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Regio- and Stereoselectivity in the Halogenation of Methyl Tricyclo[4.1.0.0^{2,7}]heptane-1-carboxylate

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Abstract—Conjugate halogenation of methyl tricyclo[4.1.0.0^{2,7}]heptane-1-carboxylate by the action of *N*-iodo- and *N*-bromosuccinimides in the presence of halide ions occurs exclusively at the central bicyclobutane C^1–C^7 bond via electrophilic attack on the C^1 atom, leading to *endo*,*syn*-adducts of the norpinane series. Reactions of the title compound with iodine, dibromotetrachloroethane, and (dichloro-λ^3-iodanyl)benzene give not only the corresponding 6,7-*endo*,*syn*-dihalonorpinane but also its epimer at C^6, indicating radical mechanism of the halogenation. The regio- and stereoselectivity observed in these ionic and radical reactions are discussed in terms of the results of nonempirical MP2/STO-3G calculations of appropriate cationic and radical intermediates.

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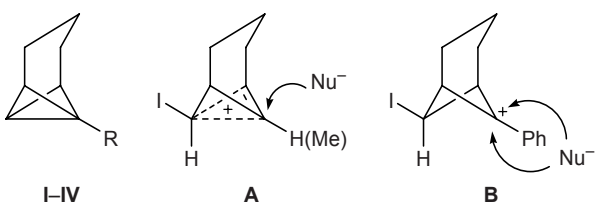
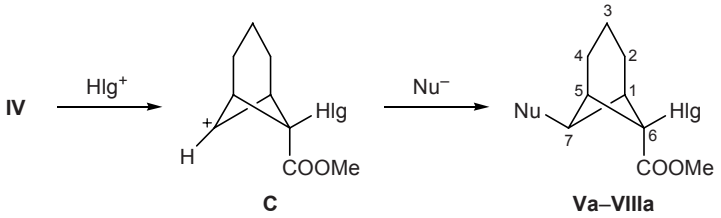
We previously showed [1–3] that tricyclo[4.1.0.0^{2,7}]-heptane (**I**) and its 1-methyl- and 1-phenyl-substituted derivatives **II** and **III** react with *N*-iodosuccinimide (NIS) in the presence of an external nucleophile (Nu = Hlg, SCN, RCOO, etc.) exclusively at the C^1–C^7 bond to give the corresponding conjugate iodination products. The addition to hydrocarbons **II** and **III** was strictly regioselective (electrophilic attack by iodine on C^7), which is consistent with the assumed ionic mechanism of the addition. The difference in the stereochemistry of the addition to compounds **I** and **II**, on the one hand, and phenyl-substituted derivative **III**, on the other, was related only to the direction of attack by external nucleophile (it is generally accepted [4] that electrophilic attack by a halogen, including iodine, always occurs from the *endo* side). In the reactions with **I** and **II**, the attack occurred exclusively from the side of the trimethylene bridge, resulting in strict *endo*,*syn* addition, whereas in the reaction with **III** the attack was not stereoselective, and two diastereoisomers were formed. The difference in the stereoselectivity was interpreted in terms of different structures of cationic intermediates. In the first case, the intermediate was cation **A** which allows only strictly selective approach of external nucleophile, while in the latter case, the intermediate is benzyl-type cation **B** which allows nucleophile approach in two directions. The reaction of elemental iodine with tricycloheptane **I** results in *endo*,*syn* addition of two iodine atoms at the C^1–C^7 bond [5, 6], indicating intermediacy of cation **A** in the process.



I, R = H; **II**, R = Me; **III**, R = Ph; **IV**, R = MeOCO.

In the present work we focused on the iodination of tricycloheptane **IV** containing an electron-withdrawing methoxycarbonyl group in position *1*. It might be expected that the presence of such substituent should reduce the nucleophilicity of the substrate and change the regioselectivity of electrophilic addition to this compound. In fact, the results confirmed our expectations. Ester **IV** reacted with NIS in the presence of 5–10 equiv of KI, LiBr, or LiCl (as source of external nucleophile) in DMF at 20°C (reaction time 5–7 days) to give only the corresponding *endo*,*syn*-addition product at the C^1–C^7 bond, dihalonorpinane **Va**–**VIIa** (Scheme 1). Compound **VIIa** was also obtained by treatment of **IV** with the triethylbenzylammonium

Scheme 1.



Va–**VIIa**, Hlg = I; **VIIIa**, Hlg = Br; **Va**, Nu = I; **VIa**, **VIIIa**, Nu = Br; **VIIa**, Nu = I.

chloride–iodine(I) chloride complex ($BzlEt_3NCl \cdot ICl$) in CH_2Cl_2 at 20°C. These results are quite consistent with ionic mechanism of the addition: the attack by electrophilic iodine was strictly regioselective (on the C^1 atom) in keeping with the orienting effect of the electron-withdrawing substituent, and cationic intermediate **C** took up external nucleophile with strict *syn* stereoselectivity.

For comparison, we also examined the reaction of **IV** with *N*-bromosuccinimide (NBS) in DMF in the presence of 5 equiv of LiBr. The only addition product was dibromide **VIIIa** which is analogous to diiodide **Va**. Thus we can contend that the reaction of **IV** with NBS also follows ionic mechanism.

