Diazo Coupling of XV with β-Naphthol. A 4-ml sample of 96% H_2SO_4 was added dropwise at room temperature to a solution of 0.6 g (4.4 mmole) of XV in 50 ml of water, after which a solution of 1.3 g (9.1 mmole) of β-naphthol in 50 ml of 2% KOH was added. The resulting precipitate was removed by filtration and washed successively with water and ethanol to give 1.2 g (63%) of a product with mp 192-194°. Found: N 19.8%. $C_{23}H_{16}N_6O_3$. Calculated: N 19.9%.

LITERATURE CITED

1. L. Knorr, Ber., 37, 3520 (1904).
2. H. Reimlinger, Ber., 94, 1036 (1961).
3. D. G. Farnum and P. Jates, J. Am. Chem. Soc., 84, 1399 (1962).
4. H. Dorn and H. Dichler, Ann., 707, 141 (1967).
5. E. Buchner and M. Fritsch, Ann., 273, 265 (1893).
6. L. Musante, Gazz. Chim. Ital., 72, 537 (1942).

SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES

XXX.* SYNTHESIS OF HETEROCYCLIC COMPOUNDS FROM 1,3-DICYANOADAMANTANE

G. A. Shvekhgeimer and L. K. Kuz'micheva

UDC 547.785.1.07

The corresponding mono- and bisheterocyclic derivatives of adamantane were obtained by reaction of the dinitrile or diimino ester of adamantane-1,3-dicarboxylic acid with ethylenediamine and related compounds.

The literature does not contain information regarding the synthesis of compounds simultaneously containing an adamantyl group and two azole residues. Feeling that compounds of this sort may be of interest as potential biologically active substances, we studied some methods for their synthesis.

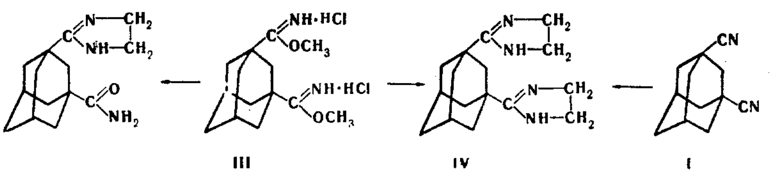
Reactions of functional derivatives of adamantane-1,3-dicarboxylic acid with ethylenediamine, o-phenylenediamine, and o-aminophenol were used to construct the heterocyclic ring. Starting dinitrile I was obtained from adamantane-1,3-dicarboxamide (II) and was used for the synthesis of the diethyl diimino ester of adamantane-1,3-dicarboxylic acid (III). The structure of III was confirmed by conversion to the known adamantane-1,3-dicarboxamide [2].

The reaction of diimino ester III with ethylenediamine under the conditions usually employed for the preparation of imidazolines leads to an inseparable mixture of two compounds, the IR spectrum of which contain absorption bands at 1600 and 1670 cm^{-1}, which we assigned, respectively, to the stretching vibrations of the C = N bond in the imidazoline ring and the C = O bond in the amide grouping. Analysis of the mass spectrum showed that the reaction product contains two compounds with molecular weights of 272 and 247; these values are in agreement with empirical formulas $C_{16}H_{24}N_3$ and $C_{14}H_{21}N_3O$. We evidently obtained a mixture of 1,3-[bis(2-imidazolinyl)]adamantane (IV) and 3-(2-imidazolinyl)adamantane-1-carboxamide. Compound IV was synthesized by condensation of diimino ester III with fivefold excess of ethylenediamine at room temperature and also by refluxing dinitrile I with ethylenediamine in acidified cumene.

---

*See [1] for communication XXIX.

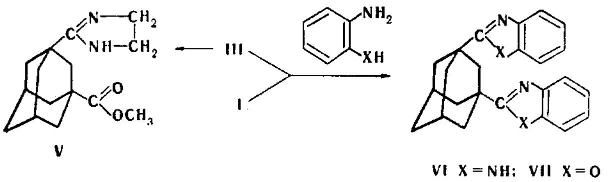
I. M. Gubkin Moscow Institute of the Petrochemical and Gas Industry. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1654-1657, December, 1976. Original article submitted July 22, 1975; revision submitted May 18, 1976.



As a result of reaction of 2 moles of o-phenylenediamine and 1 mole of diimino ester III we obtained a compound, which, according to the results of elementary analysis and the IR and mass spectra, was found to be methyl 3-[(2-benzimidazolyl)]adamantane-1-carboxylate (V) rather than the expected 1,3-[bis(2-benzimidazolyl)]adamantane.

