides **IV**.

Sodium phenylmethanethiolate. Metallic sodium, 0.69 g (30 mmol), was cut into small pieces and was added to a solution of 3.72 g (30 mmol) of phenylmethanethiolate in 50 ml of dry diethyl ether. The mixture was stirred until the metal dissolved completely, and the product was filtered off. Yield 4.2 g (96%), mp 180–182°C.

Sodium acetylacetonate. Metallic sodium, 1.38 g (60 mmol), was dissolved in 50 ml of ethanol, and 6.00 g (60 mmol) of acetylacetone was added dropwise with stirring. The mixture was cooled, and the precipitate was filtered off. Yield 6.30 g (86%), mp 234–236°C (217–219°C [6]).

Tributylstannane was prepared by the procedure reported in [7]. The other reagents used were commercial products.

***syn*-7-Bromo-*exo*-6-methoxy-2-methyl-2-azabicyclo[2.2.1]heptane (IIIa).** A solution of 1.75 g (16 mmol) of compound **Ia** in 15 ml of methanol was added under stirring and cooling with ice to

Table 2. ^{1}H NMR spectra (chemical shifts δ, ppm, and coupling constants *J*, Hz) of compounds **III**–**IIIe**, **IIIn**, **IIIo**, and **IV**–**IVm**[a]

Comp. no.	1-H, br.s	3-H	4-H	5-H	6-H	7-H	Other protons
IIIa	3.15	2.48 m (3H)		2.03 d.q (1H, *exo*-5-H, ^2J = 13.0, $J_{exo\text{-}5,4}$ = 3.7, $J_{exo\text{-}5,6}$ = 3.7, $J_{exo\text{-}5,exo\text{-}3}$ = 3.7), 1.88 d.d.d (1H, *endo*-5-H, ^2J = 13.0, $J_{endo\text{-}5,6}$ = 7.5, $J_{endo\text{-}5,7}$ = 1.3)	3.62 d.d.d (1H, $J_{6,endo\text{-}5}$ = 7.5, $J_{6,exo\text{-}5}$ = 3.7, $J_{6,7}$ = 1.3)	4.06 t (1H, $J_{7,endo\text{-}5}$ = 1.3, $J_{7,6}$ = 1.3)	3.31 s (3H, MeO), 2.40 s (3H, MeN)
IIIb	3.29	2.56 d.d.d (1H, *exo*-3-H, ^2J = 9.0, $J_{exo\text{-}3,4}$ = 3.8, $J_{exo\text{-}3,exo\text{-}5}$ = 2.7), 2.41 d (1H, *endo*-3-H, ^2J = 9.0)	2.48 m (1H)	2.05 d.d.t (1H, *exo*-5-H, ^2J = 13.0, $J_{exo\text{-}5,4}$ = 3.8, $J_{exo\text{-}5,6}$ = 3.8, $J_{exo\text{-}5,exo\text{-}3}$ = 2.7), 1.90 d.d.d (1H, *endo*-5-H, ^2J = 13.0, $J_{endo\text{-}5,6}$ = 7.5, $J_{endo\text{-}5,7}$ = 1.3)	3.62 d.d.d (1H, $J_{6,endo\text{-}5}$ = 7.5, $J_{6,exo\text{-}5}$ = 3.8, $J_{6,7}$ = 1.3)	4.03 t (1H, $J_{7,endo\text{-}5}$ = 1.3, $J_{7,6}$ = 1.3)	3.32 s (3H, MeO), 2.50 d.q and 2.63 d.q [1H each, ^2J = 11.9, J(CH_2, Me) = 7.2], 1.03 t [3H, **Me**CH_2N, J(Me, CH_2) = 7.2]
IIIc	3.27	2.56 d.d.d (1H, *exo*-3-H, ^2J = 9.1, $J_{exo\text{-}3,4}$ = 3.7, $J_{exo\text{-}3,exo\text{-}5}$ = 2.8), 2.43 d (1H, *endo*-3-H, ^2J = 9.1)	2.50 t (1H, $J_{4,exo\text{-}3}$ = 3.7, $J_{4,exo\text{-}5}$ = 3.7)	2.06 d.d.t (1H, *exo*-5-H, ^2J = 13.0, $J_{exo\text{-}5,4}$ = 3.7, $J_{exo\text{-}5,6}$ = 3.7, $J_{exo\text{-}5,exo\text{-}3}$ = 2.8), 1.93 d.d.d (1H, *endo*-5-H, ^2J = 13.0, $J_{endo\text{-}5,6}$ = 7.6, $J_{endo\text{-}5,7}$ = 1.4)	3.71 d.d.d (1H, $J_{6,endo\text{-}5}$ = 7.6, $J_{6,exo\text{-}5}$ = 3.7, $J_{6,7}$ = 1.4)	4.09 t (1H, $J_{7,endo\text{-}5}$ = 1.4, $J_{7,6}$ = 1.4)	3.26 s (3H, MeO), 3.75 d and 3.68 d (1H each, CH_2N, ^2J = 13.4), 7.19–7.33 m (5H, H_{arom})
IIId	3.13	2.47 m (3H)		2.03 d.q (1H, *exo*-5-H, ^2J = 13.0, $J_{exo\text{-}5,4}$ = 3.8, $J_{exo\text{-}5,6}$ = 3.8, $J_{exo\text{-}5,exo\text{-}3}$ = 3.8), 1.87 d.d.d (1H, *endo*-5-H, ^2J = 13.0, $J_{endo\text{-}5,6}$ = 7.6, $J_{endo\text{-}5,7}$ = 1.0)	3.71 d.d.d (1H, $J_{6,endo\text{-}5}$ = 7.6, $J_{6,exo\text{-}5}$ = 3.8, $J_{6,7}$ = 1.3)	4.05 m (1H)	3.47 d.q and 3.49 d.q [1H each, CH_2O, ^2J = 12.9, J(CH_2, Me) = 7.0], 1.18 t [3H, $MeCH_2O$, J(Me, CH_2) = 7.0], 2.39 s (3H, MeN)