On the other hand, the reaction of tricycloheptane **IV** with elemental iodine in carbon tetrachloride or diethyl ether (~75 h at 20°C) unexpectedly resulted in the formation of a mixture of diastereoisomeric norpinanes **Va** and **Vb** at a ratio of 3:1 or 2:1, respectively.* The formation of compound **Vb** is impossible in ionic process, while it is quite probable in radical reaction. Presumably, diiodides **Va** and **Vb** are formed via *endo* attack by iodine atom on the unsubstituted C^7 atom in the bridgehead position. Intermediate radical **D** takes up the second iodine atom from the reagent in a nonstereoselective mode. Insofar as diastereoisomer **Va** could also be formed via ionic process, we cannot rule out operation of both addition mechanisms whose relative contributions determine the stereoisomeric composition of the product. We concluded that, unlike tricycloheptanes **I**–**III**, electron-deficient compound **IV** is characterized by a lower reactivity as nucleophile with respect to elemental iodine, the latter being less electrophilic than *N*-iodosuccinimide or iodine(I) chloride; therefore, the contribution of radical iodination path increases.

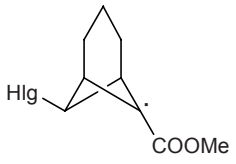
An indirect support for the radical mechanism of addition of I_2 to ester **IV** may be the data on dihalogenation of the same compound with indubitably radical reagents. The dibromination of **IV** with dibromotetrachloroethane (which is commonly used for radical bromination of alkenes [8]) in a Pyrex tube under irradiation with a KGL-500 halogen filament lamp gave a mixture of diastereoisomeric dibromides **VIIIa** and **VIIIb** at a ratio of 2.5:1. The reaction of ester **IV** with (dichloro-λ^3-iodanyl)benzene in carbon tetrachloride in a quartz tube under irradiation with a KGL-500 lamp led to the formation of analogous dichloro derivatives **IXa** and **IXb** at a ratio of 1:1.9, and the reaction mixture contained three more compounds with an overall concentration of 30%. One of these products was identified by gas chromatography–mass spectrometry as chloride **Xa** (using an authentic sample prepared by hydrodeiodination of iodochloro derivative **VIIa** with Ph_3SnH). The two other impurities were not identified.

The facts that *syn*-adduct **VIIIa** is formed as the major product in the dibromination of ester **IV** with dibromotetrachloroethanoe (as in the diiodination with I_2) and that the chlorination of **IV** with (dichloro-λ^3-iodanyl)benzene gives mainly *anti*-adduct **IXb** are interesting. Insofar as radical addition of benzenethiol [9] and benzenesulfonyl bromide [10] to the same substrate are characterized by *anti*-stereoselectivity, the pattern observed in the dibromination of **IV** may be rationalized assuming a contribution of ionic reaction path (as postulated above for the diiodination) with participation of molecular bromine which can be formed in a small amount by decomposition of dibromotetrachloroethane.

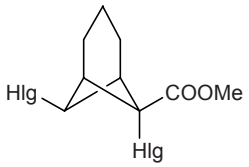
A direct evidence in favor of the radical mechanism was obtained by performing analytical experiment on the iodination of compound **IV** in the presence of 2,4,6-tribromo-1-nitrosobenzene: the mixture obtained by mixing degassed solutions of the reactants in benzene showed over a period of 2 days a strong signal in

* This result for the reaction in carbon tetrachloride was given for the first time in dissertation [7] performed under the guidance of Prof. G. Szeimies; however, the configurations of iodides **Va** and **Vb** were not assigned.

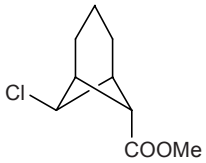
the ESR spectrum (nitrogen triplet with a_N = 14.4 G) from the corresponding nitroxyl radical formed by trapping of short-lived carbon-centered radical **D** (cf. [11]).



D



Vb, **VIIIb**, **IXb**



Xa

V, Hlg = I; **VIII**, Hlg = Br; **IX**, Hlg = Cl.

The ^{1}H NMR spectra allowed us to determine steric configuration of compounds **V**–**X** on the basis of the relations found previously for 6- and 7-substituted norpinanes [12, 13]. The *syn* configuration at C^7 for all compounds follows from the presence of a triplet signal (^3J = 5.7–5.9 Hz) from 7-H. The large difference in the chemical shifts of 7-H ($\Delta\delta \approx 1$ ppm) in each diastereoisomer couple (**Va**/**Vb**, **VIIIa**/**VIIIb**, and **IXa**/**IXb**) makes it possible to determine the configuration of C^6, taking into account known strong deshielding effect of a halogen atom (as compared to methoxycarbonyl group) [13] on the opposite 7-H proton. Almost complete coincidence of the chemical shifts of 7-H in compounds **VIa** and **VIIa** and their analogs **VIIIa** and **IXa** confirms the validity of the above assignment. The configuration at C^6 in **Xa** is established by the presence of a singlet signal from 6-H.

Table 1. Experimental and calculated chemical shifts of C^6 and C^7 in dihalonorpinanes **V**–**IX**, δ_C, ppm

Comp. no.	C^6		C^7	
	exptl.	calcd.	exptl.	calcd.
Va	36.1	38.6	15.2	23.4
Vb	34.5	36.7	35.0	26.6
VIa	39.8	34.5	39.5	49.9
VIIa	41.3	32.0	48.8	59.9
VIIIa	58.7	61.0	43.9	45.8
VIIIb	58.2	59.1	51.9	49.0
IXa[a]	68.5	–	53.3	–
IXb[a]	66.6	–	56.5	–