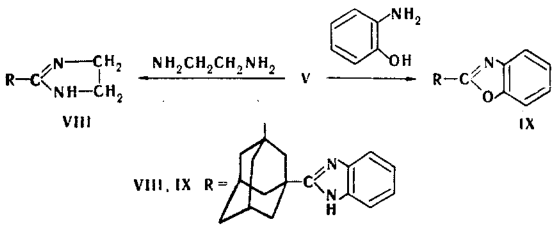
1,3-[Bis(2-benzimidazolyl)]adamantane (VI) was obtained when III was condensed with a fivefold excess of o-phenylenediamine at room temperature. Compound VI was also synthesized by refluxing dinitrile I with o-phenylenediamine in cumene in the presence of 4 N HCl.

Attempts to obtain 1,3-[bis(2-benzoxazolyl)]adamantane (VII) by condensation with 1 mole of diimino ester III with 2 moles of o-aminophenol were unsuccessful. Compound VII was obtained by reaction of dinitrile I with o-aminophenol in the presence of 4 N HCl.

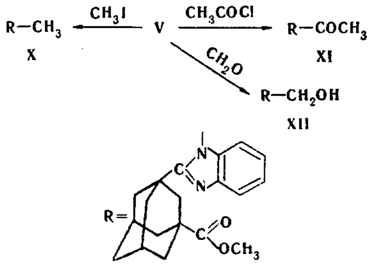


1-(2-Benzimidazolyl)-3-(2-imidazolinyl)adamantane (VIII) was obtained by refluxing a mixture of V with a large excess of anhydrous ethylenediamine in the presence of KU-2 ion-exchange resin.

Benzoxazole derivative IX was synthesized when o-aminophenol was used in place of ethylenediamine in this reaction.



The transformations of V associated with the lability of the hydrogen atom attached to the $N_{(1)}$ atom of the benzimidazole ring are shown in the scheme presented below.



EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of solutions of the compounds in acetonitrile were obtained with a Unicam SP 800 A spectrophotometer. The PMR spectra of $CDCl_3$ solutions of the compounds were recorded with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard. The molecular weights were determined with an MKh-1303 spectrometer (ionization chamber temperature 170° and ionizing voltage 50 eV). The individuality of the products was monitored by thin-layer chromatography (TLC) on activity I Al_2O_3 [elution with benzene–methanol (10 : 1) and development with iodine vapors].

Adamantane-1,3-dicarboxamide (II). This compound was obtained by the method in [2] and had mp 255° (from cyclohexane).

1,3-Dicyanoadamantane (I). A mixture of 10 g (0.045 mole) of diamide II and 46 ml of thionyl chloride in 50 ml of anhydrous benzene was refluxed in a flask equipped with a reflux condenser for 18 h, after which it was cooled and poured over ice. A 50% solution of sodium hydroxide was added to the resulting mixture until it was weakly alkaline, after which it was extracted with ether. The combined ether extracts were washed with water and dried with Na_2SO_4. The ether-benzene solution was vacuum evaporated to give 8.2 g (92%) of acid II with mp 199-200° (from aqueous methanol). IR spectrum: 2245 cm^{-1} ($C \equiv N$). Found: C 77.3; H 7.7; N 14.7%. $C_{12}H_{14}N_2$. Calculated: C 77.4; H 7.5; N 15.0%.

Adamantane-1,3-dicarboxylic Acid Methyl Diimino Ester Dihydrochloride (III). Dry hydrogen chloride was bubbled for 1.5-2 h at 5° through a solution of 0.93 g (0.005 mole) of dinitrile I and 0.32 g (0.01 mole) of anhydrous methanol in 60 ml of anhydrous dioxane, after which the mixture was allowed to stand at 0° for 24 h. The excess hydrogen chloride was removed at reduced pressure, and the resulting precipitate was removed by filtration, washed on the filter with anhydrous ether, and dried in a vacuum desiccator over sodium hydroxide to constant weight to give 1.55 g (97%) of III with mp 119-120° (dec.). Found: Cl 21.4%. $C_{14}H_{22}N_2O_2 \cdot 2HCl$. Calculated: Cl 21.2%.