Table 2. (Contd.)

Comp. no.	1-H, br.s	3-H	4-H	5-H	6-H	7-H	Other protons
IIIe	3.23	2.66 d.t (1H, *exo*-3-H, ^2J =9.0, $J_{exo\text{-}3,4}$ = 3.2, $J_{exo\text{-}3,exo\text{-}5}$ = 3.2), 2.40 d (1H, *endo*-3-H, ^2J = 9.0)	2.51 t (1H, $J_{4,exo\text{-}3}$ = 3.2, $J_{4,exo\text{-}5}$ = 3.2)	2.14 d.d.t (1H, *exo*-5-H, ^2J = 13.3, $J_{exo\text{-}5,6}$ = 3.8, $J_{exo\text{-}5,4}$ = 3.2, $J_{exo\text{-}5,exo\text{-}3}$ = 3.2), 2.04 d.d (1H, *endo*-5-H, ^2J = 13.3, $J_{endo\text{-}5,6}$ = 7.9)	4.85 d.d (1H, $J_{6,endo\text{-}5}$ = 7.9, $J_{6,exo\text{-}5}$ = 3.8)	4.10 br.s (1H)	2.03 s (3H, MeCO), 2.42 s (3H, MeN)
IIIn	3.06	2.40 d.t (1H, *exo*-3-H, ^2J = 8.9, $J_{exo\text{-}3,4}$ = 2.9, $J_{exo\text{-}3,exo\text{-}5}$ = 2.9), 2.32 d.d (1H, *endo*-3-H, ^2J = 8.9, $J_{endo\text{-}3,syn\text{-}7}$ = 1.0)	2.34 t (1H, $J_{4,exo\text{-}3}$ = 2.9, $J_{4,exo\text{-}5}$ = 2.9)	1.34 m (1H, *exo*-5-H, ^2J = 13.0), 1.65 d.d.d (1H, *endo*-5-H, ^2J = 13.0, $J_{endo\text{-}5,6}$ = 6.9, $J_{endo\text{-}5,anti\text{-}7}$ = 2.4)	3.52 d.d.d (1H, $J_{6,endo\text{-}5}$ = 6.9, $J_{6,exo\text{-}5}$ = 2.3, $J_{6,anti\text{-}7}$ = 1.3)	1.43 d.d (1H, *syn*-7-H, ^2J = 10.1, $J_{syn\text{-}7,endo\text{-}3}$ = 1.0), 1.49 d.d.d (1H, *anti*-7-H, ^2J = 10.1, $J_{anti\text{-}7,endo\text{-}5}$ = 2.4, $J_{anti\text{-}7,6}$ = 1.3)	3.27 s (3H, MeO), 2.36 s (3H, MeN)
IIIo	3.10	2.62 d.t (1H, *exo*-3-H, ^2J = 8.9, $J_{exo\text{-}3,4}$ = 3.0, $J_{exo\text{-}3,exo\text{-}5}$ = 3.0), 2.20 d.d (1H, *endo*-3-H, ^2J = 8.9, $J_{endo\text{-}3,syn\text{-}7}$ = 1.1)	2.37 m (1H)	1.45 d.d.d.d (1H, *exo*-5-H, ^2J = 3.5, $J_{exo\text{-}5,4}$ = 4.5, $J_{exo\text{-}5,exo\text{-}3}$ = 3.0, $J_{exo\text{-}5,6}$ = 2.5), 1.83 d.d.d (1H, *endo*-5-H, ^2J = 13.5, $J_{endo\text{-}5,6}$ = 7.3, $J_{endo\text{-}5,anti\text{-}7}$ = 2.5)	4.88 d.d.d (1H, $J_{6,endo\text{-}5}$ = 7.3, $J_{6,exo\text{-}5}$ = 2.5, $J_{6,anti\text{-}7}$ = 1.3)	1.47 d.d (1H, *syn*-7-H, ^2J = 10.1, $J_{syn\text{-}7,endo\text{-}3}$ = 1.1), 1.58 d.d.d (1H, *anti*-7-H, ^2J = 10.1, $J_{anti\text{-}7,endo\text{-}5}$ = 2.5, $J_{anti\text{-}7,6}$ = 1.3)	1.99 s (3H, MeCO), 2.39 s (3H, MeN)
IVf	4.10	3.74 m (1H, *exo*-3-H), 2.99 d (1H, *endo*-3-H, ^2J = 10.6)	2.82 m (1H)	2.51 d.q (1H, *exo*-5-H, ^2J = 13.7, $J_{exo\text{-}5,6}$ = 3.7, $J_{exo\text{-}5,4}$ = 3.7, $J_{exo\text{-}5,exo\text{-}3}$ = 3.7), 2.32 d.d (1H, *endo*-5-H, ^2J = 13.7, $J_{endo\text{-}5,6}$ = 7.5)	5.17 d.d (1H, $J_{6,endo\text{-}5}$ = 7.5, $J_{6,exo\text{-}5}$ = 3.7)	4.78 br.s (1H)	2.10 s (3H, MeCO), 3.18 m and 3.31 m (1H each, CH_2N), 1.54 t [3H, **Me**CH_2N, J(Me, CH_2) = 7.3], 5.76 br.s (1H, NH)
IVg	4.27	3.41 d (1H, *exo*-3-H, ^2J = 11.7), 3.24 d (1H, *endo*-3-H,	2.99 m (1H)	2.50 d.d.t (1H, *exo*-5-H, ^2J = 14.0, $J_{exo\text{-}5,6}$ = 4.5, $J_{exo\text{-}5,4}$ = 3.8,	4.41 d.d (1H, $J_{6,endo\text{-}5}$ = 8.3, $J_{6,exo\text{-}5}$ = 4.5)	Overlapped by the H_2O signal	2.93 s (3H, MeN)

Table 2. (Contd.)

