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SHORT
COMMUNICATIONS

Synthesis of 1,2,3-Thiadiazole Fused with Quinuclidine

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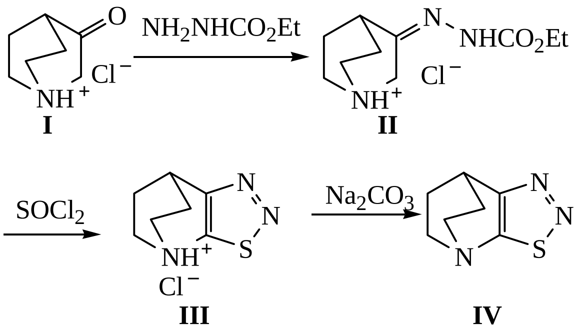
Both quinuclidine derivatives [1] and those of 1,2,3-thiadiazole [2] are endowed with a versatile biological activity. Only two [2,3-*b*]-fused derivatives of the main structural fragment of quinine, quinuclidine, are known, namely, fused derivatives of thiophene [3] and thiazole [4].

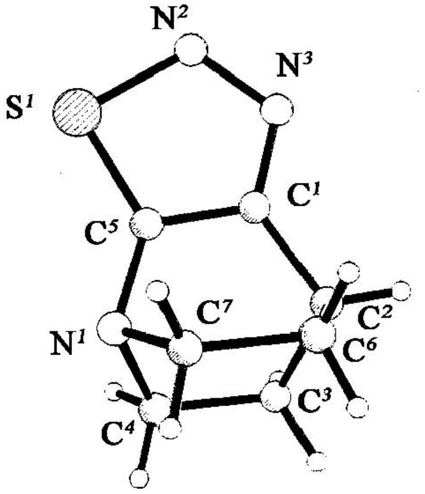
We for the first time carried out the synthesis of quinuclidine fused with 1,2,3-thiadiazole using the procedure of Hurd and Mori [5].

3-Quinuclidone hydrochloride (**I**) with ethoxycarbonylhydrazine gave 3-quinuclidone hydrochloride hydrazone **II**. Previously unknown thiadiazoloquinuclidine hydrochloride **III** was prepared by treating with thionyl chloride ethoxycarbonylhydrazone **II**. Free base **IV** was obtained by reacting hydrochloride **III** with sodium carbonate.



The structure of fused heterocycle **IV** is confirmed by ^1H, ^{13}C NMR, and mass spectra and is proved by X-ray crystallography: in all descriptions of the X-ray results the numeration of atoms is the same as in the figure.

The earlier X-ray diffraction studies were carried out on two fused 1,2,3-thiadiazole derivatives: a steroid one



Structure of the molecule of 6,7-dihydro-5*H*-4,7-ethane-1,2,3-thiadiazolo-[5,4-*b*]pyridine (**IV**) by X-ray data

[6] and 4,4,5,6-tetrachloro-4*H*-cyclopenta-1,2,3-thiadiazole [7]. The comparison of the bond distances and angles of the thiadiazole ring in molecule **IV** with the published data [6, 7] indicated that only the $N^2{=}N^3$ bond distance 1.303–1.307 Å coincided with the previous results within the experimental accuracy. The other bond lengths of the thiadiazole ring are significantly different: $S^1–C^5$ bond distance in compound **IV** was 1.688 against 1.723 Å in the steroid thiadiazole [6], $S^1–N^2$ bond distance in compound **IV** was 1.685 against 1.716 Å in 4,4,5,6-tetrachloro-4*H*-cyclopents-1,2,3-thiadiazole [7]. The bond distances and angles in the quinuclidine fragment given in the table coincide with the statistical average within the experimental accuracy [8].

