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First Synthesis of Nitro-Substituted Bicyclo[1.1.0]butane Derivatives and New Method for Generation of Tricyclo[4.1.0.0^{2,7}]hept-1(7)-ene*

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Abstract—Successive treatment of 1-phenylsulfonyltricyclo[4.1.0.0^{2,7}]heptane with butyllithium and ethyl nitrate leads to the formation of 7-nitro-7'-phenylsulfonyl-1,1'-bi(tricyclo[4.1.0.0^{2,7}]heptane) through intermediate tricyclo[4.1.0.0^{2,7}]hept-1(7)-ene which is generated by 1,2-elimination of benzenesulfinic acid from the initial compound. Analogous treatment of 1-phenyltricyclo[4.1.0.0^{2,7}]heptane gives 1-nitro-7-phenyltricyclo-[4.1.0.0^{2,7}]heptane.

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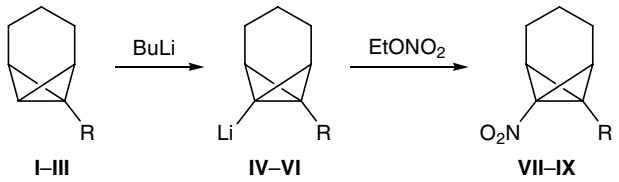
It is known [1] that metalation of tricyclo[4.1.0.0^{2,7}]-heptane (**I**) with butyllithium gives 1-lithiotricyclo-[4.1.0.0^{2,7}]heptane (**IV**) which is highly reactive toward various electrophiles. Therefore, it becomes possible to introduce various functional groups into the bridgehead position of molecule **I**. It was also shown that some electrophilic reagents can be used to effect analogous functionalization of 1-substituted tricyclo-[4.1.0.0^{2,7}]heptanes, e.g., 1-phenyl- and 1-phenylsulfonyltricyclo[4.1.0.0^{2,7}]heptanes **II** and **III** [2–4]. However, neither 1-nitrotricyclo[4.1.0.0^{2,7}]heptane nor other nitro derivatives of the bicyclo[1.1.0]butane series have not been reported, though such compounds could seemingly be available via the same approach using alkyl nitrates as electrophiles (cf. [5]).

In the present work we made an attempt to introduce a nitro group into the bridgehead position of tricyclo[4.1.0.0^{2,7}]heptane derivatives **I**–**III** through the corresponding organolithium compounds **IV**–**VI** (Scheme 1).* Metalated compound **IV** was prepared according to the procedure described in [7], i.e., by treatment of tricyclic hydrocarbon **I** with a solution of butyllithium in hexane in the presence of *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine. A solution of ethyl nitrate in diethyl ether was then added to the reaction mixture. When the reaction was complete, the mixture was treated with water, and the organic phase was separated and washed with an aqueous solution of $CuSO_4$ to remove *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine. We failed to determine the product composition, but analysis of the ^{1}H NMR spectra of different fractions isolated by distillation of the product mixture showed the absence of nitro derivative **VII**. Presumably, the use of *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine in the metalation step is a factor responsible for the formation of a complex mixture of products.

Scheme 1.