Comp. no.	1-H, br.s	3-H	4-H	5-H	6-H	7-H	Other protons
IVg		^2J = 11.7)		$J_{exo\text{-}5,exo\text{-}3}$ = 3.8), 2.40 d.d (1H, *endo*-5-H, ^2J = 14.0, $J_{endo\text{-}5,6}$ = 8.3)			
IVh	4.28	3.24 m (2H)	2.91 m (1H)	2.43 br.d (1H, *exo*-5-H, ^2J = 14.1), 2.32 d.d (1H, *endo*-5-H, ^2J = 14.1, $J_{endo\text{-}5,6}$ = 8.3)	4.36 m (1H)	4.50 br.s (1H)	3.12 d.q and 3.27 d.q [1H each, CH_2N, ^2J = 12.8, $J(CH_2, Me)$ = 7.3], 1.17 t [3H, **Me**CH_2N, $J(Me, CH_2)$ = 7.3]
IVi	4.39	3.09 m (2H)	2.90 m (1H)	2.38 m (1H, *exo*-5-H), 2.23 br.d (1H, *endo*-5-H, ^2J = 13.0)	5.05 m (1H)	5.35 br.s (1H)	4.35 d and 4.56 d (1H each, CH_2N, ^2J = 12.8), 7.28–7.93 m (5H, H_{arom}), 8.54 br.s (1H, NH)
IVj	3.85	3.60 m (1H, *exo*-3-H), 2.83 br.d (1H, *endo*-3-H, ^2J = 9.5)	2.91 m (1H)	2.36 m (1H, *exo*-5-H), 2.24 d.d (1H, *endo*-5-H, ^2J = 13.5, $J_{endo\text{-}5,6}$ = 9.1)	4.04 d.d.d (1H, $J_{6,endo\text{-}5}$ = 9.1, $J_{6,exo\text{-}5}$ = 6.5, $J_{6,7}$ = 1.3)	4.20 m (1H)	3.84 d and 3.91 d (1H each, PhC**H**$_2$S, ^2J = 13.3), 2.64 s (3H, MeN), 4.65 br.s (1H, NH), 7.22–7.58 m (5H, H_{arom})
IVk	4.09	3.41 d (1H, *exo*-3-H, ^2J = 9.2), 3.19 d (1H, *endo*-3-H, ^2J = 9.2)	2.92 m (1H)	2.20 m (2H)	4.20 m (1H)	4.56 br.s (1H)	2.90 s (3H, MeN)
IVl	4.20	3.35 m (2H)	2.96 m (1H)	2.26 m (2H)	4.28 m (1H)	4.51 br.s (1H)	3.22 m and 3.35 m (1H each, CH_2N), 1.27 t [3H, **Me**CH_2N, $J(Me, CH_2)$ = 7.1]
IVm	3.61	3.74 m (1H, *exo*-3-H), 3.13 m (1H, *endo*-3-H)	2.73 m (1H)	2.00 m (2H)	2.70 m (1H)	4.73 br.s (1H)	4.61 d [1H, $CH_\alpha(CO)_2$, $J_{\alpha,6}$ = 11.6], 2.31 s and 2.33 s (3H each, MeCO), 2.91 s (3H, MeN)