Thermal Decomposition of III. A 0.3-g (0.001 mole) sample of III was placed in a flask equipped with a reflux condenser with a calcium chloride tube and heated at 125° until methyl chloride evolution ceased, after which it was heated at 128° for 15 min. The residue was washed with benzene and recrystallized to 0.2 g (98%) of diamide II with mp 254-255° (from alcohol). No melting-point depression was observed for a mixture of a sample of diamide II with a genuine sample.

1,3-[Bis(2-imidazolinyl)]adamantane (IV). A) A 1.6-g (0.005 mole) sample of diimino ester III was added with stirring at 0° to a solution of 3 g (0.05 mole) of ethylenediamine in 30 ml of anhydrous methanol, and the mixture was stirred at 0° for 1 h and at room temperature for 28 h. It was then cooled to 0°, and a solution of 0.23 g (0.01 g-atom) of sodium in 15 ml of anhydrous methanol was added dropwise, after which the mixture was stirred at 0° for 2 h. The resulting precipitate was removed by filtration, and the filtrate was evaporated to dryness in vacuo. The residue was treated with methylene chloride, and the solvent was removed by vacuum distillation to give 1.13 g (83%) of IV with mp 293-294° (from aqueous methanol). Found: C 70.7; H 8.3; N 20.4%. $C_{16}H_{24}N_4$. Calculated: C 70.6; H 8.5; N 20.6%.

B) A mixture of 9.3 g (0.05 mole) of dinitrile I, 6.0 g (0.1 mole) of ethylenediamine, 8 ml of 4 N HCl, and 30 ml of cumene was refluxed with vigorous stirring for 36 h, after which it was cooled and filtered. The filtrate was evaporated at reduced pressure to give 11.7 g (86%) of IV with mp 292-293° (from aqueous methanol). IR spectrum: 1600 and 1620 ($C = N$); 3420 cm^{-1} (NH). PMR spectrum: 3.44 (CH_2) and 5.41 ppm (NH).

Methyl 3-(2-Benzimidazolyl)adamantane-1-carboxylate (V). A mixture of 1.6 g (0.005 mole) of III and 1.1 g (0.01 mole) of o-phenylenediamine in 30 ml of anhydrous methanol was refluxed with stirring for 2 h, after which it was cooled and poured into cold water containing 0.005 mole of $NaHCO_3$. The resulting precipitate was removed by filtration, washed on the filter with water, and dried in a vacuum desiccator over sodium hydroxide to give 0.99 g (64%) of V with mp > 350° (from methanol). IR spectrum: 1620 ($C = N$); 1730 ($C = O$); 3180, 3420 (NH) cm^{-1}. UV spectrum, λ_{max}, nm (log ε): 217 (3.10), 276 (3.41), and 282 (3.43). The product had a molecular weight of 310 (by mass spectrometry). $C_{19}H_{22}N_2O_2$. M_{calc} 310.

1,3-[Bis(2-benzimidazolyl)]adamantane (VI). A) A mixture of 0.93 g (0.005 mole) of dinitrile I, 1.08 g (0.01 mole) of o-phenylenediamine, 12 ml of 4 N HCl, and 40 ml of cumene was refluxed with vigorous stirring for 10 h, after which it was cooled and filtered. The filtrate was evaporated at reduced pressure to give 0.8 g (58%) of VI with mp > 350° (from alcohol). Found: C 77.9; H 7.5; N 15.3%. $C_{24}H_{28}N_4$. Calculated: C 78.2; H 7.6; N 15.1%.

B) A mixture of 1.6 g (0.005 mole) of III and 2.7 g (0.025 mole) of o-phenylenediamine was stirred for 4 h, after which it was poured into cold water containing Na_2CO_3; the resulting precipitate was removed by filtration and washed with water to give 1.34 g (69%) of VI with mp > 350° (from benzene). IR spectrum: 1605, 1620 ($C = N$); 3420 cm^{-1} (NH). The molecular weight of the product (by mass spectrometry) was 368. $C_{14}H_{28}N_4$. M_{calc} 368.

1,3-[Bis(2-benzoxazolyl)]adamantane (VII). A mixture of 0.93 g (0.005 mole) of dinitrile I, 1.09 g (0.01 mole) of o-aminophenol, 12 ml of 4 N HCl, and 50 ml of toluene was refluxed with stirring for 18 h, after which it was cooled and filtered, and the filtrate was evaporated at reduced pressure to give 1.15 g (62%) of VII with mp 312-314° (from methanol). IR spectrum: 1625, 1558 cm^{-1} (C=N). Found: C 77.8; H 5.9; N 7.6%. $C_{24}H_{22}N_2O_2$. Calculated: C 77.8; H 5.9; N 7.6%.

