ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 6, pp. 872–874. © Pleiades Publishing, Ltd., 2012.
Original Russian Text © Yu.R. Galina, A.N. Lobov, R.M. Sultanova, V.A. Dokichev, Yu.V. Tomilov, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 6, pp. 874–876.

## SHORT COMMUNICATIONS

# Synthesis of 3-Diazopyrrolidin-2-ones

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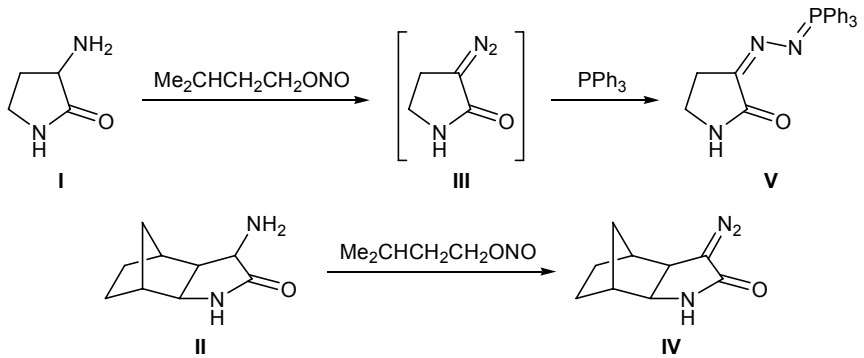
Received October 29, 2011

**DOI:** 10.1134/S1070428012060231

Aliphatic diazo compounds are reactive and unstable substances that are widely used in organic synthesis [1, 2]. At present much attention is given to preparation of four-, five-, six-, and seven-membered cyclic α-diazo amides, taking into account that nitrogen-containing heteroring is a pharmacophoric fragment responsible for a broad spectrum of physiological activity of many synthetic and natural compounds and that a diazo group provides the possibility for purposeful modification of the heterocyclic fragment [3–11]. For example, α-diazo lactams are intermediate products in the synthesis of practically important derivatives of α-oxo lactams (β-lactamase inhibitors) [4] and indolocarbazoles (protein kinase inhibitors) [8]. 3-Diazopyrrolidin-2-ones attract interest as structural fragments for the synthesis of γ-aminobutyric acid (the main neurotransmitter inhibitor in central nervous system of mammalians) analogs exhibiting nootropic and antiarrhythmic activity [12, 13].

In the present work we succeeded in developing a procedure for the synthesis of previously unknown 3-diazopyrrolidin-2-ones from 3-aminopyrrolidin-2-one (**I**) and 5-amino-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (**II**). Stable 3-diazodihydropyrroles or 3-diazopyrrolidinediones have been reported [6–8], but attempts to obtain 3-diazopyrrolidin-2-one or its alkyl-substituted derivatives were unsuccessful [14]. In particular, diazotization of 5-amino-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]-decan-4-one led to a mixture of isomeric 3-acetoxypyrrolidinones [14].

We have found that heating of a solution of 3-aminopyrrolidin-2-one (**I**) or 5-amino-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (**II**) with isopentyl nitrite in chloroform in the presence of ~15 mol % of glacial acetic acid gives 3-diazopyrrolidin-2-one (**III**) and 5-diazo-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (**IV**) in 36 and 65% yield, respectively. We failed to isolate diazo lactam **III** as individual substance; it decomposed in diethyl ether even at room temperature to produce a mixture of compounds which were difficult to identify. Therefore, the formation of **III** was proved by trapping it with triphenylphosphine. The latter reacted with 3-diazopyrrolidin-2-one (**III**) to give stable crystalline phosphazene **V**. In the synthesis of diazo lactam **III**, acetic acid was neutralized with solid $NaHCO_3$, for a saturated aqueous solution of $NaHCO_3$



induced vigorous decomposition of the diazo compound.

The structure of compounds **IV** and **V** was determined on the basis of their $^{1}H$, $^{13}C$, $^{15}N$, and $^{31}P$ NMR and IR spectra. The $^{15}N$ NMR spectrum of **IV** in $CDCl_3$ contained signals from the diazo fragment at $\delta_N$ –102.29 and 36.27 ppm and a signal at $\delta_N$ –256.94 ppm which was assigned to the amide nitrogen atom, taking into account the presence in the $^{1}H$–$^{15}N$ HSQC spectrum of a cross peak with the NH proton (δ 6.95 ppm).

To conclude, we have proposed a convenient procedure for the synthesis of 3-diazopyrrolidinones.

3-Aminopyrrolidin-2-one (**I**) and 5-amino-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (**II**) were synthesized according to the procedures described in [15, 16].

