

*Dedicated to the memory of  
Professor Cristofor I. Simionescu (1920–2007)*

## THE SYNTHESIS AND THE SPECTRAL CHARACTERIZATION OF NEW BICYCLO[2.2.1]HEPTADIENE DERIVATIVES

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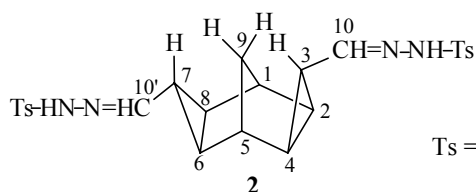
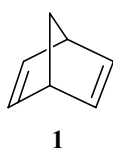
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The synthesis of 3,7-dihydroxymethyl-*exo-exo*-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>6,8] nonane(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,6 $\beta$ ,7 $\beta$ ,8 $\beta$ ) (7), 3,7-diformyl-*exo-exo*-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>6,8]-nonane(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,6 $\beta$ ,7 $\beta$ ,8 $\beta$ ) (8) and bistosylhydrazone of 3,7-diformyl-*exo-exo*-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>6,8] nonane (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,6 $\beta$ ,7 $\beta$ ,8 $\beta$ ) (2) are presented. High-resolution <sup>1</sup>H- and <sup>13</sup>C-NMR spectra of the above compounds are discussed underling the stereochemistry of 3,7-disubstituted – *exo-exo*-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>6,8] nonane. The Bamford-Stevens reaction of bistosylhydrazones 2 (corresponding to 8) affords as main product the alkene 1(BCH).

### INTRODUCTION

Our results in the stereochemistry of small rings annulated to substituted bicycloheptane<sup>1,2</sup> encouraged us to extend this investigation on the bicyclo [2.2.1]heptadienic skeleton (BCH) 1.

In this paper we report our results regarding the reaction of bistosylhydrazone 2 with natrium methoxyde/diglyme and the syntheses of the precursors.



### RESULTS AND DISCUSSION

The syntheses of bistosylhydrazone 2 (Scheme 1) was performed using a method described in lit. for obtaining of the tosylhydrazones.<sup>1</sup>

The cyclopropanation of BCH (1) was carried out with an excess of ethyl diazoacetate (EDA) in the presence of  $\pi$ -allyl palladium chloride complex at 0-5°C according to the literature method.<sup>3</sup> From this reaction was obtained a mixture of three isomeric diadducts (*anti-anti*- 3, *anti-syn*- 4 and

*syn-syn*- 5) with the *exo-exo* configuration of the cyclopropane rings.<sup>3</sup> In the next step the mixture of the diadducts 3-5 was treated with natrium methoxide in refluxing methanol for the isomers conversion to the thermodynamically more stable isomer. The epimerization of the mixture of diethyl esters 3-5 led us to the dimethyl ester 6 in an *anti-anti* configuration of carbomethoxy groups.

The configuration *anti-anti* of the totally epimerized compound 6 is proved from the shielding of the protons of methylenic bridge H<sup>9a,s</sup>

