O- and *N*-Alkylation of *N*-halosuccinimides in ionic reactions with 1-phenyltricyclo[4.1.0.0^{2,7}]heptane

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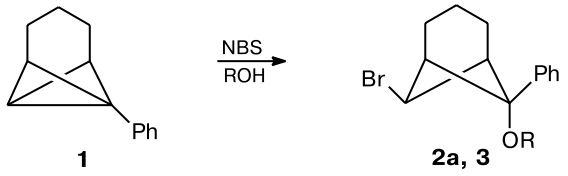
N-Bromo- and *N*-chlorosuccinimides add to 1-phenyltricyclo[4.1.0.0^{2,7}]heptane in CH_2Cl_2 with cleavage of the C(1)—C(7) bond to give isomeric 1 : 1 Markownikoff-type *endo*,*anti*-adducts of the norpinane structure in a ~3 : 7 ratio corresponding to *N*- and *O*-alkylation of succinimide.

Key words: bicyclo[3.1.1]heptane, *N*-halosuccinimides, competitive *N*- and *O*-alkylation reactions, succinimide anion, norpinane, electrophilic addition, 1-phenyltricyclo[4.1.0.0^{2,7}]heptane.

N-Halosuccinimides (NCS, NBS, and NIS) are known[1] to act as electrophilic halogen carriers in ionic addition to a multiple carbon—carbon bond. It is of note that the overwhelming majority of cases involve conjugated halogenation of olefins, where an external or internal nucleophile different from the succinimide anion acts as a coreagent. Ionic addition of *N*-halosuccinimides themselves to unsaturated compounds has been discovered only recently; this occurs with electron-rich olefins like enamines and vinyl ethers.[2] Particular emphasis should be placed on exclusive *N*-alkylation of the intermediate ambident succinimide anion in these reactions*.

Because the π-bond of olefins and the C—C bridge in bicyclo[1.1.0]butanes are known[4] to be similar in chemical behavior, *N*-halosuccinimides could be expected to effect ionic cleavage of this formally saturated carbocyclic system. Indeed, many examples of inter- and intramolecular conjugated halogenation of various derivatives of bicyclo[1.1.0]butane[5] and tricyclo[4.1.0.0^{2,7}]heptane[6—8] has been reported to date. In particular, it was shown[6,8] that in the reaction of 1-phenyltricyclo[4.1.0.0^{2,7}]heptane (**1**) with NBS in aqueous acetone or MeOH, its C(1)—C(7) bond undergoes strictly regioselective (according to the Markownikoff rule) and highly stereoselective cleavage to give norpinane adduct **2** or **3**, respectively (Scheme 1).

Scheme 1

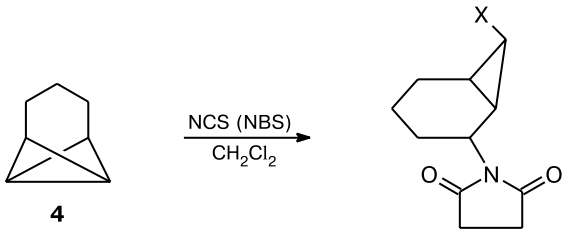


1 **2a, 3**

R = H (**2a**), Me (**3**)

The reactions of NBS and NCS with unsubstituted tricyclo[4.1.0.0^{2,7}]heptane (**4**) in an aprotic solvent afforded, through cleavage of the C(1)—C(2) bond, the corresponding adducts **5a,b** in low (2—3%) yield, which may be regarded as the ionic (electrophilic with respect to halogen) reaction products[9] (Scheme 2).

Scheme 2



4 **5a,b**

X = Br (**a**), Cl (**b**)

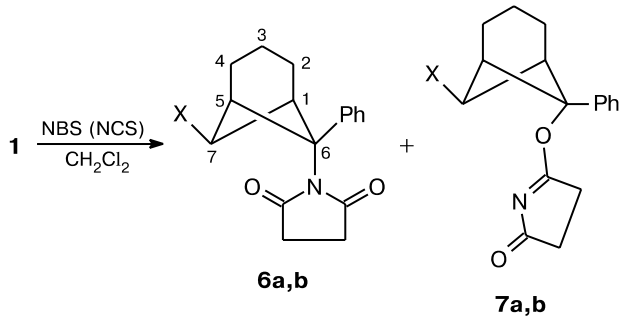
In the present work, we studied the reactions of NBS and NCS with 1-phenyltricycloheptane **1** in an aprotic

