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SHORT COMMUNICATIONS

Unusual Result of the Reaction of 5,7-Dinitroquinolin-8-ol with Hydrazine Hydrate

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Abstract—The reaction of 5,7-dinitroquinolin-8-ol with hydrazine hydrate afforded 5-aminopyrido[2,3-*d*]-pyridazin-8(7*H*)-one in 50% yield instead of expected product of reduction of the 7-nitro group, 7-amino-5-nitroquinolin-8-ol.

Keywords: nitroquinolines, pyridopyridazines, hydrazine hydrate, reduction, 5,7-dinitroquinolin-8-ol, 5-amino-pyrido[2,3-*d*]pyridazin-8(7*H*)-one, molecular spectroscopy

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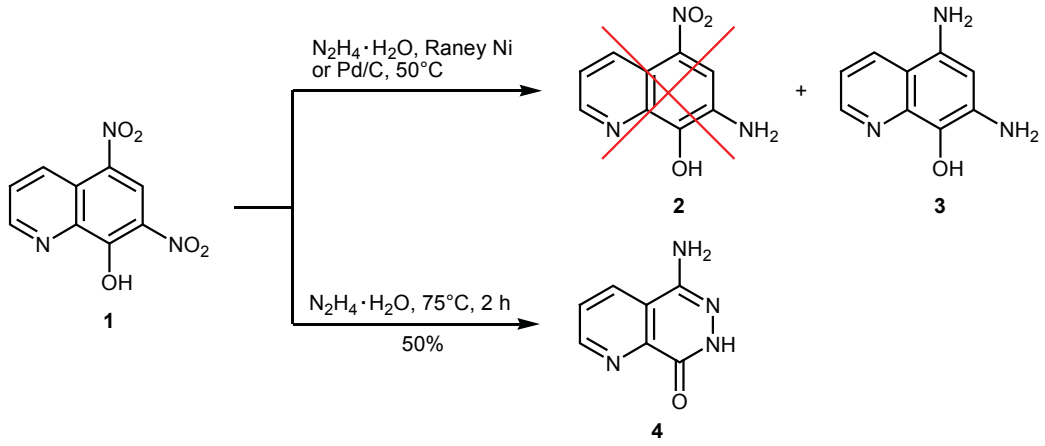
It is known that hydrazine reduces aromatic nitro compounds to the corresponding amines. These reactions are carried out in the presence of various catalysts [1–8]. There are published data on selective reduction of substituted dinitro arenes with hydrazine over Raney nickel in ethanol–dichloroethane [9] and in the presence of $FeCl_3$ in methanol [10, 11]. Ayyangar et al. [9] reported selective reduction of 2,4-dinitrophenol in the absence of a catalyst.

Nitroquinoline derivatives exhibit a broad spectrum of pharmacological activity [12–14]; therefore, synthesis of new compounds of the nitroquinoline series is practically important. The goal of the present work was aimed at studying the possibility of obtaining 7-amino-5-nitroquinolin-8-ol by selective reduction of 5,7-dinitroquinolin-8-ol with hydrazine hydrate.

We have found that catalytic reduction of 5,7-dinitroquinolin-8-ol (**1**) with hydrazine hydrate is not selective (Scheme 1). We succeeded in isolating only the product of reduction of both nitro groups, diamine **3**, as dihydrochloride. Compound **3** was identified by comparing its characteristics with those reported previously [15, 16]. We failed to obtain 7-amino-5-nitroquinolin-8-ol (**2**) despite variation of the reaction conditions.

Unexpected result was obtained when compound **1** was heated in a 60% solution of hydrazine hydrate. During the process, the reaction mixture changed in

Scheme 1.



a way typical of reduction of dinitroarenes; in particular, the mixture turned red, and the initial compound gradually dissolved. However, the NMR spectra of the isolated product were not consistent with structure **2** or **3**. The ^{1}H NMR spectrum lacked signal assignable to 6-H, whereas a downfield signal was observed at δ 11.73 ppm, which could be assigned to NH proton. In addition, a broadened singlet typical of aromatic amino group was present at δ 6.07 ppm. Protons of the pyridine ring resonated in the expected regions, at δ 7.87 (3-H), 8.48 (4-H), and 9.03 ppm (2-H). Furthermore, the ^{13}C NMR spectrum of the product displayed only seven signals instead of nine signals necessary for the quinoline structure. These findings led us to presume that compound **1** reacts with hydrazine hydrate to give a rearrangement product, 5-aminopyrido[2,3-*d*]pyridazin-8(7*H*)-one **4** (Scheme 1).

Compound **4** was studied in more detail by IR spectroscopy. As expected, no strong bands typical of symmetric and antisymmetric stretching vibrations of nitro group were observed. Amide I (νC=O) and amide II bands (δN–H) were located at 1685 and 1637 cm^{-1}, respectively, and two bands at 3205 and 3359 cm^{-1} were assigned to symmetric and antisymmetric vibrations of the primary amino group. Stretching vibrations of the exocyclic C^5–N bond appeared at 1367 cm^{-1}, and vibrations of the skeletal C–N bonds gave rise to absorption bands at 1494 and 1550 cm^{-1}. The proposed structure of **4** was also confirmed by the presence of the molecular ion peak at *m*/*z* 162 in the mass spectrum.

Interestingly, compound **4** was formed only in the reaction of **1** with 60% hydrazine hydrate. There was no reaction in more dilute solutions of hydrazine hydrate or in aqueous–alcoholic medium. Dinitroquinoline **1** remained unchanged on heating in ammonia, hydroxylamine, and alkali solutions.

We have found only one publication where the synthesis of pyridopyridazine **4** was described [17]. The data obtained by us for compound **4** were consistent with those reported in [17].