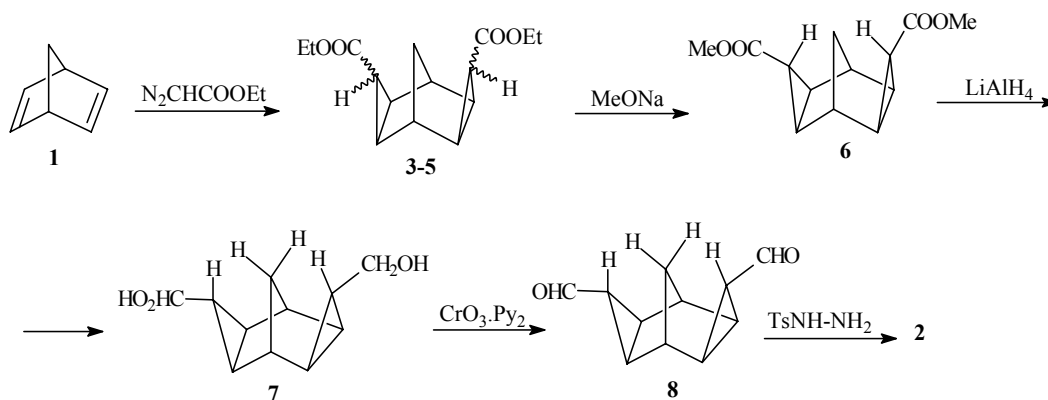
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( $\delta = 0.5$  ppm) by the cyclopropanic ring as well as of the small *trans* coupling of 2.4 Hz of the proton  $H^3$  with the protons  $H^2$  and  $H^4$ . In the Noedif experiments show that at the irradiation of the protons from the bridge  $H^{9a}$  and  $H^{9s}$  observed a increase of intensity with 15% of the signal  $H^3$  in agreement with their spatial vicinity.

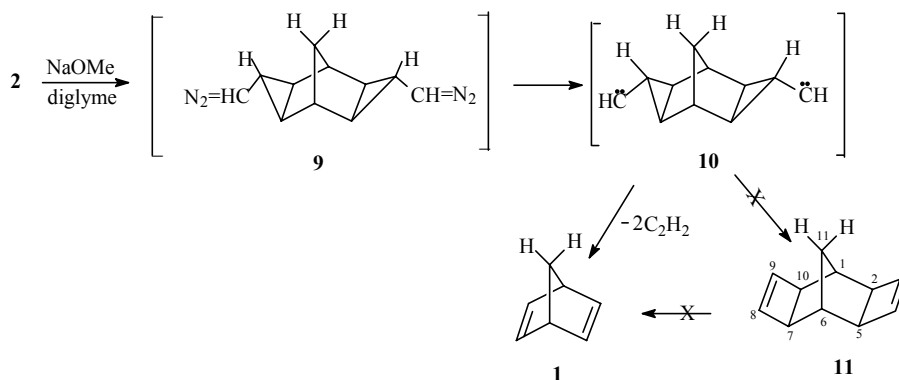
Subsequent  $LiAlH_4$ -reduction gave the diol **7** as a colourless solid (77.8%) in an *anti-anti* configuration of methylol groups. The structure of the diol **7** was assigned on the basis of the spectral data ( $^1H$ -,  $^{13}C$ -NMR and IR) and elemental analysis. The oxidation of the diol **7** with a chromium trioxide-pyridine complex in dichloromethane (Sarett procedure<sup>4</sup>) leads to the dicyclopentanedicarboxaldehyde **8** as a colourless solid product (69.5%).

The bistosylhydrazone **2** – obtained from the reaction of dialdehyde **8** with the tosylhydrazine-presented a *syn-anti* configuration of the azomethines groups. The compound **2** was subjected to Bamford-Stevens reaction using the sodium methoxide/dyglime procedure.<sup>5</sup> The  $^1H$ -NMR spectrum of crude reaction mixture revealed that the main product BCH **1**.

The products of Bamford-Stevens reactions of tosylhydrazones are usually explained admitting as intermediates carbenic species.<sup>6</sup> In the case of **2** (Scheme 2) the carbene **10** generated from diazoderivative **9** can afford as pointed out in literature<sup>1,5-8</sup> either the dicyclobutene **11** (by ring enlargement reaction) or the starting alkene **1** (by cycloreversion reaction). Formation as the main product of BCH **1** in case of **2** is unexpected.



Scheme 1



Scheme 2

## EXPERIMENTAL

The IR spectra were registered on a Carl Zeiss Jena UR-20 double beam spectrometer and a Bruker Vertex 70 spectrophotometer. Melting points are uncorrected. The NMR spectra were registered on a Varian Gemini 300 apparatus at 300 MHz ( $^1H$ ) and 75 MHz ( $^{13}C$ ) using  $CDCl_3$  as solvent and TMS as internal standard. For a correct attribution of chemical

shifts and coupling constants, as they are presented below, we performed additional 1-D and 2-D NMR experiments.