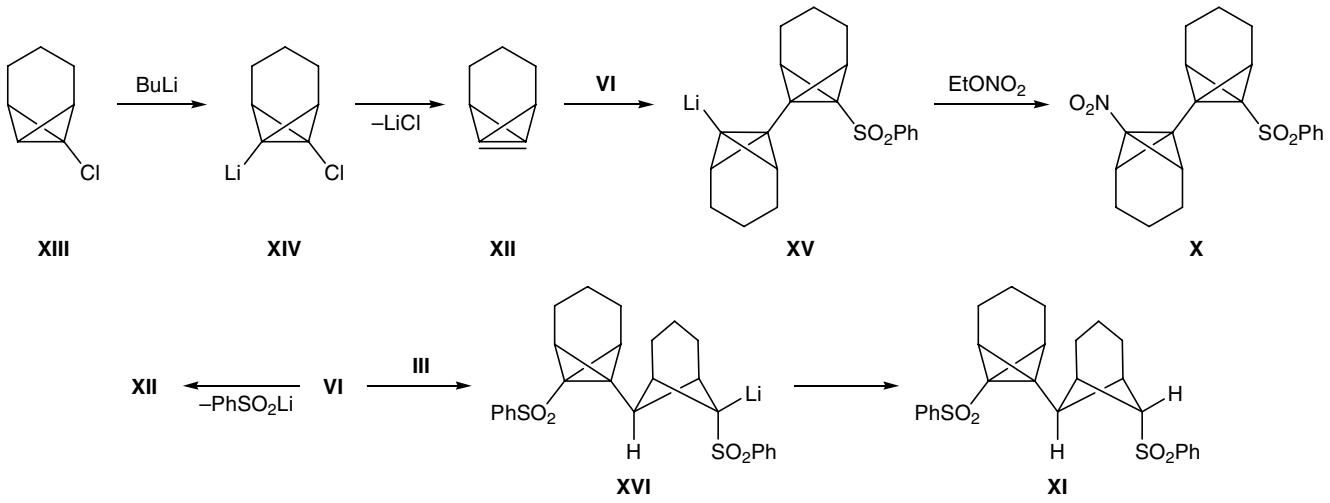


I, **IV**, **VII**, R = H; **II**, **V**, **VIII**, R = Ph; **III**, **VI**, **IX**, R = $PhSO_2$.

Insofar as tricycloheptanes **II** and **III** having electron-withdrawing substituents on C^1 are stronger CH acids than hydrocarbon **I**, their metalation can be performed without tetramethylethylenediamine [3, 4]. In fact, we succeeded in obtaining organolithium compounds **V** and **VI** by treatment of **II** and **III**, respec-

* For preliminary communication, see [6].

Scheme 2.



tively, with a hexane solution of butyllithium alone. The reaction of organolithium derivative **V** with ethyl nitrate gave nitro compound **VIII** in 73% yield (Scheme 1). The structure of **VIII** was confirmed by the NMR spectra which resembled those of 7-substituted 1-phenyltricyclo[4.1.0.0^{2,7}]heptanes [2, 3].

In the reaction of organolithium compound **VI** with a solution of ethyl nitrate in diethyl ether we isolated by column chromatography on Al_2O_3 two products: nitro sulfone **X** (yield 25%) and bis-sulfone **XI** (yield 2.5%), while the expected nitro sulfone **IX** was not detected. The structure of bi(tricycloheptane) **X** reliably followed from the ^{1}H and ^{13}C NMR spectra which were analogous to the spectra of unsubstituted and 7,7'-disubstituted 1,1'-bi(tricyclo[4.1.0.0^{2,7}]heptanes) [8]. The structure and configuration of compound **XI** was determined on the basis of the ^{1}H NMR data, primarily by analysis of the positions and multiplicities of the 6-H and 7-H signals, which corresponded to *exo*-6-*syn*-7-disubstituted bicyclo[3.1.1]heptanes [9].

The results obtained in the reaction with sulfone **III** should be discussed separately. We believe that 7-nitro-7'-phenylsulfonyl-1,1'-bi(tricyclo[4.1.0.0^{2,7}]heptane) (**X**) is formed through intermediate tricyclo[4.1.0.0^{2,7}]-hept-1(7)-ene **XII** which is generated by elimination of lithium benzenesulfinate from organolithium compound **VI**. Unsaturated hydrocarbon **XII** was postulated for the first time by Szeimies et al. [10] as a highly reactive intermediate generated by elimination of lithium chloride from organolithium compound **XIV**, the latter being formed by treatment of 1-chlorotricyclo[4.1.0.0^{2,7}]heptane (**XIII**) with butyllithium [10]. Intermediate **XII** may be regarded as a specific analog of dehydrobenzene; it then reacts with organolithium compound **VI** to give lithiated 1,1'-bi(tricyclo-[4.1.0.0^{2,7}]heptane) (**XV**) (cf. [8]) which undergoes nitration–demetalation. The fact that sulfone **III** (like chloride **XIII**) behaves as precursor of tricyclo-[4.1.0.0^{2,7}]hept-1(7)-ene (**XII**) may be interpreted in terms of similarity of phenylsulfinate and chloride ions as nucleofuges [11].** However, the nucleofugality of phenylsulfinate ion is lower than that of chloride ion; therefore, the lifetime of the corresponding organolithium compound **VI** is longer than that of **XIV**. Thus the formation of sulfone **XI** is presumed to result from nucleophilic addition of organolithium derivative **VI** to activated tricycloheptane **III** (cf. [13]). Hydrolysis of adduct **XVI** during treatment of the reaction mixture yields bis-sulfone **XI**.

