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Stereoselectivity of Halomethoxylation of 1-Phenyltricyclo-[4.1.0.0^{2,7}]heptane and Methyl 7-Phenyltricyclo[4.1.0.0^{2,7}]-heptane-1-carboxylate

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Abstract—The stereoselectivity of halomethoxylation of 1-phenyltricyclo[4.1.0.0^{2,7}]heptane and methyl 7-phenyltricyclo[4.1.0.0^{2,7}]heptane-1-carboxylate at the central bicyclobutane C^1–C^7 bond by the action of *N*-chloro-, *N*-bromo-, and *N*-iodosuccinimides in methanol depends on the halogen nature. Conjugate chlorination and bromination are characterized by pronounced *anti*-stereoselectivity; the contribution of *syn*-addition slightly increases in going from the monosubstituted tricycloheptane substrate to disubstituted. Iodomethoxylation of the latter is clearly *syn*-stereoselective.

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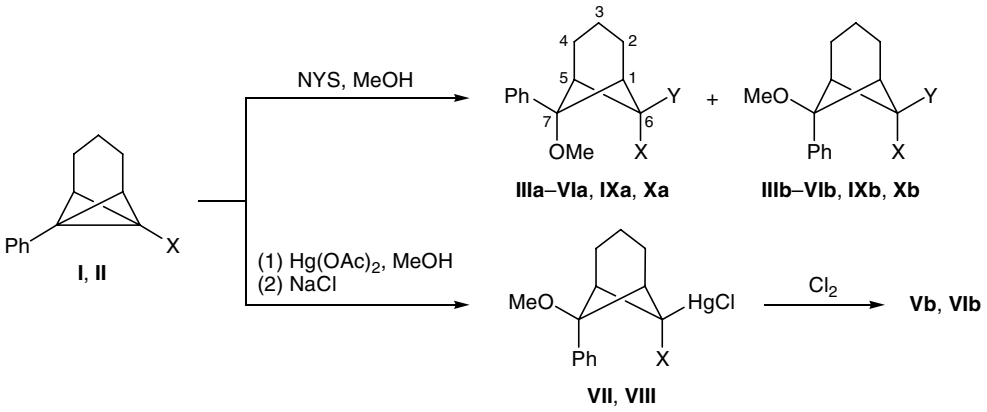
We previously found [1, 2] that *N*-bromosuccinimide (NBS) reacts with 1-phenyltricyclo[4.1.0.0^{2,7}]-heptane (**I**) and methyl 7-phenyltricyclo[4.1.0.0^{2,7}]-heptane-1-carboxylate (**II**) in methanol via addition of bromine and methoxy group at the central C^1–C^7 bond and that bromine attacks exclusively the β-position with respect to the phenyl substituent to form preferentially *anti*-adducts. The observed stereoselectivity was interpreted in terms of electrophilic mechanism of the addition. Taking into account that initial attack by electrophilic bromine atom on the C^1–C^7 bond occurs at the inner side of the bicyclobutane system [3], the intermediate benzyl-like norpinanyl cation was assumed to have a conformation in which the cationic center is shielded from nucleophilic attack by methanol at the *syn*-side either spatially or due to nonbonding interaction with the C^{3}H$_2$ group. The same hypothesis was also used to rationalize decrease in the *anti*-stereoselectivity in going from monosubstituted tricycloheptane **I** (ratio **IIIa/IIIb** 15:1) to disubstituted derivative **II** (**IVa**:**IVb** = 7:1): in the latter case, the *exo*-oriented bulky CO_2CH_3 group hinders *anti*-approach of nucleophile.

Other examples of addition to hydrocarbon **I**, initiated by electrophilic bromine, were later reported [4] (in particular, the addition of elemental bromine) and were characterized by high *anti*-stereoselectivity. However, the reaction with elemental iodine occurred as *syn*-addition [4]. In our recent study [5] on the reaction of compound **I** with *N*-halosuccinimides (NYS, Y = Cl, Br, I) in the presence of anionoid external nucleophiles (such as carboxylate and thiocyanate ions) we also observed a relation between the stereochemistry of the addition and the nature of electrophile. Conjugate chlorination and bromination showed a high *anti*-stereoselectivity, while the iodination was characterized by equally high *syn*-stereoselectivity.

With the goal of obtaining new experimental data on the effect of halogen nature and of the degree of substitution on the stereochemistry of addition to tricycloheptane substrates, we focused again on the halomethoxylation of tricycloheptane derivatives **I** and **II**. As sources of electrophilic halogens we used *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) with a view to compare the new results with those obtained previously using *N*-bromosuccinimide (NBS).

Chloromethoxylation of compounds **I** and **II** with NCS in methanol gave almost exclusively the corresponding *anti*-adducts **Va** and **VIa** which were isolated

Scheme 1.



