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SHORT COMMUNICATIONS

Products of Reaction of 1-Phenyltricyclo[4.1.0.0^{2,7}]heptane with *N*-Iodosuccinimide in Aqueous THF

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Abstract—Iodohydroxylation of 1-phenyltricyclo[4.1.0.0^{2,7}]heptane in aqueous THF at 20°C with *N*-iodosuccinimide proceeds at the central bicyclobutane bond C^1–C^7 and results in the formation of two-component mixture of diastereomeric 7-iodo-6-phenyl-6-norpinanols in the ratio 1 : 1.8 in favor of the product of the *anti*-addition. Treating of iodonorpinanols with trimethylamine in aqueous THF affords 1-benzoylcyclohex-1-ene as a result of 1,4-dehydroiodination accompanied with the Grob fragmentation of the carbon scaffold.

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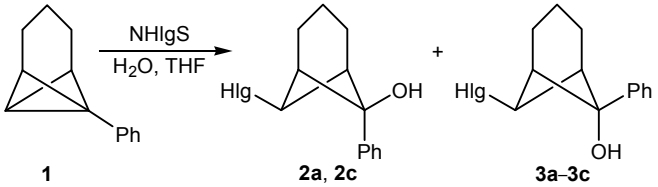
In [1] a bromohydroxylation was described of 1-phenyltricycloheptane **1** proceeding at the central bicyclobutane bond C^1–C^7 under the action of *N*-bromosuccinimide in aqueous THF at 20°C. The reaction led to the formation of two-component mixture of diastereomeric 7-bromobicyclo[3.1.1]heptan-6-ols **2a** and **3a** with a considerable prevalence (1 : 13) of the *anti*-addition product **3a**. It is also known that the reaction of compound **1** with *N*-chlorosuccinimide in aqueous acetone afforded exclusively the *anti*-addition product **3b** [2]. In this study we have established that analogous reaction of hydrocarbon **1** with *N*-iodosuccinimide (NIS) in aqueous THF occurs similarly, but with far less pronounced *anti*-stereoselectivity: the ratio of formed diastereomeric iodohydrins **2c** and **3c** is 1 : 1.8 (Scheme 1).

Compounds **2c** and **3c** were isolated in individual state by flash chromatography on silica gel. Their structure was established with the help of IR, ^{1}H and ^{13}C NMR spectra. The assignment of the signals in the ^{1}H NMR spectra of diastereomers **2c** and **3c** was carried out considering the known correlations between the spectra and structures applied to proving the structures of analogs **2a**, **3a** [1], and **3b** [2].

Having stereochemically pure samples of benzyl type norpinanols **3a** and **3c** we attempted to achieve their epimerization by keeping in aqueous THF at 20°C in the presence of catalytic amount of $HClO_4$ for 24 h. Actually this attempt was successful with iodohydrin **3c**, moreover, under these conditions this compound completely converted in diastereomer **2c**. The reason of the larger thermodynamic stability of isomer **2c** we believe to be in the difference in conformational energy of the OH group and the phenyl substituent (1.04 and 2.8 kcal mol^{-1} respectively [3]). Bromohydrin **3a** behaved differently under the chosen conditions: The initial compound disappeared to be converted in an intractable mixture of products.

It was suggested in [1, 2] that in the bromo(chloro) hydroxylation of tricycloheptane **1** a classic carbenium ion **A** formed as an intermediate, and the pronounced *anti*-stereochemistry of the addition was attributed to the effect of steric factor directing the nucleophilic attack on the cationic center from the *exo*-side [4]. We believe that the iodohydroxylation of hydrocarbon **1**

Scheme 1.