**3-[(Triphenyl-λ$^5$-phosphanylidene)hydrazinylidene]-pyrrolidin-2-one (V).** Compound **I**, 1.0 g (10 mmol), was dissolved in 35 ml of chloroform, 1.5 g (13 mmol) of isopentyl nitrite and 0.09 g (1.5 mmol) of glacial acetic acid were added in succession under stirring over a period of 10 min, and the mixture was heated for 15 min under reflux, cooled to 10°C, treated with solid $NaHCO_3$, and evaporated under reduced pressure. Cold (0°C) diethyl ether, 150 ml, was added to the residue, a solution of 2.6 g (10 mmol) of triphenylphosphine in 20 ml of diethyl ether was then added, and the mixture was left to stand for 20 h in the dark. The precipitate was filtered off and washed with diethyl ether. Yield 1.3 g (36%), light yellow crystals, mp 208–209°C (decomp.). IR spectrum, ν, cm$^{-1}$: 3176, 3074, 1691, 1591, 1456, 1437, 1379, 1307, 1115, 1059, 1000, 906, 816, 743, 719, 698, 602, 540, 527, 496. $^{1}H$ NMR spectrum ($CDCl_3$), δ, ppm: 3.06 t (2H, 4-H, $^{3}J$ = 7.1 Hz), 3.46 t (2H, 5-H, $^{3}J$ = 7.1 Hz), 7.43 t.d (6H, *m*-H, $^{3}J$ = 7.7, $^{4}J_{HP}$ = 2.9 Hz), 7.52 t.d (3H, *p*-H, $^{3}J$ = 7.7, $^{4}J$ = 1.5 Hz), 7.69 d.d.d (6H, *o*-H, $^{3}J$ = 7.7, $^{3}J_{HP}$ = 11.3, $^{4}J$ = 1.5 Hz), 8.26 br.s (1H, NH). $^{13}C$ NMR spectrum ($CDCl_3$), $\delta_C$, ppm: 24.19 ($C^4$), 38.63 ($C^5$), 128.62 ($C^m$, $^{3}J_{CP}$ = 11.4 Hz), 128.76 ($C^i$, $^{1}J_{CP}$ = 93.5 Hz), 132.09 ($C^p$, $^{4}J_{CP}$ = 2.1 Hz), 133.35 ($C^o$, $^{2}J_{CP}$ = 8.0 Hz), 149.05 (C=N, $^{3}J_{CP}$ = 42.5 Hz), 170.19 (C=O). $^{15}N$ NMR spectrum ($CDCl_3$), $\delta_N$, ppm: –257.19 (NH), –204.32 (N=P, $^{1}J_{NP}$ = 60.3 Hz), 5.64 (N=C, $^{2}J_{NP}$ = 17.1 Hz). $^{31}P$ NMR spectrum ($CDCl_3$): $\delta_P$ 19.36 ppm. Found, %: C 70.19; H 5.32; N 10.99. $C_{22}H_{20}N_3OP$. Calculated, %: C 70.77; H 5.40; N 11.25.

