

SHORT
COMMUNICATIONS

Synthesis and Some Reactions
of Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetic
Acid Azide

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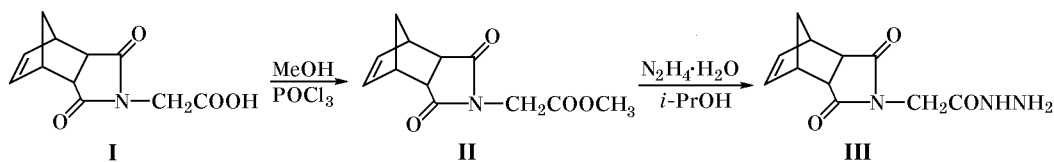
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The preparation of polyfunctional compounds containing groups capable of different transformations is an urgent task of the modern chemistry. Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetic acid (**I**) may serve as an example of such compound.

The goal of this study was the synthesis and investigation of reactions of bicyclo[2.2.1]hept-2-ene-

endo,endo-5,6-dicarboximidoacetic acid azide. To prepare azide **IV** a method was used involving conversion of acid **I** into its methyl ester, then into hydrazide with subsequent diazotization of the latter. Ester **II** was obtained by esterification of acid **I** in anhydrous alcohol in the presence of the catalytic amount of phosphorus oxychloride [2] with 86% yield of the target product.

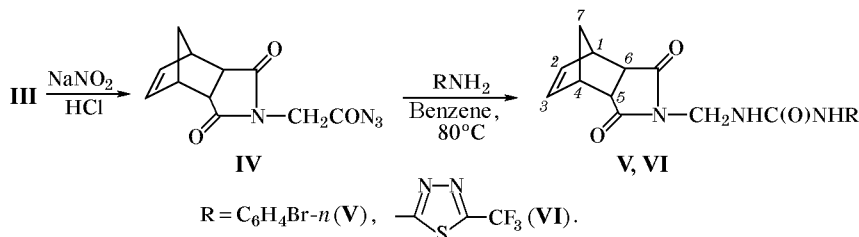


The maximum yield and purity of hydrazide **III** were achieved by carrying out the reaction at 0°C and equimolar reagents ratio. At excess hydrazine hydrate or at higher temperature apparently occurred a concurrent transhydrazination reaction in the imide ring of ester **II**, and the yield of hydrazide was considerably reduced.

The structure of compounds **II** and **III** was confirmed by the IR spectra. In the IR spectrum of compound **III** the hydrazine moiety appeared as a set of three absorption bands in the regions 3570, 3500, and 3330 cm⁻¹ corresponding to the stretching vibra-

tions of two types of NH bonds in agreement with the known published data [3]. The transformation of the ester group is obvious from the lack in the IR spectrum of hydrazide **III** of the strong band at 1220 cm⁻¹ corresponding to the stretching vibrations of the fragment C-O-C in the ester group [4] and observed in the spectrum of ester **II**.

Further hydrazide **III** was converted into azide **IV** by treatment with the nitrous acid obtained *in situ* from sodium nitrite and hydrochloric acid. Azide **IV** by heating with equimolar quantity of appropriate amines in anhydrous benzene was transformed into substituted carbamides **V**, **VI**.



Taking into consideration the low stability of carbonylazides and also to avoid the side process of azide group cycloaddition to the multiple bond of the bicyclic skeleton the azide synthesis was carried out in water medium at -15°C .

The most convincing proofs of the structure of compounds **V**, **VI** were obtained by analysis of the ^1H NMR spectra where alongside the peaks belonging to the bicyclic skeleton and substituents appeared a triplet and a singlet from protons of two nonequivalent NH groups at 6.99 and 8.51 ppm for compound **V** and at 7.30 and 11.22 ppm for compound **VI**.

Relative simplicity of the preparation and the high reactivity of azide **IV** permit recommending it as a new accessible reagent for the synthesis of biologically active compounds belonging to various classes.

Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetic acid (**I**) was synthesized by procedure from [1].

Methyl bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetate (II). To a stirred dispersion of 15.7 g (0.071 mol) of acid (**I**) in 20 ml of anhydrous methanol was added at room temperature 0.60 ml (0.0071 mol) of POCl_3 , and the stirring was continued at the same temperature till the completion of reaction (TLC monitoring). Within first 1–2 h the acid dissolved, and to the end of the process gradually separated a precipitate. The excess solvent was removed in a vacuum, the crystals of the product were filtered off and carefully washed on the filter with water and with a solution of sodium hydrogen carbonate. Then the product was dried in air and recrystallized from hexane to obtain 14.4 (86%) of ester **II**, mp $89\text{--}90^{\circ}\text{C}$. (publ.: mp $80\text{--}82^{\circ}\text{C}$ [5]). IR spectrum, cm^{-1} : 3065, 2880, 1745, 1700, 1415, 1325, 1220, 1180. Found, %: N 5.98. $\text{C}_{12}\text{H}_{13}\text{NO}_4$. Calculated, %: N 5.96.

Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetic acid hydrazide (III). To a stirred dispersion of 5.4 g (0.023 mol) of ester **II** in 15 ml of 2-propanol was added dropwise at 0°C within 30 min a solution of 1.4 ml (0.023 mol) of 80% aqueous hydrazine hydrate in 3 ml of 2-propanol. The crystalline ester within 2–3 h dissolved, and the stirring was continued till the completion of reaction (TLC monitoring). The excess alcohol was evaporated in a vacuum till the volume of the reaction mixture was 7–8 ml, the precipitate formed was filtered off, dried, and recrystallized from a small portion of 2-propanol. Yield 4.8 g (89%), mp $163\text{--}164^{\circ}\text{C}$. IR spectrum, cm^{-1} : 3570, 3500, 3330, 3070, 1755,

1680, 1620, 1490, 1418, 1325, 1175. Found, %: N 17.76. $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_3$. Calculated, %: N 17.87.

Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidoacetic acid azide (IV). Into a flask cooled in a bath of ice-salt mixture was charged 5.2 g (0.022 mol) of hydrazide **III**, 3 ml of water, 4.2 ml (0.046 mol) of 34% water solution of hydrochloric acid, and at stirring was quickly added from a dropping funnel a solution of 1.52 g (0.022 mol) of sodium nitrite in 3 ml of water. In 5 min the separated precipitate was filtered off, thoroughly washed on the filter with water till neutral washings, and dried in air for 2 days. Yield of azide **IV** 4.5 g (83%), mp $83\text{--}84^{\circ}\text{C}$ (decomp.).

N-(Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximido-methyl)-N-(p-bromophenyl)carbamide (V) was obtained by heating at reflux for 2 h of a mixture of 0.2 g (0.081 mmol) of azide **IV** and 0.18 g (0.081 mmol) of *p*-bromoaniline in 5 ml of anhydrous benzene. The separated precipitate was filtered off, washed on the filter with benzene, dried, and recrystallized from 2-propanol. Yield of compound **V** 0.25 g (71%), mp $264\text{--}265^{\circ}\text{C}$. IR spectrum, cm^{-1} : 3375, 1755, 1700, 1680, 1590, 1545, 1340, 1235. ^1H NMR spectrum, δ , ppm: 8.51 s (1H, NH), 7.29 m (4H, H arom), 6.69 t (1H, NH), 6.00 m (2H, H^2 , H^3), 4.65 d (2H, CH_2), 3.30 m (4H, H^1 , H^4 , H^5 , H^6), 1.64 d (1H, H^{7s}), 1.57 d (1H, H^{7a}). Found, %: N 10.71. $\text{C}_{17}\text{H}_{16}\text{BrN}_3\text{O}_3$. Calculated, %: N 10.77.

N-(Bicyclo[2.2.1]hept-2-ene-endo,endo-5,6-dicarboximidomethyl)-N'-2-(5-trifluoromethyl-1,3,4-thiadiazolyl)carbamide (VI) was prepared by a similar procedure from 0.6 g (2.44 mmol) of azide **IV** and 0.41 g (2.44 mmol) of 5-trifluoromethyl-1,3,4-thiadiazol-2-ylamine. Yield 0.80 g (85%), mp $226\text{--}227^{\circ}\text{C}$. IR spectrum, cm^{-1} : 3420, 3220, 1770, 1710, 1680, 1555, 1335, 1220. ^1H NMR spectrum, δ , ppm: 11.23 s (1H, NH), 7.30 t (1H, NH), 5.99 m (2H, H^2 , H^3), 4.72 d (2H, CH_2), 3.30 m (4H, H^1 , H^4 , H^5 , H^6), 1.63 d (1H, H^{7s}), 1.57 d (1H, H^{7a}). Found, %: N 17.93. $\text{C}_{14}\text{H}_{12}\text{F}_3\text{N}_5\text{O}_3\text{S}$. Calculated, %: N 18.09.

IR spectra were recorded on spectrophotometer UR-20 from samples pelletized with KBr. ^1H NMR spectra were registered on spectrometer Bruker DAX-500 (operating frequency 500 MHz) from solutions of compounds in $\text{DMSO}-d_6$. HMDS was used as internal reference. The reaction progress was monitored and the homogeneity of compounds synthesized was checked by TLC on Silufol UV-254 plates, eluent ether, development in iodine vapor. Elemental analyses were carried out on Karlo Erba analyzer.

REFERENCES

1. Tarabara, I.N., Yarovoi, M.Yu., Isaev, A.K., and Kas'yan, L.I., *Visnik DNU, Ser. Khim.*, 2002, vol. 36.
2. *Weygand-Hilgetag Organisch-chemische Experimentierkunst*, Hilgetag, G. and Martini, A., Eds., Leipzig: Johann Ambrosius Barth, 1964, 3rd ed. Translated under the title *Metody eksperimenta v organicheskoi khimii*, Moscow: Khimiya, 1968, p. 142.
3. Grekov, *Organicheskaya khimiya gidrazina* (Organic Chemistry of Hydrazine), Kiev: Tekhnika, 1966.
4. Nakanisi, K., *Infrakrasnye spektry i stroenie organicheskikh soedinenii* (IR Spectra and Structure of Organic Compounds), Moscow: Mir, 1965.
5. Biagini, S.C.G., Bush, S.M., Gibson, V.C., Mazzariol, L., North, M., Teasdale, W.G., Williams, C.M., Zagotto, G., and Zamuner, D., *Tetrahedron Lett.*, 1995, vol. 51, p. 7247.