I, **III**, **V**, **VII**, **IX**, X = H; **II**, **IV**, **VI**, **VIII**, **X**, X = CO_2Me; **III**, **IV**, Y = Br; **V**, **VI**, Y = Cl; **IX**, **X**, Y = I.

as individual substances. However, ^{1}H NMR analysis of the reaction mixtures in both cases showed the presence of a small amount of *syn*-adduct **Vb** or **VIb**. The structure of minor products **Vb** and **VIb** was reliably confirmed by their independent synthesis according to the scheme used previously for bromine analogs **IIIb** and **IVb** [1, 6], i.e., via successive methoxymercuration–halodemercuration of tricycloheptanes **I** and **II** (Scheme 1). As shown in [1, 6], methoxymercuration of compounds **I** and **II** is strictly *syn*-stereoselective, and chlorodemercuration of organomercury derivatives **VII** and **VIII** thus formed gave exclusively halo esters **Vb** and **VIb**, respectively. Unlike analogous bromodemercuration process, The yield of **Vb** and **VIb** was relatively poor. According to the TLC and ^{1}H NMR data, compounds **Vb** and **VIb** were identical to the minor products formed in the reactions of tricycloheptanes **I** and **II** with NCS in methanol.

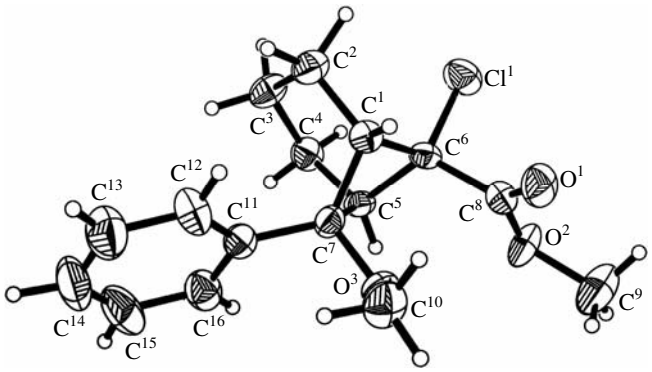


Fig. 1. Structure of the molecule of methyl *endo*-6-chloro-*anti*-7-methoxy-*syn*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (**VIa**) according to the X-ray diffraction data (one of the two crystallographically independent molecules is shown).

Iodomethoxylation of **I** and **II** with NIS in methanol also involved the central C^1–C^7 bond and led to the formation of stereoisomeric norpinanes **IXa/IXb** and **Xa/Xb**, respectively; however, the stereoselectivity of the reaction was not high. The isomer mixtures were separated into individual components by preparative thin-layer chromatography.

The ^{1}H and ^{13}C NMR spectra of chloro- and iodo derivatives **Va**, **Vb**, **VIa**, **VIb**, **IXa**, **IXb**, **Xa**, and **Xb** resemble those of the corresponding bromo derivatives **IIIa**, **IIIb**, **IVa**, and **IVb** whose structure was determined previously [1, 2]. The configuration at C^7 in trisubstituted norpinanes **IIIa**, **IIIb**, **Va**, **Vb**, **IXa**, and **IXb** was assigned according to Wiberg and Hess [7]: the presence of a triplet signal from 7-H ($J \approx 6$ Hz) indicates *anti* orientation of that proton. The configuration at the carbon atom attached to the phenyl substituent can be determined from the position of the 3-H signal. If the ^{1}H NMR spectrum contains a one-proton multiplet at about ~0.6 ppm, the phenyl group is spatially close to the C^3N_2 fragment (**IIIa–VIa**, **IXa**, **Xa**); by contrast, the lack of upfield signals up to 1.6 ppm is typical of the opposite orientation of the phenyl group (**IIIb–VIb**, **IXb**, **Xb**) [1, 2]. Shielding effect of the benzene ring on the oppositely facing groups is responsible for upfield shifts of signals from the proton at the carbon atom attached to halogen in trisubstituted norpinanes **IIIb**, **Vb**, and **IXb** and protons of the methoxycarbonyl group in tetrasubstituted norpinanes **IVb**, **VIb**, and **Xb** relative to the corresponding signals of **IIIa–VIa**, **IXa**, and **Xa**. Apart from the above differences between proton chemical shifts of diastereoisomeric norpinanes, the ^{1}H and ^{13}C NMR spectra of tetrasubstituted derivatives **IVa**, **VIa**, and **Xa** showed nonequivalence of the C^1H and C^5H fragments.

The differences in the NMR spectral patterns of stereoisomeric norpinanes were satisfactorily interpreted on the basis of the results of X-ray analysis of compounds **VIa** and **Xb** having different substituent configurations at C^7 (Figs. 1, 2). It was found that molecules **VIa** and **Xb** are characterized by considerably different geometric parameters of the carbon skeleton. The distance from the C^3 atom to the mean-square $C^1C^2C^4C^5$ plane in **VIa** is 0.2775 Å toward the phenyl group, which corresponds to a dihedral angle of 160.44° between the $C^1C^2C^4C^5$ and $C^2C^3C^4$ planes; the C^3 atom in **Xb** deviates only slightly from the $C^1C^2C^4C^5$ plane (the corresponding dihedral angle is 179.41°).* Assuming that compounds **VIa** and **Xb** in crystal have the same structure of the norpinane skeleton as in solution and that the phenyl rings are almost orthogonal to the $C^3C^6C^7$ plane in both molecules, it becomes clear why the chemical shifts of 3-H in diastereoisomers differing by the configuration at C^7 differ so strongly. The 3-H protons in compounds of the **a** series fall into the area shielded by the benzene ring, and their signals appear in a stronger field. Analogous protons in the series **b** stereoisomers suffer from deshielding effect of the opposite halogen atom and methoxy group; therefore, their signals shift downfield and become closer.