[a] The ^{1}H NMR spectra of compounds **IIIa**–**IIIe**, **IIIn**, **IIIo**, **IVf**, **IVj**, and **IVm** were recorded in chloroform-*d*, of **IVg**, **IVh**, **IVk**, and **IVl**, in D_2O, and of **IVi**, in DMSO-d_6.

Table 3. Yields, melting points, elemental analyses, and IR spectra of substituted 2-azabicyclo[2.2.1]heptane hydrochlorides **IVa**–**IVo**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			IR spectrum,[a] ν, cm^{-1}	
			C	H	N		C	H	N	C=O	NH^+
IVa	57	227[b]	37.38	5.96	5.30	$C_8H_{14}NOBr \cdot HCl$	37.45	5.89	5.46		
IVb		198[b]	39.67	6.23	5.06	$C_9H_{16}NOBr \cdot HCl$	39.93	6.28	5.18		
IVc		200[b]	50.76	5.68	4.04	$C_{14}H_{18}NOBr \cdot HCl$	50.55	5.76	4.21		
IVd		174[b]	39.64	6.32	5.27	$C_9H_{16}NOBr \cdot HCl$	39.95	6.33	5.18		
IVe	63	228[c]	37.69	5.27	4.76	$C_9H_{14}NO_2Br \cdot HCl$	37.99	5.31	4.92	1755	2435
IVf	82	134[b]	40.33	6.09	4.38	$C_{10}H_{16}NO_2Br \cdot HCl$	40.20	6.03	4.69	1755	2450
IVg	49	222[c]	33.86	4.17	9.62	$C_8H_{11}N_2SBr \cdot HCl$	33.88	4.27	9.88	2140 (SCN)	2490
IVh	34	170[c]	35.98	4.19	9.01	$C_9H_{13}N_2SBr \cdot HCl$	36.32	4.74	9.41	2170 (SCN)	2490
IVi	86	157[c]	47.14	4.64	7.63	$C_{14}H_{15}N_2SBr \cdot HCl$	46.75	4.48	7.79	2120 (SCN)	2480
IVj	55	171[c]	48.25	5.57	3.82	$C_{14}H_{18}NSBr \cdot HCl$	48.22	5.49	4.02	–[d]	
IVk	52	216[c]	31.45	4.66	20.69	$C_7H_{11}N_4Br \cdot HCl$	31.42	4.52	20.94	2130 (N_3)[e]	
IVl	52	200[c]	34.23	5.12	19.48	$C_8H_{13}N_4Br \cdot HCl$	34.12	5.01	19.90	2125 (N_3)[e]	
IVm	71	178[c]	43.85	5.59	3.93	$C_{12}H_{18}NO_2Br \cdot HCl$	44.40	5.90	4.31	1710	2530
IVn		178[b]	66.51	10.12	9.69	$C_8H_{15}NO \cdot HCl$	68.05	10.71	9.92		
IVo		195[b]	62.78	8.07	7.98	$C_9H_{15}NO_2 \cdot HCl$	63.88	8.93	8.28	1755	2440

[a] In mineral oil.