Valuable information can also be obtained by comparing the ^{13}C NMR spectra of diastereoisomers **Va**/**Vb**, **VIIIa**/**VIIIb**, and **IXa**/**IXb**. The chemical shifts of C^7 strongly differ for each diastereoisomer couple: the difference $\Delta\delta_C$ for dichloro derivatives **IXa** and **IXb** is 3.2 ppm, the $\Delta\delta_C$ value for dibromides **VIIIa** and **VIIIb** is 8.0 ppm, while the corresponding value for diiodo derivatives **Va** and **Vb** reaches 19.8 ppm; in all cases, the difference in the chemical shifts of C^6 does not exceed 2 ppm. These findings may be rationalized as follows. Let us assume that the norpinane carbon skeleton in all diastereoisomeric dihalo derivatives **V**–**X** has the same structure and that differences in the chemical shifts of C^6 or C^7 are determined exclusively by α- and γ-effects of the halogen atoms. According to [14], the α-effects of chlorine, bromine, and iodine in the ^{13}C NMR spectra of cyclobutyl halides are equal to 29.92, 19.94, and –6.62 ppm, respectively, and their γ-effects are –6.07, –3.56, and 0.54 ppm, respectively. Taking dichloride **IXa** as reference for *endo*,*syn* isomer and compound **IXb** as reference for *exo*,*syn* isomers, the chemical shifts of C^6 and C^7 in norpinanes **Va**–**VIIIa**, **Vb**, and **VIIIb** can be calculated using the additivity scheme (Table 1).

Comparison of the experimental and calculated parameters reveals considerable differences only in four instances for C^7 (the experimental values are larger than those calculated for **Vb** and **VIIIb** and smaller than those calculated for **VIa** and **VIIa**) and in two instances for C^6 (the experimental values are larger than those calculated for **VIa** and **VIIa**). We believe that these differences are related to change of the shape of the norpinane carbon skeleton in going from the reference compounds to other derivatives. In fact, there are reasons to suppose that the carbon skeleton of three dihalonorpinanes **Va**, **VIIIa**, and **IXa** has the same shape corresponding to flattened $C^1C^2C^3C^4C^5$ fragment, which was found by X-ray analysis for 6,7-*endo*,*syn*-diiodonorpinane [5] and 6,7-*endo*,*syn*-dibromo- and 6,7-*endo*,*syn*-dichloro-6-*exo*-phenylsulfonylnorpinanes [15, 16]. The $C^1C^2C^3C^4C^5$ fragment in molecules **VIa**, **VIIa**, **Vb**, and **VIIIb** should be expected to deviate from planar structure via displacement of the C^3H_2 group toward smaller substituent on C^6 and C^7 (according to [17], the van der Waals radii of I, Br, Cl, and CO_2Me groups are 1.97, 1.86, 1.73, and 1.62 Å, respectively). Therefore, approach of the C^3H_2 group to the *endo*(*syn*)-oriented halogen atom on C^6 or C^7 should be accompanied by upfield shift of the corresponding carbon signal (C^7 in

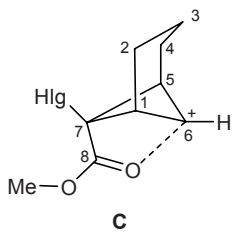
Table 2. Interatomic distances *d* (Å), bond orders (*P*), charges on atoms (*q*), and interplanar and plane–bond angles (deg) in halogen-substituted cations **C**

Cation	*l* (*P*)						*q*						Angles			
	C^1–C^6	C^5–C^6	C^1–C^7	C^5–C^7	C^6–C^7	C^6–O	C^1	C^5	C^6	C^7	C^8	Hlg	$C^1C^6C^5$/ $C^1C^7C^5$	$C^1C^6C^7$/ $C^5C^6C^7$	$C^1C^6C^5$/ C^6H^6	$C^1C^2C^4C^5$/ $C^2C^3C^4$
$\mathbf{C}_I$	1.558 (0.78)	1.559 (0.74)	1.588 (0.73)	1.588 (0.70)	2.060 (0.21)	1.499 (0.59)	–0.027	–0.027	0.076	–0.115	0.427	0.177	145.0	143.5	146.5	132.6
$\mathbf{C}_{Br}$	1.559 (0.78)	1.559 (0.74)	1.586 (0.73)	1.586 (0.70)	2.053 (0.21)	1.490 (0.59)	–0.026	–0.026	0.076	–0.063	0.429	0.103	145.2	143.5	146.4	132.9
$\mathbf{C}_{Cl}$	1.562 (0.78)	1.561 (0.74)	1.581 (0.73)	1.581 (0.70)	2.038 (0.22)	1.492 (0.59)	–0.021	–0.021	0.076	0.030	0.436	–0.060	145.8	143.7	146.2	132.9

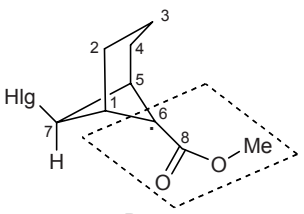
VIa and **VIIa**) as a result of steric compression [18]; deviation of the C^3H_2 group in the opposite direction should lead to downfield shift of the corresponding carbon signal (C^7 in **Vb** and **VIIIb** or C^6 in **VIa** and **VIIa**). Despite planar structure of the trimethylene bridge in norpinane dihalides **Va**, **VIIIa**, and **IXa**, the difference between the experimental and calculated chemical shifts of C^7 increases for dibromide **VIIIa** ($\Delta\delta_C$ = –1.9 ppm) and especially for diiodide **Va** ($\Delta\delta_C$ = –8.2 ppm), which may be also attributed to steric compression effect. Thus the observed increase in the difference between the chemical shifts of C^7 in diastereoisomers in going from dichlorides **IXa**/**IXb** to dibromides **VIIIa**/**VIIIb** and then to diiodides **Va**/**Vb** can be reasonably understood.