* Examples of anti-Markownikoff radical addition of *N*-halosuccinimides to unsaturated compounds under special conditions were also documented.[3]

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 457—460, February, 2005.

solvent (CH_2Cl_2) (Scheme 3). In each case, a mixture of norpinane-type structural isomers **6a**,**7a** and **6b**,**7b**, respectively, was obtained. These are *anti*-addition products of *N*-halosuccinimide to the C(1)—C(7) bond with an *endo*-attack of halogen at position 7, both the *N*- and *O*-nucleophilic centers of succinimide being involved. The ratio of the *O*- and *N*-alkylation products (**7** : **6**) in the reaction mixtures was 2.3 : 1 (**a**) and 1.8 : 1 (**b**) (^{1}H NMR data).

Scheme 3



X = Br (**a**), Cl (**b**)

Individual components **6a,b** and **7a,b** were isolated from the mixtures by fractional crystallization and characterized by IR and ^{1}H and ^{13}C NMR spectra (Tables 1, 2). Signals in the NMR spectra were assigned by comparing them with relevant data for model compounds.[6,8] The configuration of the substituent at the C(7) atom in the norpinanes is evident from the presence of a triplet signal for the H(7) proton in the ^{1}H NMR spectrum.[10,11] The configuration of the substituent at the C(6) atom is determined from a high-field signal (δ ~0.6) for one of the H(3) protons as a result of the effect of the *endo*-oriented phenyl substituent.[6,8,12] The isomeric structures of the *N*- and *O*-alkylation products are unambiguously discriminated by the ^{13}C chemical shifts of the carbon atoms of the succinimide residue and the C(6) atom. The difference in the IR spectra of the isomers is also worth noting. As in succinimide, the C=O stretching vibrations in compounds **6a,b** are observed at ~1700 cm^{-1}, while the respective absorption bands for compounds **7a,b** appear at 1747 cm^{-1}.

The structures of the *O*-alkylation products **7a,b** were additionally confirmed by their easy hydrolysis in boiling aqueous THF in the presence of Na_2CO_3 to the corresponding alcohols **2a,b** (Scheme 4). Bromide **2a** was identified by comparing it with an authentic sample,[6] while chloride **2b** was obtained by an independent synthesis from hydrocarbon **1** and NCS in aqueous acetone in the presence of Et_3N (*cf.* Ref. 8). The spectroscopic characteristics of compounds **2a,b** are given in Tables 1 and 2.

Table 1. Yields, melting points, elemental analysis data, and IR spectra of bicycloheptanes **2a,b**, **6a,b**, and **7a,b**