Analysis of the ^{1}H NMR spectrum of **VIa** provides a direct support to the fact that the conformation of the norpinane skeleton, found in crystal, is retained in going to solution. The spectrum contains strongly distant signals from *exo*-3-H (δ 0.60 ppm) and *endo*-3-H (δ 1.22 ppm) as double triplets of triplets, each showing one geminal and two vicinal spin–spin couplings. The vicinal coupling constants of these protons were estimated on the basis of the experimental dihedral angles including the *exo*-H–C^3 and *endo*-H–C^3 bonds, using the Karplus equation [8] (Table 1). The agreement between the calculated and experimental vicinal coupling constants indicates that molecule **VIa** has similar conformations of the norpinane skeleton both in crystal and in solution. Almost identical multiplets from the 3-H protons were observed in the spectra of analogous bromide **IVa** and iodide **Xa**, as well as in the spectra of trisubstituted norpinanes **IIIa**, **Va**, and **IXa**; this suggests similarity of their molecular conformations. An additional support is that the chemical shifts of *exo*-3-H and *endo*-3-H in the **a** series of norpinanes are almost insensitive to the halogen nature and the presence (or absence) of methoxycarbonyl group in the geminal position to the halogen atom.

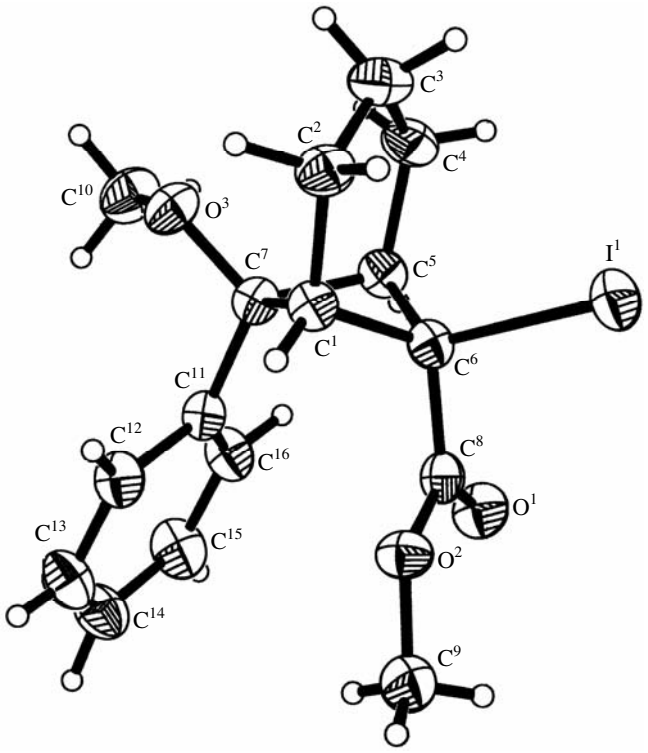


Fig. 2. Structure of the molecule of methyl *endo*-6-iodo-*syn*-7-methoxy-*anti*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (**Xb**) according to the X-ray diffraction data.

Another specificity of the ^{1}H and ^{13}C NMR spectra of tetrasubstituted norpinanes **IVa**, **VIa**, and **Xa** with *anti* orientation of the methoxy group, i.e., nonequivalence of C^1 and C^5 and protons attached thereto, can also be interpreted on the basis of the X-ray diffraction data for compound **VIa**. The methoxycarbonyl group in its molecule is oriented orthogonally to the $C^3C^6C^7$ plane. It should be noted that the CO_2Me group in iodo derivative **Xb** is arranged similarly with respect to the corresponding plane, but the C^1H and C^5H moieties in the series **b** norpinanes are equivalent in the NMR spectra. Presumably, this is the result of fast rotation of

Table 1. Dihedral angles $H^2C^2C^3H^3$ (φ, deg) and calculated[a] coupling constants (J, Hz) in compound **VIa** (averaged values for two crystallographically independent molecules)

Orientation of 2-H	φ (*exo*)	$J_{2,exo\text{-}3}$	φ (*endo*)	$J_{2,endo\text{-}3}$
exo	24.9	9.0 (10.4)	91.7	2.2 (1.7)
endo	138.2	8.3 (8.4)	21.7	9.7 (10.1)

[a] Calculated by the equation: $J = 7 - \cos(\varphi) + 5\cos(2\varphi)$ [8]; in parentheses are given the experimental values.

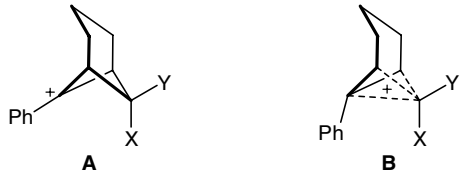
* The results of X-ray analysis of tetrasubstituted norpinanes differing by the configuration and halogen nature will be discussed in a special publication.