[b] From $CHCl_3$–Et_2O.

[c] From 95% ethanol.

[d] ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 139.1, 129.6, 129.0, 127.4 (C_{arom}); 72.6 (C^7), 58.3 ($PhCH_2S$), 45.2 (C^6), 43.0 (MeN), 42.8 (C^1), 42.7 (C^3), 40.3 (C^4), 34.9 (C^5).

[e] In ethanol.

a suspension of 6.85 g (16 mmol) of tribromide **IIa** in 15 ml of methanol, and the mixture was stirred until it became colorless. A solution of sodium methoxide prepared by dissolution of 0.75 g (32 mmol) of metallic sodium in 20 ml of methanol was added dropwise on cooling with ice. The resulting solution was heated for 30 min under reflux, the solvent was removed under reduced pressure, the residue was extracted with ether, the extract was filtered and evaporated, and the residue was distilled under reduced pressure. Yield 2.10 g (30%), bp 135°C (35 mm), n_D^{16} 1.5181. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 81.3 (C^7), 66.8 (MeO), 57.4 (C^5), 56.9 (C^3), 48.0 (C^6), 43.4 (C^1), 42.1 (MeN), 35.5 (C^4).

Compounds **IIIb**–**IIId** were synthesized following a similar procedure.

***syn*-7-Bromo-2-ethyl-*exo*-6-methoxy-2-azabicyclo[2.2.1]heptane (IIIb)** was obtained from 2.22 g (5 mmol) of tribromide **IIb**, 0.62 g (5 mmol) of amine **Ib**, and 0.23 g (10 mmol) of sodium. Yield 1.27 g (54%), bp 57°C (1 mm), n_D^{19} 1.5084.

2-Benzyl-*syn*-7-bromo-*exo*-6-methoxy-2-azabicyclo[2.2.1]heptane (IIIc) was obtained from 2.47 g (5 mmol) of tribromide **IIc**, 0.87 g (5 mmol) of amine **Ic**, and 0.23 g (10 mmol) of sodium. Yield 1.80 g (61%), bp 215°C (1 mm), mp 62–64°C.

***syn*-7-Bromo-*exo*-6-ethoxy-2-methyl-2-azabicyclo[2.2.1]heptane (IIId)** was obtained from 2.15 g (5 mmol) of tribromide **IIa**, 0.55 g (5 mmol) of amine **Ia**, and 0.23 g (10 mmol) of sodium, using ethanol as solvent. Yield 0.80 g (34%), bp 73°C (1 mm), n_D^{16} 1.5141. ^{13}C NMR spectrum, ($CDCl_3$), δ, ppm: 81.2 (C^7), 67.1 (CH_2O), 64.3 (C^5), 57.8 (C^3), 48.6 (C^6), 43.6 (C^1), 42.5 (MeN), 35.9 (C^4), 15.4 (**Me**CH_2O).

***exo*-6-Acetoxy-*syn*-7-bromo-2-methyl-2-azabicyclo[2.2.1]heptane (IIIe).** A solution of 1.09 g (10 mmol) of amine **Ia** in 10 ml of acetonitrile was added dropwise with stirring and cooling with ice to a solution of 4.29 g (10 mmol) of tribromide **IIa** in 20 ml of acetonitrile. The mixture was stirred until it became colorless, 1.64 g (20 mmol) of anhydrous sodium acetate was added, and the mixture was heated for 2 h under reflux with stirring. The precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The residue was extracted with

ether, and the extract was filtered and evaporated. Yield 2.70 g (54%), bp 110°C (1 mm), n_D^{24} 1.5083.

Hydrochloride **IVe** was obtained by adding a saturated solution of hydrogen chloride in ether to the ether extract of **IIIe** (see above). The precipitate was filtered off. Hydrochlorides **IVa**–**IVd**, **IVn**, and **IVo** were obtained in a similar way from solutions of **IIIa**–**IIId**, **IIIn**, and **IIIo** in ether.