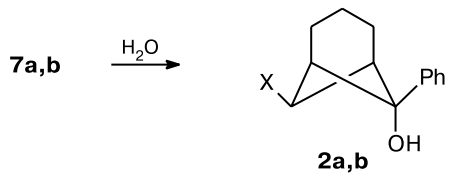
Compound	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)			Molecular formula	IR, ν/cm^{-1}
			C	H	N		
syn-7-Bromo-*endo*-6-phenylbicyclo[3.1.1]heptan-6-ol (**2a**)	35[a]	70—71 (ether)[b]	58.53 / 58.44	5.55 / 5.66	—	$C_{13}H_{15}BrO$	3211 m.br, 3025 w, 2941 m, 2938 m, 1702 m, 1448 m, 1037 m, 767 m, 700 s
syn-7-Chloro-*endo*-6-phenylbicyclo[3.1.1]heptan-6-ol (**2b**)	31[a]	64—65 (ether)	70.38 / 70.11	6.44 / 6.79	—	$C_{13}H_{15}ClO$	3363 m.br, 3025 w, 2954 m, 2939 m, 1450 m, 1072 m, 1024 s, 891 s, 765 s, 702 vs
N-(*syn*-7-Bromo-*endo*-6-phenylbicyclo[3.1.1]hept-6-yl)-succinimide (**6a**)	8	170—171 (ether—hexane)	58.75 / 58.63	5.05 / 5.21	3.97 / 4.02	$C_{17}H_{18}BrNO_2$	2948 m, 2865 w, 1708 vs, 1689 vs, 1450 m, 1351 s, 1197 s, 1107 m, 746 m, 703 m
N-(*syn*-7-Chloro-*endo*-6-phenylbicyclo[3.1.1]hept-6-yl)-succinimide (**6b**)	10	160—161 (ether)	67.32 / 67.21	5.72 / 5.97	4.44 / 4.61	$C_{17}H_{18}ClNO_2$	2953 m, 2934 w, 1694 vs, 1453 w, 1352 m, 1200 m, 1109 w, 909 w, 748 m, 706 m
5-[(*syn*-7-Bromo-*endo*-6-phenylbicyclo[3.1.1]hept-6-yl)oxy]-3,4-dihydro-2*H*-pyrrol-2-one (**7a**)	43	127—128 (CH_2Cl_2—pentane)	58.83 / 58.63	5.12 / 5.21	4.11 / 4.02	$C_{17}H_{18}BrNO_2$	2956 w, 2916 w, 2868 w, 1747 vs, 1560 s, 1554 vs, 1375 s, 1263 s, 1178 m, 775 w, 709 w
5-[(*syn*-7-Chloro-*endo*-6-phenylbicyclo[3.1.1]hept-6-yl)oxy]-3,4-dihydro-2*H*-pyrrol-2-one (**7b**)	47	114—115 (CH_2Cl_2—pentane)	67.37 / 67.21	5.86 / 5.97	4.56 / 4.61	$C_{17}H_{18}ClNO_2$	2958 w, 2939 w, 2869 w, 1747 vs, 1560 s, 1554 vs, 1375 s, 1265 s, 1182 m, 771 w, 709 w

[a] In the halohydroxylation.
[b] *cf.* Ref. 8: m.p. 78 °C (hexane).

Table 2. ^{1}H and ^{13}C NMR spectra of bicycloheptanes **2b**, **6a,b**, and **7a,b**

Compound	δ_H (*J*/Hz)						δ_C						
	H(7) (t)	H(1), H(5) (br.d)	H(2), H(4)	H(3) (1 H all)	H arom.	$C_4H_4NO_2$ [OH]	C(6)	C(7)	C(1), C(5)	C(2), C(4)	C(3)	C arom.	$C_4H_4NO_2$
2b	5.21 (5.8)	3.00 (5.8)	1.88—2.05 (2 H), 2.12—2.27 (2 H)	0.57—0.77, 1.15—1.32	7.25—7.45 (5 H)	[1.76 (s)]	79.4	59.4	49.2	23.1	12.2	125.3 (2 C), 127.8, 128.2 (2 C), 141.9	—
6a	4.76 (5.9)	4.15 (5.9)	2.12—2.31 (4 H)	0.45—0.62, 1.19—1.35	7.30—7.43 (3 H), 7.58—7.63 (2 H)	2.42—2.60, 2.60—2.78	66.9	53.0	44.8	24.6	11.3	127.0 (2 C), 127.7, 128.1 (2 C), 139.2	28.3, 177.0
6b	4.58 (6.0)	4.16 (6.0)	2.02—2.32 (4 H)	0.43—0.63, 1.17—1.35	7.25—7.40 (3 H), 7.53—7.65 (2 H)	2.42—2.59, 2.59—2.77	66.4	57.6	44.6	22.6	11.5	127.1 (2 C), 127.6, 128.1 (2 C), 138.8	28.3, 177.0
7a	5.06 (5.8)	3.65 (5.8)	2.07—2.35 (4 H)	0.51—0.72, 1.19—1.35	7.31—7.44 (3 H), 7.57—7.68 (2 H)	2.48—2.57, 2.60—2.70	93.7	52.8	48.0	25.3	11.6	127.7 (2 C), 127.8, 128.7 (2 C), 135.4	30.2, 31.1, 192.6, 193.6
7b	4.89 (5.8)	3.65 (5.8)	2.00—2.14 (2 H), 2.19—2.36 (2 H)	0.55—0.74, 1.19—1.35	7.30—7.43 (3 H), 7.59—7.66 (2 H)	2.48—2.57, 2.61—2.69	93.6	57.6	48.0	23.4	11.9	127.1 (2 C), 127.8, 128.6 (2 C), 135.1	30.3, 31.2, 192.7, 193.7

