

Heterocyclic Derivatives of Ethyl Nitroacetate *)

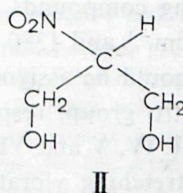
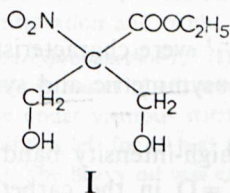
by

H. PIOTROWSKA, T. URBĄŃSKI, and I. WOŁOCHOWICZ

Presented by T. URBĄŃSKI on May 26, 1971

Summary. Ethyl nitroacetate yielded with formaldehyde 2-nitro-2-carbethoxypropanediol-1,3 which was then cyclized to 5-nitro-5-carbethoxy-1,3-dioxane, 5-nitro-5-carbethoxy-2-bora-1,3-dioxane and 5-nitro-5-carbethoxyhexahydropyrimidine derivs.

In the present work the authors tried to obtain a few heterocyclic systems starting from 2-nitro-2-carbethoxypropanediol-1,3 (**I**), which has so far been unknown. The latter was obtained by an aldolic addition of two moles of formaldehyde to ethyl nitroacetate. The attempt to obtain **I** by reacting ethyl chloroformate with sodium salt of 2-nitropropanediol (**II**) was unsuccessful, as the product was a non-crystalline mixture.



By reacting **I** with acetone or benzaldehyde, 1,3-dioxane derivatives (**III**) were obtained. Compound (**IIIb**) reacted with methylamine yielding *N*-methylamide (**V**). The reaction of (**IIIb**) with ammonia or hydrazine produced a hydrolysis of the carbethoxy group leading to **VI** through the decarboxylation.

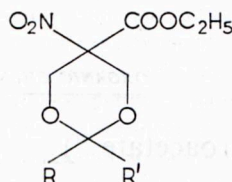
Phenylboronic acid and its *p*-chloro derivative yielded 2-bora-1,3-dioxanes (**IV**). A hexahydropyrimidine derivative (**VII**) was obtained when acting on **I** with two moles of *ter*-butylamine and one mole of formaldehyde.

Attempts to prepare tetrahydro-1,3-oxazine derivatives by acting on **I** with one mole of a primary amine (benzyl- or *ter*-butylamine) and one mole of form-

*) Dedicated to Professor M. Pailer for his 60th birthday.

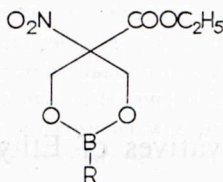
Note: Part XCVI in the series Chemistry of Nitroparaffins.

aldehyde were unsuccessful: the yield was a mixture of different products which did not give crystalline hydrochlorides.



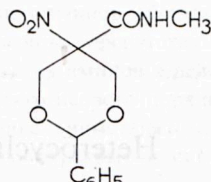
IIIa $R = R' = \text{CH}_3$

IIIb $R = \text{H}, R' = \text{C}_6\text{H}_5$

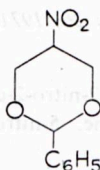


IVa $R = \text{C}_6\text{H}_5$

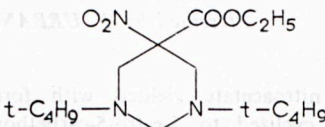
IVb $R = p\text{-ClC}_6\text{H}_4$



V



VI



VII

Infrared and NMR spectra

Infrared spectra

2-Nitro-2-carbethoxypropanediol-1,3 (**I**) shows a wide medium intensity band $3400\text{--}3200\text{ cm}^{-1}$ characterising the hydrogen bonded hydroxylic group. The band disappears in all ring compounds **III**—**VII**.

The bands 1570 cm^{-1} and $1380\text{--}1360\text{ cm}^{-1}$ were characteristic of all examined compounds. They should be assigned to the asymmetric and symmetric stretching vibrations of the nitro group, respectively.

Compounds **I**, **III**, **IV**, **V** and **VII** show a high-intensity band $1750\text{--}1740\text{ cm}^{-1}$ characterising the stretching vibrations of $\text{C}=\text{O}$ in the carbethoxylic group. *N*-methylamide **V** gives the band 1650 cm^{-1} corresponding to the same vibration in the amide group.

The ring compounds **III**—**VI** show bands of $1200\text{--}1100\text{ cm}^{-1}$ which should be assigned to the acetal $\text{C}-\text{O}-\text{C}$ bonds which in derivatives of 5-nitrotetrahydro-1,3-oxazines were manifested by a series of bands $1150\text{--}1050$, $955\text{--}925$ and $855\text{--}800\text{ cm}^{-1}$ [1].