***exo*-6-Methoxy-2-methyl-2-azabicyclo[2.2.1]-heptane (IIIn).** A solution of 1.30 g (5.9 mmol) of compound **IIIa** in 20 ml of benzene was heated to the boiling point, and a solution of 1.89 g (6.5 mmol) of tributylstannane and 0.10 g (0.6 mmol) of azobis-(isobutyronitrile) in 10 ml of benzene was added dropwise with stirring. The mixture was heated for 2 h under reflux and evaporated under reduced pressure. The residue was purified by distillation. Yield 0.68 g (82%), bp 160°C, n_D^{20} 1.4682. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 81.3 (C^6), 64.8 (MeO), 60.5 (C^3), 56.4 (C^1), 42.5 (C^4), 37.6 (C^7), 36.9 (MeN), 31.5 (C^5).

***exo*-6-Acetoxy-2-methyl-2-azabicyclo[2.2.1]-heptane (IIIo)** was synthesized as described above for amine **IIIn** from 2.70 g (10.9 mmol) of compound **IIIe**, 3.48 g (12.0 mmol) of Bu_3SnH, and 0.18 g (1.1 mmol) of azobis(isobutyronitrile). Yield 1.41 g (77%), bp 100°C (15 mm), n_D^{21} 1.4688.

***exo*-6-Acetoxy-*syn*-7-bromo-2-ethyl-2-azabicyclo-[2.2.1]heptane hydrochloride (IVf)** was synthesized without isolation of amine **IIIf**, from 0.44 g (1 mmol) of tribromide **IIb**, 0.12 g (1 mmol) of amine **Ib**, and 0.16 g (2 mmol) of sodium acetate. A saturated solution of HCl added to the ether extract obtained as described above for compound **IIIe**.

Hydrochlorides **IVg**–**IVm** were synthesized in a similar way. Their yields, melting points, elemental analyses, and IR spectral data are given in Table 3.

***syn*-7-Bromo-2-methyl-*exo*-6-thiocyanato-2-azabicyclo[2.2.1]heptane hydrochloride (IVg)** was obtained from 0.43 g (1 mmol) of tribromide **IIa**, 0.11 g (1 mmol) of amine **Ia**, and 0.19 g (2 mmol) of potassium thiocyanate.

***syn*-7-Bromo-2-ethyl-*exo*-6-thiocyanato-2-azabicyclo[2.2.1]heptane hydrochloride (IVh)** was obtained from 0.44 g (1 mmol) of tribromide **IIb**, 0.12 g (1 mmol) of amine **Ib**, and 0.19 g (2 mmol) of potassium thiocyanate.

2-Benzyl-*syn*-7-bromo-*exo*-6-thiocyanato-2-azabicyclo[2.2.1]heptane hydrochloride (IVi) was obtained from 0.50 g (1 mmol) of tribromide **IIc**, 0.19 g (1 mmol) of amine **Ic**, and 0.19 g (2 mmol) of potassium thiocyanate.

***exo*-6-Benzylthio-*syn*-7-bromo-2-methyl-2-azabicyclo[2.2.1]heptane hydrochloride (IVj)** was obtained from 2.15 g (5 mmol) of tribromide **IIa**, 0.55 g (5 mmol) of amine **Ia**, and 1.46 g (10 mmol) of sodium phenylmethanethiolate.

***exo*-6-Azido-*syn*-7-bromo-2-methyl-2-azabicyclo-[2.2.1]heptane hydrochloride (IVk)** was obtained from 2.15 g (5 mmol) of tribromide **IIa**, 0.55 g (5 mmol) of amine **Ia**, and 0.65 g (10 mmol) of sodium azide.

***exo*-6-Azido-*syn*-7-bromo-2-ethyl-2-azabicyclo-[2.2.1]heptane hydrochloride (IVl)** was obtained from 0.89 g (2 mmol) of tribromide **IIb**, 0.25 g (2 mmol) of amine **Ib**, and 0.26 g (4 mmol) of sodium azide.

***syn*-7-Bromo-*exo*-6-(diacetylmethyl)-2-methyl-2-azabicyclo[2.2.1]heptane hydrochloride (IVm)** was obtained from 2.15 g (5 mmol) of tribromide **IIa**, 0.55 g (5 mmol) of amine **Ia**, and 1.22 g (10 mmol) of sodium acetylacetonate.

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