Scheme 4



X = Br (**a**), Cl (**b**)

As expected, the chemi-, regio-, and stereoselectivity of the addition of NBS and NCS to hydrocarbon **1** proved to be similar to those for bromomethoxylation (-hydroxylation) of the same substrate. For this reason, the addition studied can well be treated in terms of the ionic (electrophilic with respect to halogen) mechanism adopted for the above addition reactions and other conjugated halogenation reactions of bicyclobutane compounds.[4] Opening of the bicyclobutane system is initiated by an attack of the halogen atom at position 7 according to the orientating effect of the phenyl substituent and occurs with inversion of the configuration at the site under attack.[4] The nucleophilic attack of the succinimide anion on the intermediate norpinanyl cation is *anti*-stereoselective, which is characteristic of other external nucleophiles.[6,8] Our case is interesting since the succinimide anion as an ambident nucleophile undergoes both *N*- and *O*-alkylation, the latter being dominant approximately in the 1 : 2 ratio. For the sake of correctness, it should be noted that several examples of competitive *N*-/*O*-alkylation in ionic addition of *N*-haloamides of carboxylic[13] and sulfonic acids[14] to alkenes have been documented. However, for *N*-haloimides of dicarboxylic acids, such a competition was discovered by us for the first time.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer (300.130 and 75.468 MHz, respectively) in $CDCl_3$. IR spectra were recorded on an InfraLUM FT-02 Fourier spectrometer (KBr pellets).

Tricycloheptane **1** [6] and NCS [15] were prepared according to known procedures; NBS ("pure" grade) was crystallized from dioxane before use.

Reactions of hydrocarbon 1 with NBS and NCS (general procedure). The corresponding *N*-halosuccinimide (10 mmol) was added in small portions under nitrogen at −10 °C for 15 min to a stirred solution of hydrocarbon **1** (1.70 g, 10 mmol) in 40 mL of dry CH_2Cl_2. The reaction mixture was stirred at −10 °C for 30 min and then at 20 °C for 4 h and concentrated. The residue was analyzed by ^{1}H and ^{13}C NMR spectroscopy. Individual products **6a,b** and **7a,b** were isolated by fractional crystallization. Their yields, physicochemical constants, elemental analysis data, and IR spectra are given in Table 1; their ^{1}H and ^{13}C NMR data are presented in Table 2.

Reaction of hydrocarbon 1 with NCS in aqueous acetone. *N*-Chlorosuccinimide (1.34 g, 10 mmol) was added in small

portions at −10 °C for 10 min to a stirred mixture of hydrocarbon **1** (1.70 g, 10 mmol) and Et_3N (1.04 g, 10 mmol) in water (20 mL) and acetone (70 mL). The reaction mixture was stirred at this temperature for 0.5 h and at 20 °C for 3.5 h. Then the product was extracted with ether (3×50 mL) and the organic layer was washed with water (3×20 mL) and dried with $MgSO_4$. The solvent was evaporated and the residue was crystallized to give chlorohydrin **2b** (0.69 g). Its physicochemical constants, elemental analysis data, and IR spectrum are given in Table 1; its ^1H and ^{13}C NMR data are presented in Table 2.

Hydrolysis of adducts 7a,b (general procedure). Sodium carbonate (0.5 g) was added to a solution of compound **7a** or **7b** (1.3 mmol) in 15 mL of aqueous THF (1 : 1). The reaction mixture was refluxed for 1 h and cooled. The products were extracted with ether (3×5 mL). The extracts were dried with $MgSO_4$. The solvent was removed and the solid residue was purified by crystallization to give compounds **2a** and **2b** in 70 and 67% yields, respectively. The physicochemical constants of compound **2a** are identical with the literature data.[6]

This work was financially supported by the Ministry of Education of the Russian Federation (Grant E 02-5.0-361).