To conclude, we were the first to obtain two representatives of previously inaccessible nitro-substituted bicyclo[1.1.0]butane derivatives and to show the possibility for generating tricyclo[4.1.0.0^{2,7}]hept-1(7)-ene (**XII**) from a new precursor, sulfone **III**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Bruker DPX-300 spectrometer (300.13 and 75.47 MHz, respectively). Analytical thin-layer chromatography was performed on Silufol UV-254 plates using hexane–diethyl ether (2:1) as eluent; spots were visualized by treatment with iodine vapor. Aluminum oxide of activity grade II was used for column chromatography; eluent light petroleum ether–

** The formation of bicyclo[1.1.0]but-1(3)-ene derivative via base-catalyzed 1,2-elimination of benzenesulfinic acid from structurally related sulfone was also postulated in [12].

diethyl ether (3:1). GLC analysis was performed on a KristalLyuks-4000 chromatograph equipped with a flame ionization detector; carrier gas nitrogen, flow rate 30 ml/min; 1200×3-mm glass column packed with 3% of OV-17 on Inetron N-Super (0.125–0.160 mm); the product compositions were determined by the internal normalization technique assuming calibration factors of all components to be equal to unity.

Tricycloheptanes **I** [7], **II** [14], and **III** [15] were synthesized by known methods.

Reaction of 1-lithiotricyclo[4.1.0.0^{2,7}]heptane (IV) with ethyl nitrate. A solution of 4.7 g (50 mmol) of compound **I** and 4 ml of *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine in 20 ml of hexane was cooled to 0°C, 100 ml of a 0.8 M solution of butyllithium in hexane was carefully added under stirring in a stream of dry argon, the mixture was stirred for 20 h at 20°C under argon and cooled to –10°C, and a solution of 5.6 g (61 mmol) of freshly distilled ethyl nitrate in 20 ml of hexane was slowly added under continuous stirring. After 1 h, 70 ml of water was added dropwise, the organic phase was separated, and the aqueous phase was extracted with diethyl ether (3×30 ml). The extracts were combined with the organic phase, washed with 30 ml of a 10% solution of $CuSO_4$, and dried over $MgSO_4$. The solvent was removed to leave an oily residue (8.3 g) which (according to the TLC and GLC data) was a multicomponent mixture of products. We succeeded in identifying only *n*-octane among these products. By vacuum distillation we isolated a fraction boiling in the range from 40 to 90°C (1 mm). According to the GLC data, it contained at least five components [R_t 0.446 (13%), 0.982 (2%), 1.236 (4%), 1.561 (27%), 5.259 (42%)]. The IR spectrum of that fraction displayed strong absorption bands at 1535 and 1377 cm^{-1}, which are typical of nitroalkanes. However, only upfield signals (δ 0.8–2.7 ppm) were observed in its ^{1}H NMR spectrum, while no expected broadened doublet at δ 3–4 ppm (assignable to 2-H and 6-H of **VII**) was present, indicating the absence of compound **VII** among the products.

1-Nitro-7-phenyltricyclo[4.1.0.0^{2,7}]heptane (VIII). A solution of 3.4 g (20 mmol) of compound **II** in 50 ml of anhydrous diethyl ether was cooled to –10°C, and 14.5 ml of a 1.7 M solution of butyllithium in hexane was added under argon. After 30 min, the cooling bath was removed, the flask was hermetically capped, and the mixture was stirred for 50 h at 20°C. The resulting solution of organolithium compound **V** was slowly added through a syringe to a solution of 2.7 g (30 mmol) of freshly distilled ethyl nitrate in 10 ml of hexane, cooled to –20°C. The mixture was stirred for 2 h, allowing it to gradually warm up to room temperature, and 30 ml of a saturated solution of ammonium chloride was added under stirring and cooling with ice water. The organic phase was separated, washed with water, dried over sodium sulfate, and evaporated on a rotary evaporator, and the residue was recrystallized from hexane. Yield 3.14 g (73%), mp 71–72°C, R_f 0.31. ^{1}H NMR spectrum, δ, ppm: 1.32–1.47 and 1.53–1.70 (1H each, 4-H), 1.75–1.95 (4H, 3-H, 5-H), 4.45 s (2H, 2-H, 6-H), 7.23–7.73 (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 19.8 (C^4), 21.2 (2C, C^3, C^5), 49.9 (2C, C^2, C^6), 51.4 (C^7), 63.9 (C^1), 125.9 (2C), 128.7, 128.75 (2C), 130.8 (C_{arom}). Found, %: C 72.42; H 6.12; N 6.72. $C_{13}H_{13}NO_2$. Calculated, %: C 72.54; H 6.09; N 6.51.