Compounds **V**–**IX** displayed in the mass spectra a common fragmentation pattern. The molecular ion peak had a low intensity, while the most abundant was tropylium ion (*m*/*z* 91); high intensity was also observed for the $[C_9H_{11}O_2]^+$ fragment ion peak (*m*/*z* 151). Differences in the mass spectra of diastereoisomers **Va**/**Vb**, **VIIIa**/**VIIIb**, and **IXa**/**IXb** were insignificant, and they included mainly intensities of some peaks.

With a view to reveal fine details of the electronic and steric structure of intermediates formed in the halogenation of ester **IV**, i.e., norpinanyl cations like **C** and radicals **D**, we performed optimization of their geometric parameters by MP2/STO-3G calculations using GAMESS program [19] (Tables 2, 3). In all cases, the most stable cations **C** had a conformation in which the C^3 atom is displaced relative to the $C^1C^2C^4C^5$ plane toward the cationic center, the dihedral angle between the $C^1C^2C^4C^5$ and $C^2C^3C^4$ planes being slightly smaller than 133°. The methoxycarbonyl group lies almost in the $C^3C^6C^7$ plane, and the carbonyl oxygen atom is directed toward C^6.



C



D

The calculations showed that cations **C** are characterized by effective donor–acceptor interaction between the carbonyl oxygen atom and C^6. First, the interatomic distance $C^6\cdots O$ is much shorter than the sum of the corresponding van der Waals radii (3.00 Å [20]); second, the C^6 atom has a tetrahedral configuration: the angle between the $C^1C^6C^5$ plane and the C^6–H bond is ~146°; and third, the interatomic distance $C^6\cdots C^7$ is relatively short as compared, e.g., to the corresponding distance in unsubstituted norpinane (2.148 Å according to MP2/STO-3G calculations). Thus the calculated structure of cations **C** implies strictly selective attack by external nucleophile on the C^6 cationic center from the side opposite to the ester group. This attack is hampered to some extent by steric shielding of the cationic center by the C^3H_2 group. The halogen nature affects the electronic structure of intermediates **C** as follows. The positive charge in cations $\mathbf{C}_I$ and $\mathbf{C}_{Br}$ is also partially localized on the halogen atom which stabilizes the cation via homohyperconjugation (cf. [1]), while no analogous pattern is observed for cation $\mathbf{C}_{Cl}$ having more electronegative halogen atom. In addition, the interatomic distance $C^6\cdots C^7$ in cation $\mathbf{C}_{Cl}$ is the shortest among the examined intermediates, and positive charge exists not only on C^6 but also on C^7. Such charge distribution allows attack by nucleophile to be directed at C^7 in cation $\mathbf{C}_{Cl}$. In fact, experimental proofs for this reaction direction were recently obtained by us [21] while studying the reaction of ester **IV** with NO_2Cl.

Geometry optimization of radicals **D** gave structures with the C^3 atom displaced relative to the

Table 3. Interatomic distances *d* (Å), bond orders (*P*), and interplanar and plane–bond angles (deg) in halogen-substituted radicals **D**

Radical	*d* (*P*)							Angle			
	C^1–C^6	C^5–C^6	C^1–C^7	C^5–C^7	C^6–C^7	C^6–H^7	C^3–C^6	$C^1C^6C^5$/ $C^1C^7C^5$	$C^1C^6C^7$/ $C^5C^6C^7$	$C^1C^6C^5$/ C^6C^8	$C^1C^2C^4C^5$/ $C^2C^3C^4$
$\mathbf{D}_I$	1.527 (0.79)	1.528 (0.75)	1.562 (0.75)	1.563 (0.73)	2.085 (0.18)	2.497	2.690	135.8	135.0	177.1	130.0
$\mathbf{D}_{Br}$	1.527 (0.79)	1.528 (0.75)	1.563 (0.75)	1.563 (0.73)	2.089 (0.18)	2.495	2.692	135.4	134.7	177.6	130.1
$\mathbf{D}_{Cl}$	1.528 (0.79)	1.529 (0.75)	1.558 (0.75)	1.558 (0.73)	2.079 (0.18)	2.529	2.694	135.6	134.8	177.7	130.3

$C^1C^2C^4C^5$ plane toward the radical center (C^6) which has a trigonal configuration (the angle between the $C^1C^6C^5$ plane and the C^6–C^8 bond is ~177°, and the $C^1C^2C^4C^5$ and $C^2C^3C^4$ planes form a dihedral angle of about 130°). The methoxycarbonyl group is almost orthogonal to the $C^3C^6C^7$ plane, so that it almost does not hamper approach of a radical reagent to C^6 from both possible sides. The interatomic distance $C^6\cdots C^7$ in radicals **D** does not exceed ~2.08 Å and is slightly longer than the corresponding distance in cations **C**. Comparison of the nonvalence distances between the *anti*-oriented 7-H atom and C^6 radical center, on the one hand, and between the C^3 and C^6 atoms, on the other, shows that chlorine-containing radical $\mathbf{D}_{Cl}$ is more accessible for *exo*-attack by external reagent, as compared to bromo- and iodo-substituted analogs. The energies of the semioccupied molecular orbitals in intermediates $\mathbf{D}_{Cl}$ (–8.23 eV), $\mathbf{D}_{Br}$ (–7.94 eV), and $\mathbf{D}_I$ (–7.32 eV) suggest stronger electrophilicity and reactivity of the chlorine-containing radical intermediate. Presumably, this is the reason why appreciable amounts of monochloro derivatives are formed in the radical reaction with $PhICl_2$; these impurities result from hydrogen abstraction from the substrate by $\mathbf{D}_{Cl}$.