3-Quinuclidone hydrochloride ethoxycarbonylhydrazone (II). A mixture of 16.2 g (0.1 mol) of 3-quinuclidone hydrochloride (**I**), 11.5 g (0.11 mol) of

Bond distances d (Å) and bond angles ω (deg) in the molecule of 6,7-dihydro-5*H*-4,7-ethane-1,2,3-thiadiazolo-[5,4-*b*]pyridine (**IV**)

Bond	d	Angle	ω
S^1–N^2	1.6850(19)	$N^2S^1C^5$	91.82(10)
S^1–C^5	1.688(2)	$C^5N^1C^4$	106.39(16)
N^1–C^5	1.421(2)	$C^5N^1C^7$	106.27(15)
N^1–C^4	1.492(3)	$C^4N^1C^7$	107.11(16)
N^1–C^7	1.493(2)	$N^3N^2S^1$	112.49(13)
N^2–N^3	1.304(3)	$N^2N^3C^1$	112.32(17)
N^3–C^1	1.353(3)	$N^3C^1C^5$	114.97(19)
C^1–C^5	1.361(3)	$N^3C^1C^2$	132.22(19)
C^1–C^2	1.483(3)	$C^5C^1C^2$	112.81(17)
C^2–C^6	1.537(3)	$C^1C^2C^6$	106.76(19)
C^2–C^3	1.539(3)	$C^1C^2C^3$	106.42(19)
C^3–C^4	1.540(3)	$C^6C^2C^3$	107.0(2)
C^6–C^7	1.538(3)	$C^2C^3C^4$	108.82(19)
		$N^1C^4C^3$	112.25(17)
		$C^1C^5N^1$	117.84(17)
		$C^1C^5S^1$	108.40(15)
		$N^1C^5S^1$	133.77(15)
		$C^2C^6C^7$	108.89(18)
		$N^1C^7C^6$	112.24(17)

ethoxycarbonylhydrazine, and 200 ml of ethanol was boiled for 3 h. Then 100 ml of ethanol was distilled off, and the reaction mixture was left standing for crystal-lization. The separated precipitate was filtered off, washed with ethanol and ether, and dried. The reaction product proved to be chromatographically pure and was used without further purification (eluents chloroform–methanol, 9:1; chloroform–methanol–ammonia 5:2:0.5). Yield 19.2 g (77%). Colorless fine needle crystals, mp 202–204°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.21 t (3H, CH_3),1.96 m (4H, 2CH_2 N), 2.72 m (1H, CH), 3.27 m (4H, 2CH_2 CH_2N), 4.03 s (2H, $NCH_2C{=}N$), 4.12 q (2H, OCH_2), 10.12 s (1H, NH), 11.66 br.s (1H, HCl). Found, %: C 48.29, 48.54; H 7.15, 7.29. $C_{10}H_{18}ClN_3O_2$. Calculated, %: C 48.48; H 7.32.

6,7-Dihydro-5*H*-4,7-ethane-1,2,3-thiadiazolo-[5,4-*b*]pyridine hydrochloride (III). In a flask equipped with a magnetic stirrer, reflux condenser, and a system for removing and absorption of gaseous HCl, to 12.4 g (0.05 mol) of hydrazone hydrochloride **II** was added 35 ml of freshly distilled thionyl chloride, and the mixture was stirred for 1 h at room temperature and 1.5 h at 35–40°C; to the end of the reaction a colorless precipitate separated. On cooling to 20–25°C the excess thionyl chloride was distilled off in a vacuum. To the residue 80 ml of tetrachloromethane was added, and the mixture was boiled for 10 min. The reaction mixture was cooled, the precipitate was filtered off and washed with tetrachloromethane and ether. Yield of the crude reaction product was 7.8 g. On recrystallization from 50 ml of water with 1 g of activated carbon we obtained 5.5 g (55%) of hydrochloride **III**. Colorless plate-like crystals, mp 175–177°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.63 m (2H, CH_2N), 2.14 m (2H, CH_2N), 2.82 m (2H, CH_2CH_2N), 3.61 m (2H, CH_2CH_2N), 4.15 m (1H, CH), 5.4 br.s (3H, HCl + H_2O). Mass spectrum, m/z (I_{rel}, %): 167 (22) $[M{-}HCl]^+$, 138 (100) $[M{-}HCl{-}2N{-}H]^+$, 124 (8), 111 (28), 97 (27), 80 (25), 67 (40), 58(48), 39 (65) $[C_3H_3]^+$. Found, %: C 41.37, 41.53; H 5.21, 5.18. $C_7H_{10}ClN_3S$. Calculated, %: C 41.28; H 4.95.