References

1. J. Beger, *J. Prakt. Chem.*, 1991, **333**, 677; J. Rodriguez and J.-P. Dulcère, *Synthesis*, 1993, 1177.
2. S. Erbeck and H. Prinzbach, *Tetrahedron Lett.*, 1997, **38**, 2653; R. Lavilla, O. Coll, R. Kumar, and J. Bosch, *J. Org. Chem.*, 1998, **63**, 2728.
3. J. Lessard, Y. Couture, M. Mondon, and D. Touchard, *Can. J. Chem.*, 1984, **62**, 105; U. Lüning and P. S. Skell, *Tetrahedron*, 1985, **41**, 4269; J. Tuaillon, Y. Couture, and J. Lessard, *Can. J. Chem.*, 1987, **65**, 2194.
4. M. Christl, *Advances in Strain in Organic Chemistry*, 1995, **4**, 163; V. V. Razin, in *Sovremennye problemy organicheskoi khimii* [*Modern Problems of Organic Chemistry*], Collection by Schools of Higher Education, St. Petersburg State University, St. Petersburg, 1996, Issue 11, 54 (in Russian).
5. V. V. Razin and N. Yu. Zadonskaya, *Zh. Org. Khim.*, 1990, **26**, 2342 [*J. Org. Chem. USSR*, 1990, **26**, 2021 (Engl. Transl.)]; V. V. Razin, N. Yu. Zadonskaya, A. G. Alekseev, and Yu. A. Makarychev, *Zh. Org. Khim.*, 1992, **28**, 972 [*Russ. J. Org. Chem.*, 1992, **28**, 750 (Engl. Transl.)].
6. V. V. Razin, N. Yu. Zadonskaya, and Kh. T. Shamurzaev, *Zh. Org. Khim.*, 1991, **27**, 1253 [*J. Org. Chem. USSR*, 1991, **27**, 1093 (Engl. Transl.)].
7. V. V. Razin, N. Yu. Zadonskaya, and Yu. A. Makarychev, *Zh. Org. Khim.*, 1990, **26**, 674 [*J. Org. Chem. USSR*, 1990, **26**, 578 (Engl. Transl.)]; V. V. Razin and Yu. A. Makarychev, *Zh. Org. Khim.*, 1992, **28**, 2490 [*Russ. J. Org. Chem.*, 1992, **28**, 2009 (Engl. Transl.)]; V. V. Razin, R. N. Zolotarev, and M. E. Yakovlev, *Zh. Org. Khim.*, 1998, **34**, 859 [*Russ. J. Org. Chem.*, 1998, **34**, 809 (Engl. Transl.)]; V. A. Vasin, A. V. Semenov, and V. V. Razin, *Zh. Org. Khim.*, 2002, **38**, 845 [*Russ. J. Org. Chem.*, 2002, **38**, 803 (Engl. Transl.)].
8. E. Gerstner, R. Kemmer, and M. Christl, *Chem. Ber.*, 1994, **127**, 381.
9. V. A. Vasin, I. Yu. Bolusheva, S. G. Kostryukov, E. P. Sanaeva, A. A. Ramzevich, and V. V. Razin, *Zh. Org. Khim.*, 1996, **32**, 698 [*Russ. J. Org. Chem.*, 1996, **32**, 668 (Engl. Transl.)].
10. K. B. Wiberg and B. A. Hess, *J. Org. Chem.*, 1966, **31**, 2250.
11. V. V. Razin, V. A. Vasin, and I. E. Blinkov, *Zh. Org. Khim.*, 1993, **29**, 916 [*Russ. J. Org. Chem.*, 1993, **29**, 759 (Engl. Transl.)].
12. G. Szeimies, A. Schloßer, F. Philipp, P. Dietz, und W. Mickler, *Chem. Ber.*, 1978, **111**, 1922.
13. S. Wolfe and D. V. C. Awang, *Can. J. Chem.*, 1971, **49**, 1384.
14. F. A. Daniker, M. T. Melchior, and P. E. Butler, *J. Chem. Soc., Chem. Commun.*, 1968, 931; T. A. Foglia, E. T. Hocberer, and G. Maerker, *J. Am. Oil Chem. Soc.*, 1979, **47**, 27.
15. E. L. Hirst and A. K. Macbeth, *J. Chem. Soc.*, 1922, **121**, 2169.

Received February 3, 2004;
in revised form October 11, 2004