Thus the calculated structural and electronic parameters of intermediates **C** and **D** agree satisfactorily with the experimental stereochemical results of ionic and radical halogenation of ester **IV**.

EXPERIMENTAL

The elemental compositions were determined on a Hewlett–Packard HP-185B CHN analyzer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer at 300.130 and 75.468 MHz, respectively, using $CDCl_3$ as solvent and tetramethylsilane as internal reference. The ESR spectra were obtained on an EPA-2M spectrometer; magnetic field calibration was performed using Mn^{2+} ions in MgO lattice as reference. The IR spectra were measured in KBr on an InfraLYuM FT-02 spectrometer with Fourier transform. GLC analyses were performed on a Crystallyuks-4000 chromatograph equipped with a flame ionization detector and a glass column, 1000×3 mm, packed with 3% of OV-17 on Inerton N-Super (0.125–0.160 mm); carrier gas nitrogen, flow rate 40 ml/min; oven temperature 160°C, injector temperature 200°C. The components were quantitated by peak areas using internal normalization technique; the calibrating factors for all compounds were assumed to be equal to unity. The chromatograms were processed using NetChrom 1.5 program. The mass spectra (electron impact, 70 eV) were obtained on an Agilent GC–MS system (6890N chromatograph coupled with a mass-selective detector); Agilent 19091S-433 (HP-5MS) column, 30 m×0.25 mm, 5% of phenylmethylsilicone; oven temperature programming from 70 to 300°C; carrier gas helium, 1 ml/min. Analytical thin-layer chromatography was performed on Silufol UV-254 plates using hexane–diethyl ether (2:1) as eluent; development with iodine vapor. Aluminum oxide of activity grade II was used for column chromatography; eluent light petroleum ether–diethyl ether, (2–3):1.

Methyl tricyclo[4.1.0.$0^{2,7}$]heptane-1-carboxylate (**IV**) [22], dibromotetrachloroethane [23], (dichloro-λ^3-iodanyl)benzene [24], 2,4,6-tribromo-1-nitrosobenzene [25], and $BzlEt_3NCl\cdot ICl$ [26] were synthesized by known methods.

Nonempirical quantum-chemical calculations (MP2/STO-3G) were performed in terms of restricted (for radicals) and unrestricted (for cations) Hartree–Fock theory using GAMESS program [19] with the initial PM3 parametrization [27] (gradient norm 0.01 kcal/mol).

Conjugate halogenation of tricycloheptane IV with *N*-halosuccinimides. The corresponding *N*-halosuccinimide, 10 mmol, was added in small portions over a period of 10–15 min with stirring under argon to a solution of 1.52 g (10 mmol) of tricycloheptane **IV** and 100 mmol of appropriate inorganic salt (KI, LiBr, or LiCl) in 40 ml of anhydrous DMF. The mixture was stirred for 5–7 days at 20°C, diluted with 40 ml of water, and extracted with diethyl ether (3×30 ml). The extracts were combined, washed with water, dried over $MgSO_4$, and evaporated under reduced pressure (water-jet pump), and the residue was subjected to column chromatography on aluminum oxide.

Methyl *endo*-6,*syn*-7-diiodobicyclo[3.1.1]heptane-*exo*-6-carboxylate (Va). Yield 30%, mp 58–59°C (from methanol), R_t 5.66 min, R_f 0.79. IR spectrum, ν, cm^{-1}: 2933 w, 1709 v.s (C=O), 1440 m, 1273 s (O–C–O), 1246 m, 1200 m, 1065 w, 862 w, 767 w, 669 w. ^1H NMR spectrum, δ, ppm: 1.55–1.94 m (2H, 3-H), 2.25–2.55 m (4H, 2-H, 4-H), 3.05 br.s (2H, 1-H, 5-H), 3.85 s (3H, OMe), 4.35 t (1H, 7-H, J = 5.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.7 (C^3), 15.2 (C^7), 30.9 (C^2, C^4), 36.1 (C^6), 49.7 (C^1, C^5), 53.4 (OMe), 172.6 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 406 (0.02) $[M]^+$, 375 (0.6) $[M - 31]$, 279 (10) $[M - 127]$, 247 (6) $[C_8H_8IO]^+$, 219 (2) $[C_7H_8I]^+$, 152 (100) $[C_9H_{12}O_2]^+$, 151 (35) $[C_9H_{11}O_2]^+$, 118 (8), 120 (10) $[C_8H_8O]^+$, 119 (12) $[C_8H_7O]^+$, 105 (7), 93 (41), 92 (27), 91 (85) $[C_7H_7]^+$, 79 (12), 78 (8), 77 (36) $[C_6H_5]^+$, 65 (20) $[C_5H_5]^+$, 63 (8), 59 (20) $[CO_2Me]^+$, 53 (10), 51 (9). Found, %: C 26.67; H 2.96. $C_9H_{12}I_2O_2$. Calculated, %: C 26.63; H 2.98.