6,7-Dihydro-5*H*-4,7-ethane-1,2,3-thiadiazolo-[5,4-*b*]puridine (IV). In 50 ml of water 5.1 g (0.025 mol) thiadiazole hydrochloride **III** was dissolved, and thiadiazole **IV** was precipitated by adding saturated solution of sodium carbonate. The precipitate was filtered off, washed with water, and dried at 40–45°C. Yield 2.6 g (62%). Colorless fine plate-like crystals, mp 110–112°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.46 m (2H, CH_2N), 1.95 m (2H, CH_2N), 2.52 m (2H, CH_2CH_2N), 3.25 m (2H, CH_2CH_2N), 3.98 m (1H, CH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.64 ($\underline{C}H_2CH_2N$), 27.89 (CH), 50.00 (CH_2N), 162.55 (CN=), 166.16 (CS). Mass spectrum, m/z (I_{rel}, %): 167 (14) $[M]^+$, 138 (78) $[M{-}2N{-}H]^+$, 124 (14), 111 (27), 97 (28), 80 (27), 67 (51), 58(61), 39 (100) $[C_3H_3]^+$. Found, %: C 50.42, 50.21; H 5.73, 5.84. $C_7H_9N_3S$. Calculated, %: C 50.27; H 5.42. M 167.23.

Melting points were measured on a Boëtius heating block. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker AMX-400 (at 400 and 100 MHz respectively), as internal reference were used the signals of residual protons (^{1}H) and of carbon nuclei (^{13}C) of deuterated solvents. Mass spectra were measured on a mass spectrometer Kratos MS-890 with a direct admission of the sample into the ion source, ionizing electrons energy 70 eV, ionizing chamber temperature 200°C. The reaction progress was monitored by TLC on Silufol UV-254 plates, development under UV irradiation or in iodine vapor. All solvents used in the study were purified and dried by standard procedures.

X-ray diffraction analysis of compound **IV** single crystal was carried out on an automatic diffractometer Enraf-Nonius CAD-4 (MoK_α-radiation, β-filter, 2Θ/Θscanning, $2.20 \leq \Theta \leq 25.18°$). Crystals monoclinic, $C_7H_9N_3S$, a 10.419(2), b 14.236(3), c 11.521(2) Å, β 115.91(3)°, V 1537.1 (5) $Å^3$, space group P2(1)/n , Z 8, d_{calc} 1.445 g/cm^3. The structure was solved by the direct method [2887 reflections with $I > 2\sigma(I)$] in the full-matrix approximation, anisotropic for N, C, and S atoms and isotropic for hydrogen atoms till R 0.0265, R_W 0.0638. Crystallographic coordinates of nonhydrogen and hydrogen atoms and their equivalent thermal factors are available from the authors.

REFERENCES

1. Hoffmann, H.M.R. and Frackenpohe, J.F., *Eur. J. Org. Chem.*, 2004, p. 4293.
2. Bakulev, V.A. and Mokrushin, V.S., *Khim. Geterotsikl. Soedin.*, 1986, p. 1011.
3. Kaminka, M.E., Vorob’eva, V.Ya., Nikitin, V.B., Mikhlina, E.E., Zhirnikova, M.L., and Yakhontov, L.N., *Khim.-Farm. Zh.*, 1987, vol. 21, p. 945.
4. Arya, V.P. and Shenoy, S.J., *Indian J. Chem. B*, 1976, vol. 14, p. 759.
5. Hurd, C.D. and Mori, R.I., *J. Am. Chem. Soc.*, 1955, vol. 77, p. 5359.
6. Britton, T.C., Lobl, T.J., and Chidester, C.G., *J. Org. Chem.*, 1984, vol. 49, p. 4773.
7. Christensen, T.B., Jorgensen, K.A., Larsen, F.K., Martiny, L., Moller, J., Senning, A., and Vichi, L., *J. Chem. Soc., Chem. Commun.*, 1993, p. 489.
8. Allen, F.H., Kennard, O., Watson, D.G., Brammer, L., Orpen, A.G., and Taylor, R., *J. Chem. Soc., Perkin Trans. 2*, 1987, p. 1.