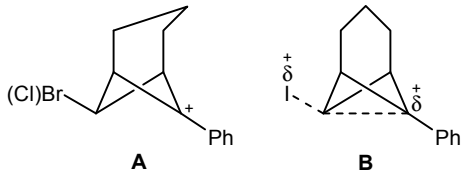


1 **2a**, **2c** **3a**–**3c**

Hlg = Br (**a**), Cl (**b**), I (**c**).

and the epimerization of norpinanol **3c** proceed through a somewhat different cationic intermediate more alike in its structure to nonclassic carbonium ion **B** stabilized by the homohyperconjugation of the iodine atom [5]. An ion of similar structure was suggested for reactions of solvoxymercuration of tricycloheptanes [1, 4, 6, 7]. Chlorine and bromine atoms do not have analogous effects on the cationic intermediate due to their enhanced electronegativity. The higher stability of intermediate **B** explains the result of the reversible acid catalyzed epimerization of iodohydrin **3c** under the conditions of the thermodynamic control. The less stable carbenium ion **A** is capable to suffer a known cyclobutyl-cyclopropylcarbonyl rearrangement [4, 8]. Intermediate **B** in iodohydroxylation reaction of tricycloheptane **1** is subjected to the nucleophilic attack under the conditions of a kinetic control and shows the growing part of the *syn*-addition compared to the bromo(chloro) hydroxylation, but to a lesser extent than in the reaction of solvoxymercuration (Scheme 2).

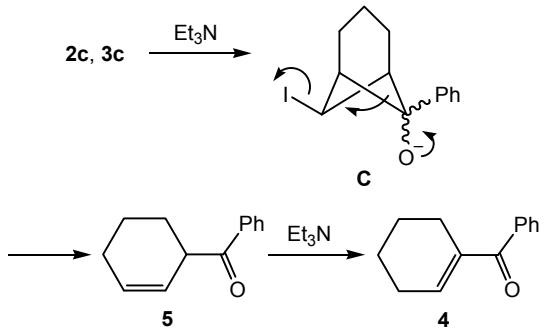
Scheme 2.



Iodohydrins **2c** and **3c** at keeping in aqueous THF in the presence of trimethylamine at 20°C are converted in a known [9] conjugated ketone **4**[1]. It is presumable that this compound formed as a result of a prototropic rearrangement of ketone **5** which formed in its turn by 1,4-dehydroiodination of iodohydrins **2c** and **3c** via anion **C** in keeping with Grob fragmentation process [10] (Scheme 3).

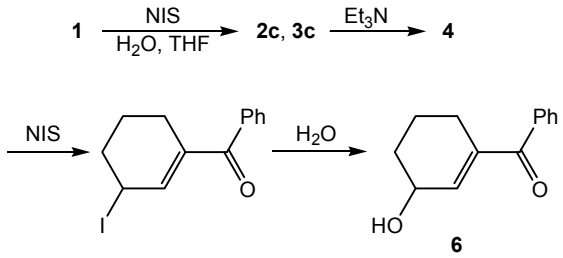
An unexpected result was obtained at performing the iodohydroxylation of hydrocarbon **1** in the presence of triethylamine: A single reaction product isolated in 32% yield was hydroxyketone **6** whose structure was confirmed by spectral data. The IR spectrum contained a strong band of the conjugated carbonyl group at 1644 cm^{-1} and a broad band of the hydroxy group at 3407 cm^{-1} [12], and in the ^{13}C NMR spectrum along with the carbonyl group signal (198.8 ppm) 6 signals

Scheme 3.



appear in the weak field and 4 are seen upfield. In assignment of signals in the ^{13}C NMR spectrum DEPT experiment was used. ^1H NMR spectrum contains a multiplet of the olefin proton (δ 6.42 ppm) and a broadened signal of the hydroxy group (δ 2.12 ppm). We believe that the formation of hydroxyketone **6** in the reaction of tricycloheptane **1** with NIS in the presence of triethylamine occurs due to allylic iodination of ketone **4** with the subsequent hydrolysis of the arising iodide (Scheme 4).

Scheme 4.



Such transformation was not observed at the bromohydroxylation of hydrocarbon **1** with *N*-bromosuccinimide in the presence of triethylamine. It obviously is connected with the fact that bromohydrins **2a** and **3a** are less prone to Grob fragmentation since the carbon–bromine bond is stronger than the carbon–iodine bond.