Table 2. Fractions of the *anti*-adduct (%) in the halomethoxylation of compounds **I** and **II**

Tricycloheptane	Cl	Br	I
I	96	92	56
II	94	86	30

the methoxycarbonyl group about the C^6–C^8 bond in molecule **Xb** in solution. Analogous fragments are equivalent in the spectra of both diastereoisomers of trisubstituted norpinanes **IIIa/IIIb**, **Va/Vb**, and **IXa/IXb** having no CO_2Me substituent. In the molecules of series **a** norpinanes, rotation of the methoxycarbonyl group about the C^6–C^8 bond is restricted, presumably due to donor–acceptor interaction with the opposite methoxy group. The degree of restriction (and hence nonequivalence of C^1H and C^5H) increases in going from chloride **VIa** to iodide **Xa**; a probable reason is enhanced repulsion between the CO_2Me group and the geminal halogen atom.

Table 2 contains data on the stereoselectivity of halomethoxylation of compounds **I** and **II**, obtained from the ^1H NMR spectra of the reaction mixtures. It is seen that the stereoselectivity depends on both halogen nature and substituent X in the substrate. Assuming that the reaction involves intermediate formation of a classical carbenium ion like **A**, decrease in the *anti*-stereoselectivity of halomethoxylation of tricycloheptanes **I** and **II** as the size of the halogen atom increases cannot be explained only in terms of deviation of the C^3H_2 fragment toward the cationic center according to [1, 2]. Presumably, we must take into account the effect of geminal repulsion between the X substituent (X = H, CO_2Me) and the halogen atom (Y), which makes the X substituent closer to the cationic center as the size of the halogen atom increases; as a result, the fraction of the *anti*-adduct decreases. The importance of that factor for the stereoselectivity of iodination of **I** was noted previously [4]. However, a sharp change in the stereoselectivity in going from bromine to iodine (but not from chlorine to bromine) suggests the existence of an additional factor favoring *syn*-nucleophilic attack in the iodomethoxylation process. We believe that this factor may be variation of charge delocalization in the cationic intermediate upon replacement of bromine or chlorine by iodine. It is also possible that the iodine-containing intermediate has a structure similar to bicyclobutyl cation **B** due to low electronegativity and appreciable positive resonance effect of iodine; nucleophilic attack on cation like **B** can occur only from the *syn* side. An analogous structure of cationic intermediate was postulated previously for the methoxymercuration of unsubstituted tricyclo[4.1.0.$0^{2,7}$]heptane [9] and compounds **I** and **II** [1, 2], as well as for the conjugate iodination of unsubstituted and 1-methyl-substituted tricyclo[4.1.0.$0^{2,7}$]heptanes [10, 11]. More electronegative bromine and especially chlorine atoms preferentially give rise to classical carbenium intermediate like **A**; therefore, the *anti*-stereoselectivity decreases only slightly.



X = H, CO_2Me; Y = Cl, Br.

Our treatment of the stereochemistry of halomethoxylation of compounds **I** and **II** with respect to the halogen nature is fully consistent with the results of conjugate halogenation of compound **I** and conclusions drawn therefrom [5]. In the presence of a stronger anionoid nucleophile than methanol, the conjugate iodination of **I** was almost completely *syn*-stereoselective. Decrease in the fraction of the *anti*-adduct in going from monosubstituted tricycloheptane **I** to its disubstituted analog **II** was observed in each halomethoxylation reaction, regardless of the halogen nature. This is the result of steric effect of the methoxycarbonyl group, which was discussed previously [1, 2] while studying the bromomethoxylation process.

EXPERIMENTAL

The elemental compositions were determined on an HP-185B CHN analyzer. The ^1H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Bruker DRX-300 spectrometer at 300 and 75.4 MHz, respectively; the chemical shifts were measured relative to the solvent signals (residual $CHCl_3$, δ 7.26 ppm; $CDCl_3$, δ_C 76.9 ppm). Signals in the ^1H and ^{13}C NMR spectra of **IVa**, **VIa**, and **Xb** were assigned using two-dimensional COSY, NOESY, and HETCOR techniques (Bruker Avance DRX-600 instrument). Solid products were recrystallized from hexane–diethyl ether unless otherwise stated. Analytical thin-layer chromatography was performed on Silufol UV-254 plates (development with iodine vapor); Silica gel LSL (5–40 μm) was used for preparative TLC, and silica gel L (40–100 μm), for column chromatography; eluent diethyl ether–hexane,

1:(1–3). Compounds **I** [1] and **II** [6, 12] and *N*-chloro- [13] and *N*-iodosuccinimides [14] were prepared by known methods.