The cyclopropanation of BCH was carried out with an excess of ethyl diazoacetate (EDA) in the presence of  $\pi$ -allyl palladium chloride complex at 0–5°C according to the method described in lit.<sup>3</sup> The diadducts **3-5** were not isolated from the reaction mixture.

3,7-Dicarbomethoxy-exo-exo-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>0<sup>6,8</sup>] nonane (1 $\alpha$ , 2 $\beta$ , 3 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 6 $\beta$ , 7 $\beta$ , 8 $\beta$ ), **6**

The *anti-anti-exo*-dimethylester **6** was obtained by epimerization with methanol and sodium methoxide of the mixture of diethyl esters **3-5** according to lit.<sup>3</sup> The dimethylester **6** was obtained as a colourless solid (2.7 g; 75%), mp 139-140°C (methanol).

IR (CS<sub>2</sub>, CCl<sub>4</sub>, cm<sup>-1</sup>): 718 m; 841 m; 1179 vs; 1271 vs; 1385 s; 1440 s; 1730 s; 2840 vw; 2904 w; 2951 m; 2971 m; 2999 s.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>,  $\delta$  ppm, J Hz): 0.48 (s, 2H, H-9a, H-9b); 1.70 (d, 2.4, 4H, H-2, H-4, H-6, H-8); 2.00 (t, 2.4, 2H, H-3, H-7); 2.56 (s, 2H, H-1, H-5); 3.63 (s, 6H, CH<sub>3</sub>);

<sup>13</sup>C-NMR (CDCl<sub>3</sub>,  $\delta$  ppm): 17.67 (C-9); 21.50 (C-3, C-7); 28.71 (C-2, C-4, C-6, C-8); 51.58 (CH<sub>3</sub>); 173.20 (CO).

3,7-Dihydroxymethyl-exo-exo-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>0<sup>6,8</sup>] nonane (1 $\alpha$ , 2 $\beta$ , 3 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 6 $\beta$ , 7 $\beta$ , 8 $\beta$ ), (**7**)

A solution of dimethylester **6** (5.4g (22.88 mmoles) in ethyl ether (100 mL) was added dropwise to a magnetically stirred suspension of lithium aluminum hydride (6g; 24 mmoles) in 200 mL of ethyl ether. The reaction mixture was stirred 3 hours at room temperature and 24 hours at reflux. It was then cooled and quenched with chilled water added dropwise, followed by addition of a 10% solution of sulfuric acid until the precipitate was completely dissolved. The aqueous phase was separated and was extracted with ether (3 x 50 mL). The combined organic phases were washed with a saturated aqueous sodium chloride solution and dried over anhydrous MgSO<sub>4</sub>. After the removal of the solvent the dicyclopropyl carbinol **7** (3.2g; 77.8%) was obtained as a colourless solid, mp 145°C.

IR (KBr, cm<sup>-1</sup>): 1040 s; 1130 m; 1270 w; 1330 m; 1390 m; 1460 w; 1490 w; 2850 m; 2920 s; 2950 s; 3020 m; 3350 s.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>,  $\delta$  ppm, J Hz): 0.42 (bs, 2H, H-9); 0.79 (d, 2.5, 4H, H-2, H-4, H-6, H-8); 1.27 (tt, 6.6; 2.5; 2H, H-3, H-7); 2.25 (bs, 2H, H-1, H-5); 3.10 (t, 6.6, 4H, H-10, H-10'); 4.37 (t, 5.5, 2H, OH)

<sup>13</sup>C-NMR (CDCl<sub>3</sub>,  $\delta$  ppm): 17.61 (C); 21.20 (C); 24.31 (C); 35.34 (C); 62.89 (C)

Anal. Calcd. For C<sub>11</sub>H<sub>16</sub>O<sub>2</sub> : C, 73.30; H, 8.95; Found: C, 73.51; H, 8.85.