Methyl *syn*-7-bromo-*endo*-6-iodobicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIa). Yield 43%, mp 42–43°C (from methanol), R_t 4.4 min, R_f 0.75. IR spectrum, ν, cm^{-1}: 2955 w, 1728 v.s (C=O), 1443 m, 1259 s (O–C–O), 1240 m, 1202 m, 1065 w, 866 w, 787 w, 779 w. ^1H NMR spectrum, δ, ppm: 1.59–1.73 m (2H, 3-H), 2.10–2.26 m and 2.31–2.50 m (2H each, 2-H, 4-H), 3.10 br.s (2H, 1-H, 5-H), 3.81 s (3H, OMe), 4.37 t (1H, 7-H, J = 5.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 10.5 (C^3), 29.0 (C^2, C^4), 39.5 (C^7), 39.8 (C^6), 49.9 (C^1, C^5), 53.4 (OMe), 172.5 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 360/358 (0.3)/(0.3) $[M]^+$, 329/327 (2.0)/(2.0) $[M - 31]$, 233/231 (36)/(37) $[M - 127]^+$, 201/199 (11)/(11) $[C_8H_8BrO]^+$, 151 (52) $[C_9H_{11}O_2]^+$, 119 (23) $[C_8H_7O]^+$, 91 (100) $[C_7H_7]^+$, 77 (28) $[C_6H_5]^+$, 65 (20) $[C_5H_5]^+$, 59 (23) $[CO_2Me]^+$. Found, %: C 30.09; H 3.39. $C_9H_{12}BrIO_2$. Calculated, %: C 30.11; H 3.37.

Methyl *syn*-7-chloro-*endo*-6-iodobicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIIa). Yield 45%, oily substance, R_t 2.1 min, R_f 0.72. IR spectrum (film, neat), ν, cm^{-1}: 2957 m, 2930 m, 1736 v.s (C=O), 1445 m, 1267 s (O–C–O), 1240 s, 1203 m, 1065 m, 879 w, 685 w. ^1H NMR spectrum, δ, ppm: 1.57–1.72 m (2H, 3-H), 2.03–2.17 m and 2.37–2.51 m (2H each, 2-H, 4-H), 3.10 br.s (2H, 1-H, 5-H), 3.82 s (3H, OMe), 4.28 t (1H, 7-H, J = 5.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 10.9 (C^3), 27.7 (C^2, C^4), 41.3 (C^6), 48.8 (C^7), 49.9 (C^1, C^5), 53.3 (OMe), 172.5 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 316/314 (0.12)/(0.25) $[M]^+$, 285/283 (0.2)/(0.8) $[M - 31]^+$, 189/187 (6)/(18) $[M - 127]^+$, 151 (24) $[C_9H_{11}O_2]^+$, 155/157 (14)/(5) $[C_8H_8ClO]^+$, 119 (12) $[C_8H_7O]^+$, 91 (100) $[C_7H_7]^+$, 77 (23) $[C_6H_5]^+$, 65 (19) $[C_5H_5]^+$, 59 (28) $[CO_2Me]^+$. Found, %: C 34.72; H 3.74. $C_9H_{12}ClIO_2$. Calculated, %: C 34.37; H 3.85.

Methyl *endo*-6,*syn*-7-dibromobicyclo[3.1.1]heptane-*exo*-6-carboxylate (VIIIa). Yield 40%, oily substance, R_t 2.15 min, R_f 0.61. IR spectrum, ν, cm^{-1}: 2959 m, 2932 m, 1738 v.s (C=O), 1444 m, 1267 s, 1234 s, 1205 m, 1066 m, 871 w, 698 w. ^1H NMR spectrum, δ, ppm: 1.55–1.75 m (2H, 3-H), 2.22–2.33 m (4H, 2-H, 4-H), 3.14 br.s (2H, 1-H, 5-H), 3.82 s (3H, OMe), 4.26 t (1H, 7-H, J = 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.0 (C^3), 26.3 (C^2, C^4), 43.9 (C^7), 49.1 (C^1, C^5), 53.3 (OMe), 58.7 (C^6), 170.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 310/312/314 (0.1)/(0.15)/(0.1) $[M]^+$, 279/281/283 (0.4)/(0.8)/(0.4) $[M - 31]^+$, 233/231 (19)/(20) $[M - Br]^+$, 201/199 (10)/(10) $[C_8H_8BrO]^+$, 151 (40) $[C_9H_{11}O_2]^+$, 119 (26) $[C_8H_7O]^+$, 91 (100) $[C_7H_7]^+$, 77 (29) $[C_6H_5]^+$, 65 (25) $[C_5H_5]^+$, 59 (27) $[CO_2Me]^+$. Found, %: C 34.76; H 3.96. $C_9H_{12}Br_2O_2$. Calculated, %: C 34.65; H 3.88.

Reaction of tricycloheptane IV with the complex $BzlEt_3NCl \cdot ICl$. Benzyltriethylammonium chloride–iodine chloride complex, 3.90 g (10 mmol), was added in small portions over a period of 10–15 min to a solution of 1.52 g (10 mmol) of tricycloheptane **IV** in 30 ml of anhydrous methylene chloride under stirring in an argon atmosphere. The mixture was stirred for 24 h at 20°C, 40 ml of water was added, and the mixture was extracted with methylene chloride (3×30 ml). The extracts were combined, washed with water, dried over $MgSO_4$, and evaporated under reduced pressure (water-jet pump), and the residue was subjected to column chromatography on Al_2O_3 to isolate 1.41 g (45%) of dihalide **VIIa**.