The X-ray diffraction data for single crystals of **VIa** and **Xb** were acquired on a Siemens CCD-SMART diffractometer (MoK_α irradiation, λ = 0.71073 Å, temperature 223(2) K, graphite monochromator, θ/2θ scanning). The structures were solved by the direct method, followed by successive electron density syntheses. The positions of non-hydrogen atoms were refined by the full-matrix least-squares procedure (with respect to F^2) in anisotropic approximation. The positions of hydrogen atoms were calculated from the geometry considerations and were involved in the refinement procedure using the *riding* model [U(H) = 1.2U(C), where U(C) is the equivalent temperature factor of that carbon atom to which the corresponding hydrogen atom is attached]. All calculations were performed using SHELXTL 5.1 software package [15]. In all cases, U_{eq} was defined as one third of the orthogonalized U_{ij} tensor. The coordinates and equivalent isotropic thermal parameters of hydrogen atoms and anisotropic thermal parameters of non-hydrogen atoms are available from the authors. The structures of molecules **VIa** and **Xb** are shown in Figs. 1 and 2, respectively.

***syn*-7-Bromo-*exo*-6-methoxy-*endo*-6-phenylbicyclo[3.1.1]heptane (IIIa)** [2]**.** ^{1}H NMR spectrum, δ, ppm: 0.61 d.t.t (1H, *endo*-3-H, J = 14.8, 10.4, 8.5 Hz), 1.22 d.t.t (1H, *exo*-3-H, J = 14.8, 9.9, 1.6 Hz), 1.93–2.08 m (2H, *endo*-2-H, *endo*-4-H), 2.13–2.28 m (2H, *exo*-2-H, *exo*-4-H), 2.97 s (3H, OCH_3), 3.10 br.s (2H, 1-H, 5-H, halfwidth 14 Hz), 5.23 br.t (1H, *exo*-7-H, J = 5.8 Hz), 7.23–7.45 m (5H, Ph).

Methyl *endo*-6-bromo-*anti*-7-methoxy-*syn*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (IVa) [1]**.** ^{1}H NMR spectrum, δ, ppm: 0.59 d.t.t (1H, *exo*-3-H, J = 14.9, 10.5, 8.4 Hz), 1.21 d.t.t (1H, *endo*-3-H, J = 14.9, 9.8, 1.8 Hz), 2.10–2.27 m (2H, *exo*-2-H, *exo*-4-H), 2.27–2.42 m (2H, *endo*-2-H, *endo*-4-H), 2.86 s (3H, OCH_3), 3.41 br.s and 3.53 br.s (1H each, 1-H, 5-H, halfwidth 16 Hz), 3.85 s (3H, CO_2CH_3), 7.22–7.30 m (2H, H_{arom}), 7.35–7.45 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 11.4 (C^3); 26.8 and 26.9 (C^2, C^4); 47.0 and 49.4 (C^1, C^5); 49.7 and 52.6 (OCH_3); 68.5 (C^6); 84.2 (C^7); 126.9 (2C), 128.0, 128.1 (2C), and 136.9 (Ph); 171.1 (C=O).

***syn*-7-Chloro-*exo*-6-methoxy-*endo*-6-phenylbicyclo[3.1.1]heptane (Va).** *N*-Chlorosuccinimide, 0.35 g (2.6 mmol), was dissolved in 15 ml of methanol, 50 mg of powdered $CaCO_3$ was added, and a solution of 0.43 g (2.5 mmol) of compound **I** in 10 ml of methanol was then added. The mixture was stirred for 4 h at 20°C and evaporated under reduced pressure, the residue was dissolved in 25 ml of methylene chloride, the solution was washed with water (2×10 ml) and dried over $MgSO_4$, and the solvent was removed. According to the ^{1}H NMR data, the residue contained mainly compound **Va** and ~5% of its isomer **Vb**. By preparative thin-layer chromatography we isolated 0.44 g (75%) of isomer **Va** as a light yellow oily substance, R_f 0.61 (hexane–diethyl ether, 4:1). ^{1}H NMR spectrum, δ, ppm: 0.61 d.t.t (1H, *endo*-3-H, J = 14.6, 10.4, 8.5 Hz), 1.22 d.t.t (1H, *exo*-3-H, J = 14.6, 9.9, 1.8 Hz), 1.85–1.98 m (2H, *endo*-2-H, *endo*-4-H), 2.13–2.28 m (2H, *exo*-2-H, *exo*-4-H), 2.99 s (3H, OCH_3), 3.10 br.s (2H, 1-H, 5-H, halfwidth 14 Hz), 5.04 br.t (1H, *exo*-7-H, J = 6.0 Hz), 7.25–7.47 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 12.3 (C^3); 22.9 (2C, C^2, C^4); 46.0 (2C, C^1, C^5); 50.2 (OCH_3); 59.7 (C^6); 84.1 (C^7); 127.1 (2C), 127.6, 128.0 (2C), and 137.5 (Ph). Found, %: C 70.93; H 7.41. $C_{14}H_{17}ClO$. Calculated, %: C 71.03; H 7.24.