3,7-Diformyl-exo-exo-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>0<sup>6,8</sup>] nonane (1 $\alpha$ , 2 $\beta$ , 3 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 6 $\beta$ , 7 $\beta$ , 8 $\beta$ ), (**8**)

The chromium trioxide (4 g; 40 mmoles) was added to a solution of pyridine (6.32 g; 80 mmoles) in 300 mL dichloromethane cooled to 5°C. The yellow precipitate and the dark solution were stirred for 5 min at 5°C and then at room temperature until the solution became clear (1h). Then, the dicyclopropylcarbinol (2.5g; 13.9 mmoles) was added. After the mixture was stirred at room temperature, for 15 min, the dark residue formed was separated and washed with 5 x 40mL of ether. The combined organic phases were washed with a cold aqueous sodium hydroxide solution (5%, 3 x 100mL), then with 5% HCl aqueous solution (100mL), 5% sodium carbonate solution (100mL) and then a saturated aqueous sodium chloride solution (100 mL), and dried over anhydrous MgSO<sub>4</sub>. After the removal of solvents at reduced pressure, the dicyclopropanedicarboxaldehyde **8** (1.7g; 69.5%) was obtained as a colourless solid, mp 79° (methanol).

IR (CCl<sub>4</sub>, cm<sup>-1</sup>): 1120 m; 1180 m; 1390 w; 1700 vs; 2740 w; 2850 m; 2920 s; 2980 s; 3010 s; 3070 m.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>,  $\delta$  ppm, J Hz): 0.58 (t, 1.6, 2H, H-9); 1.82 (d, 2.4, 2H, H-2); 2.31 (dt, 4.6, 2.4, H-3); 2.66 (bs, 2H, H-1 H-5); 9.19 (d, 4.6, 2H, H-10, H-10').

<sup>13</sup>C-NMR (CDCl<sub>3</sub>,  $\delta$  ppm): 17.91 (C-9); 28.65 (C-2); 31.81 (C-3); 36.43 (C-1); 199.26 (C-10).

Anal. Calcd. for C<sub>11</sub>H<sub>12</sub>O<sub>2</sub> : C, 74.97; H, 6.86; Found: C, 75.17; H, 6.97.

Bistosylhydrazone of 3,7-diformyl-exo-exo-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>0<sup>6,8</sup>] nonane(1 $\alpha$ , 2 $\beta$ , 3 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 6 $\beta$ , 7 $\beta$ , 8 $\beta$ ), (**2**)

The dicyclopropyldicarboxyaldehyde (2g; 11.36 mmoles) and 5g Na<sub>2</sub>SO<sub>4</sub> were added to a solution of tosylhydrazine (3.6 g; 22.8 mmoles) in 200 mL chloroform. The mixture was kept three days in refrigerator. After filtration and solvent removal, the bistosylhydrazone **2** (3.6 g; 80%) was obtained, as a colorless solid, m.p. 192° (methanol).