Hydrodeiodination of compound VIIa. A round-bottom flask equipped with a reflux condenser and

an oil seal was flushed with argon and charged with a solution of 0.28 g (0.89 mmol) of compound **VIIa**, 0.3 g (1.07 mmol) of Ph_3SnH, and 7 mg of azobis(isobutyronitrile) in 10 ml of anhydrous benzene. The mixture was heated for 4 h under reflux, the solvent was removed under reduced pressure (water-jet pump), and the residue was subjected to column chromatography to isolate 0.126 g (75%) of methyl *syn*-7-chlorobicyclo[3.1.1]heptane-*exo*-6-carboxylate (**Xa**), R_f 0.63, R_t 2.0 min. ^{1}H NMR spectrum, δ, ppm: 1.45–1.65 m (2H, 3-H), 1.98–2.13 m (4H, 2-H, 4-H), 2.85 m (2H, 1-H, 5-H), 3.70 s (1H, 6-H), 3.75 s (3H, CO_2Me), 4.35 t (1H, 7-H, J = 5.8 Hz). Mass spectrum, m/z (I_{rel}, %): 190/188 (1.3)/(4.6) $[M]^+$ ($C_9H_{13}ClO_2$), 153 (25), 152 (30), 137 (10), 125 (6), 124 (8), 121 (19), 120 (10), 93 (100), 91 (65), 79 (28), 78 (11), 77 (55), 67 (8), 65 (21), 59 (15), 55 (11), 53 (15), 51 (12).

Reaction of tricycloheptane IV with molecular iodine. *a. Analytical experiment*. A special heat-resistant glass ampule equipped with two arms (one of which was designed for insertion into the probe of an ESR spectrometer) was charged with ~70 mg of tricycloheptane **IV** in 1 ml of anhydrous benzene and (into another arm) with a mixture of 60 mg of I_2 and 60 mg of 2,4,6-tribromo-1-nitrosobenzene in 1 ml of the same solvent. The ampule was thrice frozen with liquid nitrogen and evacuated at a residual pressure of 1 mm and sealed. After mixing the reactants, a triplet signal due to nitroxyl radical (a_N = 14.4 G) was observed in the ESR spectrum over a period of 2 days,.

b. Preparative experiment. A solution of 2.54 g (10 mmol) of iodine in 50 ml of anhydrous diethyl ether was added to a solution of 1.52 g (10 mmol) of compound **IV** in 10 ml of anhydrous diethyl ether. The mixture was stirred for 3 days at 20°C, washed with a 5% aqueous solution of Na_2SO_3 and with water, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. According to the GLC and ^{1}H NMR data, the crystalline residue, 2.95 g (72%), was a mixture of stereoisomeric diiodides **Va** and **Vb** at a ratio of 2:1. Found, %: C 26.47; H 2.85. $C_9H_{12}I_2O_2$. Calculated, %: C 26.63; H 2.98.

In an analogous experiment performed in carbon tetrachloride, diiodides **Va** and **Vb** were obtained at a ratio of 3:1 with a n overall yield of 77%. By fractional crystallization from hexane we isolated pure isomer **Va** and isomer **Vb** with a stereochemical purity of ~70%.

Methyl *exo*-6,*syn*-7-diiodobicyclo[3.1.1]heptane-*endo*-6-carboxylate (Vb). R_t 4.9 min. ^{1}H NMR spectrum, δ, ppm: 1.18–1.33 m and 1.38–1.55 m (1H each, 3-H), 1.95–2.09 m and 2.45–2.59 m (2H each, 2-H, 4-H), 2.83 m (2H, 1-H, 5-H), 3.85 s (3H, OMe), 5.48 t (1H, 7-H, J = 5.5 Hz). ^{13}C NMR spectrum, δ, ppm: 11.1 (C^3), 27.2 (C^2, C^4), 34.5 (C^6), 35.0 (C^7), 52.5 (C^1, C^5), 52.9 (OMe), 170.7 (C=O). Mass spectrum, m/z (I_{rel}, %): 406 (0.01) $[M]^+$, 279 (13.8), 247 (6.4), 153 (9.2), 152 (83), 151 (24), 137 (7), 120 (16), 119 (15), 93 (64), 92 (36), 91 (100), 79 (16), 76 (14), 66 (7), 65 (24), 63 (10), 59 (23), 53 (14), 52 (6), 51 (14).

Reaction of tricycloheptane IV with dibromotetrachloroethane. A Pyrex tube was charged with a mixture of 1.52 g (10 mmol) of tricycloheptane **IV** and 3.25 g (10 mmol) of dibromotetrachloroethane in 10 ml of carbon tetrachloride. The tube was tightly capped, and the mixture was irradiated with a KGL-500 lamp for 50 h at 20°C until it turned homogeneous. According to the GLC and ^{1}H NMR data, the product was a mixture of stereoisomeric dibromides **VIIIa** and **VIIIb** at a ratio of 72:28. Yield 1.62 g (52%), bp 75–80°C (1 mm).

Methyl *exo*-6,*syn*-7-dibromobicyclo[3.1.1]heptane-*endo*-6-carboxylate (VIIIb). R_t 8.25 min. ^{1}H NMR spectrum, δ, ppm: 1.15–1.38 m (2H, 3-H), 1.45–1.70 m and 2.10–2.41 m (2H each, 2-H, 4-H), 2.96 m (2H, 1-H, 5-H), 3.83 s (3H, OMe), 5.24 t (1H, 7-H, J = 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.8 (C^3), 24.9 (C^2, C^4), 51.4 (C^1, C^5), 51.9 (C^7), 52.8 (OMe), 58.2 (C^6), 168.9 (C=O). Mass spectrum, m/z (I_{rel}, %): 312 (0.1) $[M]^+$, 279/281/283 (0.5)/(0.7)/(0.4) $[M - 31]^+$, 233/231 (11)/(12) $[M - Br]^+$, 201/199 (10)/(9) $[C_8H_8BrO]^+$, 151 (33) $[C_9H_{11}O_2]^+$, 119 (32) $[C_8H_7O]^+$, 91 (100) $[C_7H_7]^+$, 77 (35) $[C_6H_5]^+$, 65 (30) $[C_5H_5]^+$, 59 (28) $[CO_2Me]^+$.