***syn*-7-Chloro-*endo*-6-methoxy-*exo*-6-phenylbicyclo[3.1.1]heptane (Vb).** A stream of dry chlorine was passed through a suspension of 0.87 g (2 mmol) of compound **VII** in 15 ml of methylene chloride until a yellow–green transparent solution was obtained (about 15–20 min). After 2 h, excess chlorine and the solvent were removed under reduced pressure, and the residue was subjected to column chromatography. Yield 0.24 g (51%), light yellow oily substance, R_f 0.70 (hexane–diethyl ether, 4:1). ^{1}H NMR spectrum, δ, ppm: 1.65–1.94 m (2H, 3-H), 2.10–2.29 m (2H, 2-H, 4-H), 2.94 s (3H, OCH_3), 3.06 d.t (2H, 1-H, 5-H, J = 5.7, 1.3 Hz), 4.12 br.t (1H, 6-H, J = 5.7 Hz), 7.29–7.52 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 13.6 (C^3); 22.2 (2C, C^2, C^4); 47.5 (2C, C^1, C^5); 51.9 (OCH_3); 54.8 (C^6); 78.9 (C^7); 127.3 (2C), 127.6, 128.4 (2C), and 140.9 (Ph). Found, %: C 71.12; H 7.17. $C_{14}H_{17}ClO$. Calculated, %: C 71.03; H 7.24.

Reaction of ester II with *N*-chlorosuccinimide. *N*-Chlorosuccinimide, 0.40 g (3 mmol), was added to a solution of 0.69 g (3 mmol) of compound **II** in 20 ml of methanol, and the mixture was stirred for 6 h at 20°C. The solvent was removed under reduced pressure, the residue was dissolved in 50 ml of diethyl ether, and the solution was washed with water and dried over Na_2SO_4. Removal of the solvent, followed

by recrystallization of the residue, gave 0.64 g (72%) of chloride **VIa**. The mother liquor contained isomer **VIb** (^{1}H NMR data).

Methyl *endo*-6-chloro-*anti*-7-methoxy-*syn*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIa). mp 84–85°C, R_f 0.56 (hexane–diethyl ether, 1:1). ^{1}H NMR spectrum, δ, ppm: 0.60 d.t.t (1H, *exo*-3-H, J = 14.6, 10.4, 8.4 Hz), 1.22 d.t.t (1H, *endo*-3-H, J = 14.6, 10.1, 1.7 Hz), 2.01–2.15 m (2H, *exo*-2-H, *exo*-4-H), 2.22–2.40 m (2H, *endo*-2-H, *endo*-4-H), 2.86 s (3H, OCH_3), 3.47 br.s (2H, 1-H, 5-H, halfwidth 24 Hz), 3.85 s (3H, CO_2CH_3), 7.23–7.32 m (2H, H_{arom}), 7.35–7.45 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 11.7 (C^3); 24.7 (2C, C^2, C^4); 47.0 and 47.8 (C^1, C^5); 49.6 and 52.6 (OCH_3); 71.1 (C^6); 84.0 (C^7); 127.0 (2C), 128.0 (2C), 128.1, and 136.5 (Ph); 170.7 (C=O). Found, %: C 65.25, 64.96; H 6.52, 6.58. $C_{16}H_{19}ClO_3$. Calculated, %: C 65.19; H 6.50.

X-Ray diffraction data for compound VIa. Triclinic crystals, space group P-1; unit cell parameters: a = 10.8729(13), b = 11.6741(15), c = 13.2390(17) Å; α = 114.179(2), β = 91.584(3), γ = 100.465(3)°; V = 1497.7(3) Å^3. Crystal habit 0.20×0.20×0.05 mm; Z = 4; d_{calc} = 1.307 g/cm^3. Total of 10061 reflections were measured, 6960 of which were independent (R_{int} = 0.0544), F(000) = 624, υ_{max} = 28.86°. A correction for absorption (μ = 0.259 mm^{-1}) was introduced using SADABS algorithm. The final divergence factors were R_1 = 0.0584 [for 6960 reflections with $I > 2\sigma(I)$; calculated by F_{hkl}] and wR_2 = 0.0765 (for all 10061 reflections involved in the final refinement stage; calculated by F_{hkl}^2); number of refined parameters 515; GOOF 0.772. Each unit cell contains two crystallographically independent atropoisomer molecules.

Methyl *endo*-6-chloro-*syn*-7-methoxy-*anti*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIb). A stream of chlorine was passed over a period of 30 min through a solution of 495 mg (1 mmol) of compound **VIII** in 20 ml of methylene chloride until the mixture turned persistently yellow–green. After 2 h, the mixture was filtered, the filtrate was washed with an aqueous solution of $NaHCO_3$ and water and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by preparative TLC on silica gel. Yield 86 mg (29%), mp 49–51°C, R_f 0.63 (hexane–diethyl ether, 1:1). ^{1}H NMR spectrum, δ, ppm: 1.62–1.75 m and 1.75–1.89 m (1H each, 3-H), 2.27–2.42 m (4H, 2-H, 4-H), 2.90 s (3H, OCH_3), 3.18 s (3H, CO_2CH_3), 3.55 br.s (2H, 1-H, 5-H), 7.30–7.47 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 13.6 (C^3); 24.6 (2C, C^2, C^4); 49.2 (2C, C^1, C^5); 49.0 and 52.1 (OCH_3); 67.3 (C^6); 78.8 (C^7); 127.4 (2C), 128.0 (2C), 128.5, and 137.9 (Ph); 170.2 (C=O). Found, %: C 65.29, 65.25; H 6.67, 6.68. $C_{16}H_{19}ClO_3$. Calculated, %: C 65.19; H 6.50.