The bond $\text{B}-\text{O}$ in compound **IV** is characterised by a stretching vibration high-intensity band and a frequency of about 1320 cm^{-1} .

The aromatic rings of compounds **IIIb** and **IVa** are manifested by the presence of bands 700 cm^{-1} which should probably be assigned to $\text{C}-\text{H}$ bending vibrations. In compound **IVb** the corresponding frequency is higher: 825 cm^{-1} .

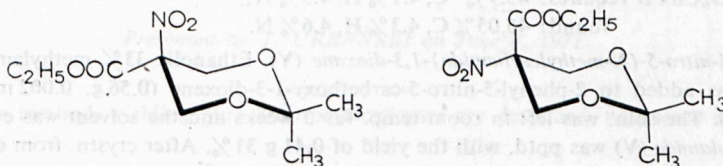
Amide **V** was manifested by $\text{N}-\text{H}$ amide stretching and bending vibrations 3270 and 1560 cm^{-1} , respectively.

NMR spectra

NMR spectra confirmed the structural formulae of the compounds.

Compounds **I**—**IV** and **VII** gave CH_2 quartets at 5.57—5.72 ppm and CH_3 triplets at 8.64—9.72 ppm which should be assigned to CH_2 and CH_3 groups, respectively, in $\text{COOCH}_2\text{CH}_3$. Compounds **III**—**IV** and **VII** showed heterocyclic ring protons quartets corresponding to the CH_2 groups at 5.20—5.45 ppm and 6.60—7.20 ppm, respectively. Particular attention should be drawn to compound **IIIa**, where two CH_3 groups are attached to C (2).

Here, two singlets were recorded, at 8.51 and 8.85 ppm. They should be assigned to their axial and equatorial positions.



The conformations of the carbethoxy and the nitro groups could not be definitely established.

Compounds **IIIb**, **IV**—**VI** show aromatic proton signals 2.49—2.67 ppm of the aromatic substituents in position 2.

Experimental

Ethyl nitroacetate was prepd. according to Rodinov *et al.* [2] starting from ethyl acetacetic ester through the nitrosation and oxidn. The fraction collected had b.p. 58°/0.5 mm Hg.

2-Nitro-2-carbethoxypropanediol-1,3 (I). 40% aq. formaldehyde (10 ml, 0.1 mol), and sodium acetate (1 g) dissolved in water (5 ml) were cooled to 0°. Ethyl nitroacetate (6 g, 0.045 mol) was introduced dropwise under vigorous stirring keeping the temp. below 5°. Stirring was continued for 2 h at 10° and all was left for 40 h at room temp. and poured on ice (40 g) with concd. hydrochloric acid (0.7 ml). The heavy oil was extd. with ether, the ext. dried over magnesium sulphate, ether evapd. The residual oil crystd. overnight in long needles of **I**. They were washed with benzene. The yield was 2.9 g 33%, m.p. 71—72°.

$\text{C}_6\text{H}_{11}\text{O}_6\text{N}$ requires: 37.3% C, 5.7% H, 7.25% N;

found: 37.4% C, 5.9% H, 7.4% N.

2,2-Dimethyl-5-nitro-5-carbethoxy-1,3-dioxane (IIIa). **I** (2 g, 0.01 mol) was dissolved in acetone (50 ml). Anhydrous magnesium sulphate (15 g) and a small amount of *p*-toluene sulphonic acid were added. All was refluxed for 30 h. Magnesium sulphate was filtered off, acetone evapd., the residue was treated with an aq. (5%) soln. of sodium carbonate. The product was extd. with ether, dried over magnesium sulphate, ether evapd. The oily residue was dissolved in anh. ethanol, boiled with charcoal, filtered, ethanol was evapd. The yield was 1.8 g (42%) of **IIIa**. After crystn. from ethanol m.p. was 73—75.5°.

$\text{C}_9\text{H}_{15}\text{O}_6\text{N}$ requires: 46.3% C, 6.4% H, 6.1% N;

found: 46.45% C, 6.6% H, 6.2% N.