Iodohydroxylation of tricycloheptane (1). To a solution of 2.06 g (12 mmol) of hydrocarbon **1** [1] in 10 mL of aqueous THF (1 : 1) at 0°C was added while stirring by small portions within 30 min 3.4 g (15 mmol) of NIS [13]. The cooling was removed and the mixture was stirred at 20°C for 2 h. Then to the mixture 30 mL of ethyl ether was added, the organic layer was separated, washed with water (3 × 10 mL), dried with anhydrous Na_2SO_4. On removing the solvent on the rotary evaporator in the residue ^1H NMR spectrum

[1] Formerly [11] ketone **4** was obtained from bromohydrin **3a** by treating with sodium hydride in THF.

showed the presence of iodohydrins **2c** and **3c** in a ratio 1 : 1.8. These compounds were isolated in an individual state by flash chromatography on silica gel.

7-*syn*-Iodo-6-*endo*-phenylbicyclo[3.1.1]heptan-6-ol (2c). Yield 1.43 g (38%), light yellow oily substance. IR spectrum, ν, cm^{-1}: 3399 m (OH), 2944 s, 2867 m, 1451 m, 1200 m, 1177 m, 1073 m, 1015 m, 988 m, 933 m, 884 m, 822 m, 775 m, 702 s. ^{1}H NMR spectrum, δ, ppm: 0.54–0.67 m (1H, H^3), 1.13–1.25 m (1H, H^3), 1.99–2.07 m (2H, H^{2,4}), 2.10–2.18 m (2H, H^{2,4}), 2.93 m (2H, H^{1,5}), 5.54 t.t (1H, *anti*-H^7, *J* 5.7, 1.4 Hz), 7.27–7.30 m (2H, H$_{arom}$), 7.31–7.35 m (1H, H$_{arom}$), 7.37–7.42 m (2H, H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 11.8 (C^3), 28.7 (C^{2,4}), 39.5 (C^7), 49.5 (C^{1,5}), 79.5 (C^6), 125.2 (2C$_{arom}$), 128.2 (C$_{arom}$), 129.0 (2C$_{arom}$), 143.0 (C$_{arom}$). Found, %: C 50.05; H 4.92. $C_{13}H_{15}IO$. Calculated, %: C 49.70; H 4.81.

7-*syn*-Iodo-6-*exo*-phenylbicyclo[3.1.1]heptane-6-ol (3c). Yield 0.75 g (20%), light yellow oily substance. IR spectrum, ν, cm^{-1}: 3398 m (OH), 2940 s, 2863 m, 1493 m, 1447 m, 1277 m, 1188 m, 1119 m, 1038 m, 884 m, 822 m, 764 s, 698 v.s. ^{1}H NMR spectrum, δ, ppm: 1.65–1.85 m (2H, H^3), 2.03–2.10 m (2H, H^{2,4}), 2.37–2.45 m (2H, H^{2,4}), 3.00 br.d (2H, H^{1,5}, *J* 5.8 Hz), 4.18 t (1H, *anti*-H^7, *J* 5.8 Hz), 7.31–7.36 m (2H, H$_{arom}$), 7.39–7.43 m (1H, H$_{arom}$), 7.49–7.52 m (2H, H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 12.4 (C^3), 26.5 (C^{2,4}), 28.1 (C^7), 49.6 (C^{1,5}), 74.6 (C^6), 126.4 (2C$_{arom}$), 128.3 (C$_{arom}$), 129.0 (2C$_{arom}$), 143.8 (C$_{arom}$). Found, %: C 50.15; H 4.98. $C_{13}H_{15}IO$. Calculated, %: C 49.70; H 4.81.

Acid catalyzed epimerization of iodonorpinanol 3c. To a solution of 150 mg (0.47 mmol) of compound **3c** in 2 mL of anhydrous ethyl ether was added 50 μL of conc. $HClO_4$. The mixture was stirred for 24 h at 20°C. On removing the solvent on the rotary evaporator in the residue ^{1}H NMR spectrum showed the presence of iodonorpinanol **2c** without the traces of the initial compound. This product (113 mg, 75%) was isolated by flash chromatography on silica gel.