***syn*-7-Chloromercurio-*endo*-6-methoxy-*exo*-6-phenylbicyclo[3.1.1]heptane (VII)** was synthesized according to the procedure described in [2]. The ^{1}H NMR spectrum of **VII** was identical to that given in [2]. ^{13}C NMR spectrum, δ_C, ppm: 13.5 (C^3); 26.7 (2C, C^2, C^4); 48.4 (2C, C^1, C^5); 49.6 (C^7); 51.1 (OCH_3); 81.4 (C^6); 127.3 (2C), 127.5, 128.2 (2C), and 141.4 (Ph).

Methyl *endo*-6-chloromercurio-*syn*-7-methoxy-*anti*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIII). Ester **II**, 1.15 g (5 mmol), was added to a solution of 1.6 g (5 mmol) of $Hg(OAc)_2$ in 30 ml of methanol, and the mixture was stirred for 3 h at 20°C. A solution of 1.49 g (20 mmol) of potassium chloride in 10 ml of aqueous methanol (1:1) was then added, and the mixture was stirred for 1 h, concentrated on a rotary evaporator to a volume of ~20 ml, and diluted with 30 ml of water. The precipitate was filtered off, washed with water, and dried under reduced pressure. Yield 1.88 g (76%), mp 216–217°C (from $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 1.85–2.0 m and 2.15–2.2.3 m (1H each, 3-H), 2.0–2.15 m and 2.3–2.45 m (2H each, 2-H, 4-H), 2.83 s (3H, OCH_3), 3.13 s (3H, CO_2CH_3), 3.68 br.s (2H, 1-H, 5-H), 7.25–7.7.47 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 13.7 (C^3); 28.9 (2C, C^2, C^4); 50.7 (2C, C^1, C^5); 51.0 and 51.4 (OCH_3); 68.9 (C^6); 81.3 (C^7); 127.7 (2C), 128.0, 128.5 (2C), and 138.6 (C_{arom}); 173.3 (C=O). Found, %: C 39.03; H 3.79. $C_{16}H_{19}ClHgO_3$. Calculated, %: C 38.79; H 3.87.

Reaction of tricycloheptane I with *N*-iodosuccinimide. *N*-Iodosuccinimide, 1.13 g (5 mmol), was slowly added at room temperature to a solution of 0.85 g (5 mmol) of compound **I** in 15 ml of methanol. The mixture was stirred for 6 h, the solvent was removed under reduced pressure, and the residue was treated with 25 ml of a 5% aqueous solution of Na_2CO_3 and 25 ml of $CHCl_3$. The organic phase was separated, washed in succession with a 10% solution of Na_2SO_3, a 5% solution of Na_2CO_3, and water, and dried over $CaCl_2$. The solvent was removed, and the residue was separated by column chromatography to isolate 0.51 g (31%) of methoxy iodide **IXb**, R_f 0.71 (hexane–diethyl ether, 4:1), and 0.72 g (44%) of isomer **IXa**, R_f 0.62.

syn*-7-Iodo-*exo*-6-methoxy-*endo*-6-phenylbicyclo-[3.1.1]heptane (IXa).* mp 97–98°C. ^{1}H NMR spectrum, δ, ppm (cf. [4]): 0.59 d.t.t (1H, *endo*-3-H, *J* = 15.0, 10.3, 8.6 Hz), 1.20 d.t.t (1H, *exo*-3-H, *J* = 15.0, 9.6, 1.8 Hz), 2.01–2.20 m (4H, 2-H, 4-H), 33.0 br.d (3H, OCH_3), 3.04 br.d (2H, 1-H, 5-H, *J* = 5.7 Hz), 5.40 t (1H, 6-H, *J* = 5.7 Hz), 7.20–7.47 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 11.6 (C^3); 28.2 (2C, C^2, C^4); 39.6 (C^6); 46.0 (2C, C^1, C^5); 50.3 (OCH_3); 83.9 (C^7); 126.6 (2C), 127.6, 127.8 (2C), and 138.2 (Ph). Found, %: C 51.26; H 5.28. $C_{14}H_{17}IO$. Calculated, %: C 51.36; H 5.35.

syn*-7-Iodo-*endo*-6-methoxy-*exo*-6-phenylbicyclo-[3.1.1]heptane (IXb).* mp 86–87°C. ^{1}H NMR spectrum, δ, ppm (cf. [4]): 1.66–1.85 m (2H, 3-H), 1.92–2.14 m and 2.28–2.48 m ((2H each, 2-H, 4-H), 2.91 s (3H, OCH_3), 3.01 br.d (2H, 1-H, 5-H, *J* = 5.7 Hz), 4.28 t.t (1H, 6-H, *J* = 5.7, 1.5 Hz,), 7.29–7.49 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 12.7 (C^3); 26.5 (2C, C^2, C^4); 29.1 (C^6); 47.9 (2C, C^1, C^5); 51.6 (OCH_3); 78.9 (C^7); 127.2 (2C), 127.7, 128.3 (2C), and 140.7 (Ph). Found, %: C 51.38; H 5.25. $C_{14}H_{17}IO$. Calculated, %: C 51.36; H 5.35.