IR(solid in ATR, cm<sup>-1</sup>): 545.16 m; 671.14 s; 815.15 w; 928.01 w; 1022.09 w; 1088.90 m; 1161.44 vs; 1260.57 m; 1312.42 w; 1640.73 w; 2971.62 w; 3025.39 w; 3220.25 s.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>,  $\delta$  ppm, J Hz): 0.58 (bs, 2H, H-9); 1.28 (d, 2.3, 2H, H-2 s (a)); 1.33 (d, 2.2, 2H, H-2 s(a)); 1.87 (dt, 7.4, 2.3, 1H, H-3a(s)); 2.34 (dt, 7.9, 2.2, 1H, H-3a(s)); 2.39 (s, 3H, H-14 a(s)); 2.43 (s, 2H, H-1); 6.00 (d, 7.8, 1H, H-10 a (s)); 6.79 (d, 7.4, 1H, H-1 a(s)); 7.38 (d, 7.9, 2H, H-12 a(s)); 7.4 d (d, 7.9, 2H, H-12a (s)); 7.69 (d, 7.9, 2H, H-11 a(s)); 7.72 (d, 7.9, 2H, H-11 s(a)); 10.66 (s, 1H, NH); 10.85(s, 1H, NH).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>,  $\delta$  ppm): 16.61 (C-9a(s)); 17.41 (C-9 s(a)); 20.98 (CH); 21.60 (CH); 26.40 (CH); 26.61 (CH); 35.90 (CH); 127.16 (C-12 a(s)); 127.35 (C-8 s(a)); 129.45 (C-11a); 129.54 (C-11 s); 136.26 (C<sub>q</sub>); 143.18 (C<sub>q</sub>); 151.38 (C-1); 152(C-1)

Anal. Calcd. for C<sub>26</sub>H<sub>28</sub>N<sub>4</sub> : C, 78.75; H, 7.12; N, 14.13; Found: C, 78.9; H, 7.22; N, 14.30.

Bamford- Stevens reaction of bistosylhydrazone of 3,7-diformyl-exo-exo-tetracyclo[2.2.1.1.1.0<sup>2,4</sup>0<sup>6,8</sup>] nonane (1 $\alpha$ , 2 $\beta$ , 3 $\beta$ , 4 $\beta$ , 5 $\alpha$ , 6 $\beta$ , 7 $\beta$ , 8 $\beta$ ), (**2**)

The bistosylhydrazone **2** (4g; 10 mmoles) was added in small portions over a stirred suspension of freshly prepared and dried sodium methoxyde (1.1 g; 20 mmoles) in 80 mL anhydrous diglyme at 110-120°. The reaction mixture was stirred at 120-130° for 2 hrs (evolution of gaseous nitrogen). The cooled reaction mixture was then poured in water and ether extracted (5 x 30 mL). The combined organic solutions were washed with water, dried over anhydrous MgSO<sub>4</sub> and evaporated. The residual product (0.5 g; 54% calculated for **1**)- thick oil-was subsequently chromatographed on neutral Al<sub>2</sub>O<sub>3</sub> (Merck, activity I) with petroleum ether (b. p. 30-35°) as solvent. The main product obtained in first eluates is the BCH **1** (IR, <sup>1</sup>H-NMR).

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## CONCLUSIONS

In this paper we realized the Bamford- Stevens reaction of bistosylhydrazone **2** and the syntheses and the spectral characterization of new bicyclo[2.2.1] derivatives: diol **7**, dialdehyde **8** and bistosylhydrazone **2**.

## REFERENCES

1. M. D. Gheorghiu and E. Olteanu, *Rev. Roum. Chim.*, **1989**, *34*, 1931-1944.
2. M. D. Gheorghiu and E. Olteanu, *J. Org. Chem.*, **1987**, *52*, 5158-5162.
3. E. Olteanu, M.T. Căproiu and C. Drăghici, *Rev. Roum. Chim.*, **1996**, *41*, 953-958.
4. G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Am. Chem. Soc.*, **1953**, *75*, 422-431.
5. L. Friedman and Schechter, *J. Amer. Chem. Soc.*, **1960**, *82*, 1003-1005.
6. R. H. Shapiro, in "Organic Reactions" vol. 23, Wiley, New York, 1976, p. 405
7. R.R. Sauers, S. B. Schlosberg and P. E. Pfeffer, *J. Org. Chem.*, **1968**, *33*, 2175-2179; W. Kirmse and K. H. Pook, *Chem Ber.*, **1965**, *98*, 4022.
8. A. Banciu, C. Drăghici, I. Ghivirigă, M. D. Banciu and E. Cioranescu, *Rev. Roum. Chim.*, **1992**, *37*, 1133-1144.