Cyclohex-1-ene-1-yl(phenyl)methanone (4). To a solution of 150 mg (0.478 mmol) of the mixture of iodonorpinanols **2c** and **3c**, 1 : 2, in 2.5 mL of THF was added 0.5 mL of triethylamine and 0.5 mL of water. The mixture was stirred at 20°C for 7 h. The organic layer was separated, the water layer was extracted with ethyl ether (5 × 10 mL). Combined extracts were dried with $MgSO_4$. On removing the solvent on the rotary evaporator the residue was subjected to flash chromatography on silica gel to isolate 66 mg (74%) of compound **4** as transparent oily fluid. ^{1}H NMR spectrum, δ, ppm: 1.59–1.76 m (4H, 2CH$_2$), 2.23–2.28 m (2H, CH$_2$), 2.38–2.43 m (2H, CH$_2$), 6.57–6.59 m (1H, H$_{olef}$), 7.40 t (2H, H$_{arom}$, *J* 7.7 Hz), 7.48 t (1H, H$_{arom}$, *J* 7.2 Hz), 7.62 d (2H, H$_{arom}$, *J* 7.2 Hz). ^{13}C NMR spectrum, δ, ppm: 21.7, 22.1, 24.0, 26.2, 128.1 (2C$_{arom}$), 129.2 (2C$_{arom}$), 131.3, 138.75, 138.76, 144.4, 198.4 (C=O). Found, %: C 76.95; H 7.12. $C_{13}H_{14}O$. Calculated, %: C 83.82; H 7.58.

(3-Hydroxycyclohex-1-ene-1-yl)(phenyl)methanone (6) was obtained in the reaction of 2.06 g (12 mmol) of hydrocarbon **1** with 3.4 g (15 mmol) of NIS in the presence of 1.2 mL of triethylamine. The reaction mixture was stirred at 20°C for 24 h and worked up as described above. By flash chromatography on silica gel we isolated 0.78 g (32%) of compound **6** as colorless oily substance. IR spectrum, ν, cm^{-1}: 3407 m (OH), 2940 m, 2863 w, 1644 v.s (C=O), 1597 m, 1447 m, 1304 m, 1269 s, 1246 m, 1123 m, 961 w, 714 s, 660 w. ^{1}H NMR spectrum, δ, ppm: 1.57–1.72 m (2H, H^4), 1.85–1.93 m (1H, H^5), 1.96–2.03 m (1H, H^5), 2.12 br.s (1H, OH), 2.36–2.41 m (2H, H^6), 4.42 m (1H, H^3), 6.42 m (1H, H$_{olef}$), 7.39–7.42 m (2H, H$_{arom}$), 7.49–7.53 m (1H, H$_{arom}$), 7.65–7.68 m (2H, H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 19.2 (C^5), 24.3 (C^4), 31.5 (C^6), 66.4 (C^3), 128.3 (2C$_{arom}$), 129.4 (2C$_{arom}$), 132.0 (C$_{arom}$), 137.8 w (C$_{olef}$), 140.0 w (C$_{arom}$), 142.8 (C$_{olef}$), 198.3 (C=O). Found, %: C 76.95; H 7.12. $C_{13}H_{14}O_2$. Calculated, %: C 77.20; H 6.98.

^{1}H and ^{13}C NMR spectra of solutions of compounds in $CDCl_3$ were registered on a spectrometer JNM-ECX400 JEOL. The residual proton signal (δ 7.26 ppm) and the carbon signal (δ 77.16 ppm) of deuteron-chloroform served as internal reference. IR spectra were recorded on a Fourier spectrophotometer InfraLyum FT-02 from thin films. Elemental analysis was carried out on a CHNS-analyzer VarioMICRO. Flash chromatography was performed on a silica gel Merck 60 (for thin layer chromatography), eluent ethyl ether–light petroleum ether, 1 : 4.

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