Reaction of compound II with *N*-iodosuccinimide. *N*-Iodosuccinimide, 0.90 g (4 mmol), was added under stirring to a solution of 0.92 g (4 mmol) of ester **II** in 30 ml of methanol, and the mixture was stirred for 8 h at 20°C. The solvent was removed under reduced pressure, the residue was dissolved in 50 ml of diethyl ether, the solution was washed with water, dried over $MgSO_4$, and evaporated, and the residue was separated by preparative TLC to isolate 0.62 g (39.5%) of iodo ester **Xb** and 0.29 g (18.5%) of isomer **Xa** (R_f 0.64 and 0.57, respectively; hexane–diethyl ether, 1:1).

Methyl *endo*-6-iodo-*anti*-7-methoxy-*syn*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (Xa). Oily substance which failed to crystallize. ^{1}H NMR spectrum, δ, ppm: 0.55 d.t.t (1H, *exo*-3-H, *J* = 14.8, 10.5, 8.0 Hz), 1.17 d.t.t (1H, *endo*-3-H, *J* = 14.8, 9.7, 1.7 Hz), 2.10–2.26 m (2H, *exo*-2-H, *exo*-4-H), 2.26–2.41 m (2H, *endo*-2-H, *endo*-4-H), 2.86 s (OCH_3), 3.34 br.s and 3.46 br.s (1H each, 1-H, 5-H, halfwidth 17 Hz), 3.82 s (CO_2CH_3), 7.20–7.30 m (2H, H_{arom}), 7.32–7.42 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 11.1 (C^3); 30.6 and 30.7 (C^2, C^4); 47.6 and 49.8 (C^1, C^5); 50.1 and 52.6 (OCH_3); 56.4 (C^6); 83.1 (C^7); 126.6 (2C), 127.9, 128.0 (2C), and 137.7 (Ph); 172.7 (C=O). Found, %: C 50.03; H 4.78. $C_{16}H_{19}IO_3$. Calculated, %: C 49.76; H 4.96.

Methyl *endo*-6-iodo-*syn*-7-methoxy-*anti*-7-phenylbicyclo[3.1.1]heptane-*exo*-6-carboxylate (Xb). mp 105–107°C. ^{1}H NMR spectrum, δ, ppm: 1.65–1.87 m (2H, 3-H), 2.12–2.28 m and 2.51–2.68 m (2H each, 2-H, 4-H), 2.87 s (OCH_3), 3.13 s (CO_2CH_3), 3.49 br.s (2H, 1-H, 5-H), 7.26–7.47 m (5H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 12.9 (C^3); 30.0 (2C, C^2, C^4); 48.1 (C^6); 50.3 (2C, C^1, C^5); 51.4 and 52.0 (2C, OCH_3); 77.1 (C^7); 127.6 (2C), 128.1, 128.7 (2C), and 137.9 (Ph); 172.5 (C=O). Found, %: C 49.87; H 4.99. $C_{16}H_{19}IO_3$. Calculated, %: C 49.76; H 4.96.

X-Ray diffraction data for compound Xb. Monoclinic crystals, space group C_2/c; unit cell parameters: a = 17.081(3), b = 13.148(2), c = 14.968(3) Å; β = 116.330(3)°; V = 3012.9(9) Å^3. Crystal habit 0.30×0.30×0.10 mm; Z = 8; d_{calc} = 1.703 g/cm^3. Total of 9960 reflections were measured, 3711 of which were independent (R_{int} = 0.0227), $F(000)$ = 1536, υ_{max} = 29.12°. A correction for absorption (μ = 2.130 mm^{-1}) was introduced using SADABS algorithm. The final divergence factors were R_1 = 0.0229 [for 3711 reflections with $I > 2\sigma(I)$; calculated by F_{hkl}] and wR_2 = 0.0604 (for all 9960 reflections involved in the final refinement stage; calculated by F_{hkl}^2); number of refined parameters 252; GOOF 0.966.

Reactions of compounds I and II with *N*-halosuccinimides (NYS, Y = Br, Cl, I) in methanol (*analytical experiments*). A mixture of ~0.2 mmol of compound **I** or **II** and a small excess (~10%) of the corresponding *N*-halosuccinimide in 5 ml of methanol was stirred at 25°C for 2 h (for compound **I**) or 10 h (for **II**). The solvent was distilled off under reduced pressure, the residue was dissolved in diethyl ether, and the solution was washed with water and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the residue was analyzed by ^{1}H NMR spectroscopy. The diastereoisomer ratios of halomethoxylation products **III**–**VI**, **IX**, and **X** were determined from the intensities of the singlets from the methoxy protons and triplets from the CH protons. The results are given in Table 2 (average values from three parallel runs).

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