Reaction of 1-lithio-7-phenylsulfonyltricyclo[4.1.0.0^{2,7}]heptane (VI) with ethyl nitrate. A three-necked flask equipped with a mechanical stirrer, reflux condenser, and oil seal, was charged with 4 g (17 mmol) of sulfone **III** in 20 ml of anhydrous THF. The flask was purged with dry argon, the mixture was cooled to –10°C, and 30 ml of a solution of butyllithium in hexane [prepared from 0.5 g (70 mmol) of lithium foil and 2.8 g (30 mmol) of butyl chloride] was carefully added under stirring. The mixture was stirred for 10 min at 0°C, a solution of 2.2 g (24 mmol) of freshly distilled ethyl nitrate in 15 ml of anhydrous diethyl ether was added, the mixture was stirred for 0.5 h at 20°C, and 30 ml of water was added dropwise. The organic phase was separated, the aqueous phase was extracted with methylene chloride (3×40 ml), and the extracts were combined with the organic phase, dried over $CaCl_2$, and evaporated under reduced pressure (water-jet pump). The residue was a brown oily substance which was subjected to column chromatography on Al_2O_3 to isolate 0.79 g (25%) of crystalline nitro sulfone **X** (R_f 0.38), 0.1 g (2.5%) of bis-sulfone **XI** (R_f 0.15), and 0.05 g of initial sulfone **III** (R_f 0.36).

7-Nitro-7'-phenylsulfonyl-1,1'-bi(tricyclo[4.1.0.0^{2,7}]heptane) (X). mp 120–121°C (from $CHCl_3$–hexane, 1:3). ^{1}H NMR spectrum, δ, ppm: 0.90–1.30 (2H), 1.30–1.55 (6H), and 1.65–1.90 (4H, 3-H, 4-H, 5-H, 3'-H, 4'-H, 5'-H); 3.60 s and 4.22 s (2H each, 2-H, 6-H, 2'-H, 6'-H); 7.53–7.68 (3H) and 7.85–7.99 (2H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 19.5 and 19.8 (C^4, $C^{4'}$), 20.3 and 21.1 (2C each, C^3, C^5, $C^{3'}$, $C^{5'}$), 33.0 and 33.8 (C^1, $C^{1'}$), 47.4 and 52.4 (2C each, C^2, C^6, $C^{2'}$, $C^{6'}$), 49.0 and 50.9 (C^7, $C^{7'}$); 126.4 (2C), 129.2 (2C), 133.0,

142.3 (C_{arom}). Found, %: C 65.01; H 5.62; N 3.82. $C_{20}H_{21}NO_4S$. Calculated, %: C 64.67; H 5.70; N 3.77.

***exo*-6-Phenylsulfonyl-*syn*-7-(7-phenylsulfonyltricyclo[4.1.0.0^{2,7}]hept-1-yl)bicyclo[3.1.1]heptane (XI).** mp 193–194°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 1.15–1.29 and 1.29–1.41 (1H each, 4'-H), 1.41–1.59 (4H, 3'-H, 5'-H), 1.62–1.80 (1H, 3-H), 2.10–2.30 (3H, 2-H, 3'-H, 4-H), 2.58–2.81 (2H, 2-H, 4-H), 2.87 br.d (2H, 1-H, 5-H), 3.35 s (1H, 6-H), 3.56 s (2H, 2'-H, 6'-H), 4.31 t (1H, 7-H, J = 6.0 Hz), 7.50–7.71 (6H) and 7.88–8.00 (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.1 (C^3), 19.3 (2C, $C^{3'}$, $C^{5'}$), 19.6 ($C^{4'}$), 23.2 (2C, C^2, C^4), 32.6 ($C^{1'}$), 36.2 ($C^{7'}$), 38.7 (C^7), 46.9 (2C, C^1, C^5), 50.2 (2C, $C^{2'}$, $C^{6'}$), 60.8 (C^6), 126.45 (2C), 127.30 (2C), 129.15 (2C), 129.25 (2C), 133.20 (2C), 140.65, 141.55 (C_{arom}). Found, %: C 66.21; H 5.92. $C_{26}H_{28}O_4S_2$. Calculated, %: C 66.64; H 6.02.

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