2-Phenyl-5-nitro-5-carbethoxy-1,3-dioxane (IIIb). **I** (0.96 g, 0.005 mol) and benzaldehyde (0.63 g, 0.006 mol) and a small amount of *p*-toluenesulphonic acid were dissolved in benzene (100 ml) and refluxed for 2 h under a condenser with an azeotropic head. After cooling the soln. was shaken

with aq. sodium carbonate and dried over magnesium sulphate. After the evapn. of benzene the oily residue was dissolved in anh. ethanol, the solvent evapd. and the cryst. product (**IIIb**) collected. After another crystn. from ethanol m.p. was 72°, the yield 0.84 g 60%.

$C_{11}H_{14}O_6N$ requires: 55.7% C, 5.35% H, 5.0% N;

found: 55.7% C, 5.5% H, 5.1% N.

2-Phenyl-(IVa) and 2-p-Chlorophenyl-2-bora-5-nitro-5-carbethoxy-1,3-dioxacyclohexane (IVb). A soln. of **I** (0.96 g, 0.005 mol), phenyl- and *p*-chlorophenyl boronic acid (0.61 g and 0.78 g, respectively, 0.005 mol) in acetone (20 ml) was refluxed for 2 h. The solvent was evapd. and the residue was crystd. from benzene. The yield of **IVa** and **IVb** was 1.25 g (90.5%) and 1.05 g (67%), resp. M.ps. were 134–136° and 99–100°, resp.

IVa: $C_{12}H_{14}O_6NB$ requires: 51.6% C, 5.0% H, 5.0% N;

found: 51.8% C, 5.2% H, 5.1% N.

IVb: $C_{12}H_{13}O_6ClNB$ requires: 45.9% C, 4.1% H, 4.5% N;

found: 46.05% C, 4.3% H, 4.6% N.

2-Phenyl-5-nitro-5-(N-methylcarbamido)-1,3-dioxane (V). Ethanolic 33% methylamine (0.5 ml, 0.005 mol) was added to 2-phenyl-5-nitro-5-carbethoxy-1,3-dioxane (0.56 g, 0.002 mol) in anh. ethanol (5 ml). The soln. was left in room temp. for 3 weeks and the solvent was evapd. White cryst. *N*-methylamide (**V**) was pptd. with the yield of 0.41 g 31%. After crystn. from ethanol m.p. was 123–125°.

2-Phenyl-5-nitro-1,3-dioxane (VI). **IIIb** (0.84 g, 0.003 mol), hydrazine hydrate (0.3 g, 0.006 mol) and ethanol were refluxed for 8 h. The soln. was concd. and the ppt. filtered off. The yield of **VI** was 0.30 g (46%). After crystn. from ethanol m.p. was 124–125° [3].

1,3-Di(ter-butyl)-5-nitro-5-carbethoxyhexa-hydropyrimidine (VII). **I** (0.96 g, 0.005 mol) in ethanol (5 ml) was refluxed for 2 h with aq. (40%) formaldehyde (0.4 ml, 0.005 mol) and *ter*-butylamine (0.73 g, 0.01 mol). The soln. became coloured orange-yellow. It was kept for 40 h in a refrigerator. The product **VII** was pptd. and crystd. from ethanol. The yield was 0.58 g 25%, m.p. 84–87°.

Infrared spectroscopy. The infrared spectra were taken in nujol mull on the Perkin–Elmer spectrophotometer 2376.

INSTITUTE OF ORGANIC CHEMISTRY AND TECHNOLOGY, TECHNICAL UNIVERSITY, WARSAW, KOSZYKOWA 75

(INSTYTUT CHEMII I TECHNOLOGII ORGANICZNEJ, POLITECHNIKA, WARSZAWA)

REFERENCES

- [1] Z. Eckstein, P. Gluziński, W. Hofman, T. Urbański, J. Chem. Soc., **1961**, 489.
- [2] V. M. Rodinov, V. M. Belikov, I. V. Makhinskaya, Zh. Obshch. Khimii, **18**, 917 (1948).
- [3] Z. Eckstein, Roczniki Chem., **27**, 246 (1953).

Г. Пиотровска, Т. Урбаньски, И. Волохович, Гетероциклические производные гтилнитро-ацетата

Содержание. Этилнитроацетат реагируя с формальдегидом дает 2-нитро-2-карбозтоксипропандиол-1,3. Это соединение послужило к проведению синтеза некоторых производных 5-нитро-5-карбозтоксид-1,3-диоксана, 5-нитро-5-карбозтоксид-2-бора-1,3-диоксана и 5-нитро-5-карбозтоксидгексагидропиримидина.