1-(2-Benzimidazolyl)-3-(2-imidazolinyl)adamantane (VIII). A mixture of 0.15 g of KU-2 resin (COE—4.85 meq/g), 2 ml of anhydrous ethylenediamine, and 0.31 g (0.001 mole) of V was stirred at 115-116° for 12 h, after which the contents of the flask were dissolved in hot methanol. The precipitate was removed by filtration and washed with hot methanol. The filtrate was evaporated at reduced pressure to give 0.24 g (71%) of VIII with mp 310-311° (from acetonitrile). IR spectrum: 1655, 1615 (C=N); 3200, 3340 cm^{-1} (NH). Found: C 75.6; H 8.7; N 17.5%. $C_{20}H_{38}N_4$. Calculated: C 75.8; H 8.7; N 17.2%.

1-(2-Benzimidazolyl)-3-(2-benzoxazolyl)adamantane (IX). A mixture of 0.31 g (0.001 mole) of V, 0.11 g (0.001 mole) of o-aminophenol, 0.1 g of KU-2 ion-exchange resin, and 50 ml of p-xylene was stirred in a flask equipped with a Dean—Stark trap, after which it was refluxed with vigorous stirring until water liberation ceased (18 h). The catalyst was removed by filtration, and the filtrate was evaporated at reduced pressure to give 2.1 g (59%) of IX with mp > 350° (from benzene). IR spectrum: 1620, 1655, and 1540 cm^{-1} (C=N). Found: C 77.5; H 5.9; N 11.5%. $C_{24}H_{23}N_3O$. Calculated: C 77.8; H 6.0; N 11.3%.

Methyl 3-(1-Methyl-2-benzimidazolyl)adamantane-1-carboxylate (X). A 1.42-g (0.01 mole) sample of methyl iodide was added dropwise with cooling and stirring in the course of 30 min to a solution of 0.1 g (0.0075 mole) of potassium hydroxide and 1.55 g (0.005 mole) of V in 7 ml of anhydrous methanol, and the mixture was stirred at room temperature for 5 h. The potassium iodide was removed by filtration, and the filtrate was evaporated at reduced pressure to give 1.4 g (84%) of X with mp 242-243° (from methanol). IR spectrum: 1620 (C=N) and 1732 cm^{-1} (C=O). PMR spectrum: 2.05 (NCH_3), 3.6 ($COOCH_2$), and 7.2-7.6 ppm (C_6H_4).

Methyl 3-(1-Acetyl-2-benzimidazolyl)adamantane-1-carboxylate (XI). A solution of 0.31 g (0.001 mole) of V and 0.07 ml (0.001 mole) of freshly distilled acetyl chloride in 20 ml of anhydrous benzene was stirred for 20 h, and the precipitate was removed by filtration and dried in a vacuum desiccator to constant weight to give 0.3 g (86%) of XI with mp 192-193° (from acetonitrile). IR spectrum: 1620 (C=N) and 1730 cm^{-1} (C=O). PMR spectrum: 3.63 (CH_3) and 7.3-7.7 ppm (C_6H_4).

Methyl 3-(1-Hydroxymethyl-2-benzimidazolyl)adamantane-1-carboxylate (XII). A mixture of 0.31 g (0.001 mole) of V, 0.3 g (0.001 mole) of paraformaldehyde, and 15 ml of anhydrous methanol was refluxed for 10 h, after which it was cooled and poured into cold water. The resulting precipitate was removed by filtration and dried in a vacuum desiccator over sodium hydroxide to give 0.33 g (96%) of XII with mp 265-266° (from methanol). IR spectrum: 1620 (C=N), 1730 (C=O), 3450 (OH), and 1050 cm^{-1} (OH). Found: C 70.8; H 7.0; N 8.5%. $C_{20}H_{24}N_2O_3$. Calculated: C 70.6; H 7.2; N 8.2%.

LITERATURE CITED

1. G. A. Shvekhgeimer and A. Baran'ski, Summaries of Papers Presented at the Fifth Conference on the Chemistry of Nitro Compounds [in Russian], Nauka, Moscow (1974), p. 8.
2. V. Prelog, Ber., 74, 1769 (1971).