**5-Diazo-3-*exo*-azatricyclo[5.2.1.$0^{2,6}$]decan-4-one (IV).** Compound **II**, 6.6 g (40 mmol), was dissolved in 85 ml of chloroform, 6.0 g (51 mmol) of isopentyl nitrite and 0.36 g (6.0 mmol) of glacial acetic acid were added in succession under stirring over a period of 10 min. The mixture was heated for 15 min under reflux, cooled to 10°C, washed with 25 ml of a saturated solution of $NaHCO_3$, and evaporated under reduced pressure. Diethyl ether, 300 ml, was added to the residue, the precipitate was filtered off, the filtrate was evaporated under reduced pressure, and the residue was washed with hexane and dried under reduced pressure. Yield 4.6 g (65%), orange crystals, decomposition point 126°C. IR spectrum, ν, cm$^{-1}$: 3221, 3072, 2069 (C=$N_2$), 1678, 1647, 1417, 1394, 1377, 1313, 1290, 1269, 1248, 1080, 939, 867, 817, 738, 648. $^{1}H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.17 d.d.d.d (1H, *endo*-9-H, $^{2}J$ = 16.1, $^{3}J_{endo\text{-}9,endo\text{-}8}$ = 12.4, $^{3}J_{endo\text{-}9,exo\text{-}8}$ = 3.5, $^{4}J_{endo\text{-}9,syn\text{-}10}$ = 2.2 Hz), 1.23 d.d.d.d (1H, *endo*-8-H, $^{2}J$ = 15.9, $^{3}J_{endo\text{-}8,endo\text{-}9}$ = 12.4, $^{3}J_{endo\text{-}8,exo\text{-}9}$ = 3.2, $^{4}J_{endo\text{-}8,syn\text{-}10}$ = 2.2 Hz), 1.26 d.t.t (1H, *anti*-10-H, $^{2}J$ = 10.7, $^{3}J_{anti\text{-}10,1}$ = 4.7, $^{3}J_{anti\text{-}10,7}$ = 4.7, $^{4}J_{anti\text{-}10,2}$ = 1.8, $^{4}J_{anti\text{-}10,6}$ = 1.8 Hz), 1.60 d.d.d.d (1H, *exo*-8-H, $^{2}J$ = 15.9, $^{3}J_{exo\text{-}8,exo\text{-}9}$ = 10.4, $^{3}J_{exo\text{-}8,endo\text{-}9}$ = 3.5, $^{3}J_{exo\text{-}8,7}$ = 4.7 Hz), 1.57 d.d.d.d (1H, *exo*-9-H, $^{2}J$ = 16.1, $^{3}J_{exo\text{-}9,exo\text{-}8}$ = 10.4, $^{3}J_{exo\text{-}9,endo\text{-}8}$ = 3.2, $^{3}J_{exo\text{-}9,1}$ = 4.7 Hz), 1.78 d.t.t (1H, *syn*-10-H, $^{2}J$ = 10.7, $^{3}J_{syn\text{-}10,1}$ = 3.9, $^{3}J_{syn\text{-}10,7}$ = 3.9, $^{4}J_{syn\text{-}10,endo\text{-}8}$ = 2.2, $^{4}J_{syn\text{-}10,endo\text{-}9}$ = 2.2 Hz), 2.21 t.d (1H, 1-H, $^{3}J_{1,exo\text{-}9}$ = 4.7, $^{3}J_{1,anti\text{-}10}$ = 4.7, $^{3}J_{1,syn\text{-}10}$ = 3.9 Hz), 2.26 t.d (1H, 7-H, $^{3}J_{7,exo\text{-}8}$ = 4.7, $^{3}J_{7,anti\text{-}10}$ = 4.7, $^{3}J_{7,syn\text{-}10}$ = 3.9 Hz), 3.30 d.d (1H, 6-H, $^{3}J_{6,2}$ = 7.5, $^{4}J_{6,anti\text{-}10}$ = 1.8 Hz), 3.56 d.d.d (1H, 2-H, $^{3}J_{2,6}$ = 7.5, $^{3}J_{2,3}$ = 1.2, $^{4}J_{2,anti\text{-}10}$ = 1.8 Hz), 6.95 br.s (1H, NH). $^{13}C$ NMR spectrum ($CDCl_3$), $\delta_C$, ppm: 25.15 ($C^9$), 27.26 ($C^8$), 31.54 ($C^{10}$), 39.67 ($C^7$), 42.30 ($C^1$), 43.40 ($C^6$), 54.88 ($C^5$), 59.91 ($C^2$), 172.06 (CO). $^{15}N$ NMR spectrum ($CDCl_3$), $\delta_N$, ppm: –256.94 (NH), –102.29 (C=**N**=N), 36.27 (C=N=**N**). Mass spectrum, *m*/*z* ($I_{rel}$, %): 177.1 (100) $[M]^+$, 165.0 (9), 149.1 (40) $[M - N_2]^+$, 120.0 (50), 108 (100). Found: *m*/*z* 178.0975 $[M + H]^+$. $C_9H_{11}N_3O$. Calculated: 178.0975 $[M + H]^+$.

The $^{1}H$, $^{13}C$, $^{15}N$, and $^{31}P$ NMR spectra were recorded on a Bruker Avance III spectrometer at 500, 126, 51, and 202 MHz, respectively; the chemical shifts were determined relative to tetramethylsilane ($^{1}H$ and $^{13}C$, internal reference), $MeNO_2$ ($^{15}N$, external), and $H_3PO_4$ ($^{31}P$, external). The IR spectra were measured on a Shimadzu IR Prestige-21 instrument from samples dispersed in mineral oil. The mass spectra (electron impact, 70 eV) were obtained on a Thermo Finnigan MAT 95 XP high-resolution mass spectrometer (ion source temperature 250°C, direct inlet probe temperature 50–270°C, heating rate 10 deg/min). The

melting points were measured on a Boetius melting point apparatus. The elemental compositions were determined on a EURO EA-3000 C,H,N,S-analyzer.

This study was performed under financial support by the Chemistry and Materials Science Department, Russian Academy of Sciences (basic research program "Theoretical and Experimental Studies on the Nature of Chemical Bond and Mechanisms of the Most Important Chemical Reactions and Processes").

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