Methyl *endo*-6,*syn*-7-dichlorobicyclo[3.1.1]heptane-*exo*-6-carboxylate (IXa) and methyl *exo*-6,*syn*-7-dichlorobicyclo[3.1.1]heptane-*endo*-6-carboxylate (IXb). A Pyrex tube was charged with a mixture of 1.52 g (10 mmol) of ester **IV** and 2.74 g (10 mmol) of freshly prepared (dichloro-λ^3-iodanyl)benzene in 10 ml of anhydrous carbon tetrachloride. The tube was tightly capped, and the mixture was irradiated with a KGL-500 lamp for 18 h at 20°C until it turned homogeneous. The solvent was removed under reduced pressure. According to the GLC data, the residue contained iodobenzene and five more substances at a ratio of 7:13:24.5:45.5:10 (in the order of leaving of the chromatographic column). The first minor component (R_t 2 min) was identified by GC–MS data (using an authentic sample) as monochloride **Xa**. The

second and the last components (R_t 2.2 and 3.9 min, respectively) had the compositions $C_9H_{13}ClO_2$ and $C_9H_{12}Cl_2O_2$ (MS). The two major components (R_t 3.6 and 3.0 min) were dichlorides **IXa** and **IXb**, respectively. Vacuum distillation of the product mixture gave 1.4 g (62%) of a mixture of stereoisomers **IXa** and **IXb** with bp 70–75°C (1 mm). Found, %: C 48.13; H 5.32. $C_9H_{12}Cl_2O_2$. Calculated, %: C 48.45; H 5.42.

Isomer **IXa**. R_t 3.6 min. ^{1}H NMR spectrum, δ, ppm: 1.55–1.75 m (2H, 3-H), 2.22–2.33 m (4H, 2-H, 4-H), 3.15 br.s (2H, 1-H, 5-H), 3.85 s (3H, OMe), 4.24 t (1H, 7-H, J = 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.7 (C^3), 23.2 (C^2, C^4), 48.9 (C^1, C^5), 53.3 (C^7), 53.6 (OMe), ~68.5 (C^6), 170.4 (C=O). Mass spectrum, m/z (I_{rel}, %): 225/224/223/222 (0.2)/(1.6)/(0.3)/(2.5) $[M]^+$, 189/187 (2.3)/(7.9) $[M - HCl]^+$, 151 (18) $[C_9H_{11}O_2]^+$, 150 (19) $[C_9H_{10}O_2]^+$, 129/127 (6)/(19) $[C_7H_8Cl]^+$, 119 (13) $[C_8H_7O]^+$, 93 (15), 92 (13), 91 (100) $[C_7H_7]^+$, 79 (15), 77 (19) $[C_6H_5]^+$, 65 (22) $[C_5H_5]^+$, 59 (22) $[CO_2Me]^+$, 53 (10), 51 (10).

Isomer **IXb**. R_t 3.0 min. ^{1}H NMR spectrum, δ, ppm: 1.55–1.75 m (2H, 3-H), 2.22–2.33 m (4H, 2-H, 4-H), 2.96 m (2H, 1-H, 5-H), 3.85 s (3H, OMe), 5.04 t (1H, 7-H, J = 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.2 (C^3), 23.0 (C^2, C^4), 51.2 (C^1, C^5), 52.8 (OMe), 56.5 (C^7), 66.6 (C^6), 168.3 (C=O). Mass spectrum, m/z (I_{rel}, %): 225/224/223/222 (0.09)/(0.7)/(0.1)/(1.1) $[M]^+$, 189/187 (28)/(85) $[M - HCl]^+$, 155 (10), 152 (7), 151 (57) $[C_9H_{11}O_2]^+$, 127 (14), 125 (6), 119 (30) $[C_8H_7O]^+$, 118 (21), 111 (11), 105 (6), 93 (10), 92 (13), 91 (100), 81 (8), 79 (14), 78 (6), 77 (27), 75 (10), 65 (27), 63 (7), 59 (21), 53 (15), 51 (14).

Unidentified compound (R_t 2.2 min). $C_9H_{13}ClO_2$. Mass spectrum, m/z (I_{rel}, %): 190/188 (1.4)/(4.5) $[M]^+$, 159/157 (6)/(17), 154 (4), 153 (41), 126 (20), 125 (9), 124 (17), 122 (5), 121 (40), 120 (18), 119 (7), 113 (4), 112 (7), 111 (69), 100 (9), 98 (6), 95 (5), 94 (14), 93 (100), 81 (19), 80 (5), 79 (40), 78 (12), 77 (52), 75 (8), 68 (8), 67 (26), 66 (20), 65 (26), 63 (7), 59 (22), 55 (22), 54 (5), 53 (26), 52 (7), 51 (16).

Unidentified compound (R_t 3.9 min). $C_9H_{12}Cl_2O_2$. Mass spectrum, m/z (I_{rel}, %): 224/222 (0.5)/(0.7) $[M]^+$, 151 (18), 150 (12), 119 (14), 118 (9), 93 (12), 92 (12), 91 (100), 79 (10), 65 (20), 59 (22), 53 (9), 51 (10).

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