Thus, we were the first to synthesize 5-aminopyrido[2,3-*d*]pyridazin-8(7*H*)-one (**4**) by reaction of 5,7-dinitroquinolin-8-ol (**1**) with hydrazine hydrate.

Initial 5,7-dinitroquinolin-8-ol (**1**) was synthesized from commercially available quinolin-8-ol according to the procedure described in [18].

5-Aminopyrido[2,3-*d*]pyridazin-8(7*H*)-on (4). A mixture of 1 g (4 mmol) of compound **1** and 20 mL of 60% hydrazine hydrate was heated at 75–80°C for 2 h. After cooling, the off-white solid was filtered off, washed with water and ethanol, and dried in air. Yield 328 mg (50%), off-white powder, mp 320–322°C (from water); published data [17]: mp 320–330°C. IR spectrum, ν, cm^{-1}: 3205, 3359 br (NH_2), 1685 s (C=O), 1637 v.s (NH), 1494, 1550 m (C–N), 1367 w (C–NH_2). ^{1}H NMR spectrum (500 MHz), δ, ppm: 6.07 br.s (2H, NH_2), 7.87 d.d (1H, 3-H, J = 4.6, 8.2 Hz), 8.48 d.d (1H, 4-H, J = 1.53, 8.24 Hz), 9.03 d.d (1H, 2-H, J = 1.5, 4.6 Hz), 11.73 br.s (1H, CONH). ^{13}C NMR spectrum (126 MHz), δ_C, ppm: 121.61 (C^{4a}), 127.32 (C^3), 132.65 (C^4), 143.88 (C^{8a}), 145.93 (C^5), 153.34 (C^2), 157.41 (C^8). Mass spectrum, *m*/*z* (I_{rel}, %): 162 (100) $[M]^+$, 147 (1), 131 (4), 104 (21), 79 (29), 52 (17), 29 (14).

The IR spectrum was recorded in KBr on a Nicolet iS10 spectrometer. The NMR spectra were recorded on a Bruker Avance III spectrometer from solutions in DMSO-d_6 using hexamethyldisiloxane as internal standard. The mass spectrum (electrospray ionization) was obtained on a Bruker maXis instrument. The melting point was measured on a Boetius hot stage. The progress of the reaction was monitored by TLC on Sorbfil UV-254 plates using DMF–toluene (2:5 by volume) as eluent; detection under UV light.

CONFLICT OF INTEREST

The authors declare the absence of conflict of interest.

REFERENCES

1. Lü, S., Zheng, W., Ji, L., Luo, Q., Hao, X., Li, X., and Wang, F., *Eur. J. Med. Chem*., 2013, vol. 61, p. 84. https://doi.org/10.1016/j.ejmech.2012.07.036
2. Li, F., Frett, B., and Li, H., *Synlett*, 2014, vol. 25, p. 1403. https://doi.org/10.1055/s-0033-1339025
3. Rashidi, A., Afghan, A., Baradarani, M.M., and Joule, J.A., *J. Heterocycl. Chem*., 2009, vol. 46, p. 428. https://doi.org/10.1002/jhet.18
4. Lauwiner, M., Rys, P., and Wissmann, J., *Appl. Catal., A*, 1998, vol. 172, p. 141. https://doi.org/10.1016/s0926-860x(98)00110-0
5. Feng, H., Li, Y., Lin, S., Van der Eycken, E.V., and Song, G., *Sustainable Chem. Processes*, 2014, vol. 2, article no. 14. https://doi.org/10.1186/2043-7129-2-14
6. Mokhov, V.M., Popov, Y.V., and Nebykov, D.N., *Russ. J. Gen. Chem*., 2014, vol. 84, p. 1515. https://doi.org/10.1134/S107036321408012X
7. Ignatovich, Z.V., Ermolinskaya, A.L., Koroleva, E.V., and Eremin, A.N., *Rus. J. Org. Chem*., 2018, vol. 54, p. 943. https://doi.org/10.1134/S1070428018060192
8. Kadam, H.K. and Tilve, S.G., *RSC Adv*., 2015, vol. 5, p. 83391. https://doi.org/10.1039/c5ra10076c

9. Ayyangar, N.R., Kalkote, U.R., Lugade, A.G., Nikrad, P.V., and Sharma, V.K., *Bull. Chem. Soc. Jpn*., 1983, vol. 56, p. 3159. https://doi.org/10.1246/bcsj.56.3159
10. Samet, A.V., Zakharov, E.P., Semenov, V.V., Buchanan, A.C. III, and Gakh, A.A., *Synth. Commun*., 2001, vol. 31, p. 1441. https://doi.org/10.1081/scc-100104054
11. Shevelev, S.A., Shakhnes, A.K., Ugrak, B.I., and Vorob'ev, S.S., *Synth. Commun*., 2001, vol. 31, p. 2557. https://doi.org/10.1081/SCC-100105379
12. Mohan, S., Thiagarajan, K., Sundaramoorthy, B., Gurung, V., Barpande, M., Agarwal, S., and Chandrasekaran, R., *BMC Complementary Altern. Med*., 2016, vol. 16, article no. 229. https://doi.org/10.1186/s12906-016-1186-x
13. Chen, L.S., Ma, Y., Chen, L.J., Zhao, C.H., Maubois, J.L., Jiang, T.M., Li, H.M., and He, S.H., *Int. J. Food Sci. Technol*., 2010, vol. 45, p. 555. https://doi.org/10.1111/j.1365-2621.2009.02165.x
14. Paloque, L., Verhaeghe, P., Casanova, M., Castera-Ducros, C., Dumètre, A., Mbatchi, L., Hutter, S., Kraiem-M'Rabet, M., Laget, M., Remusat, V., Rault, S., Rathelot, P., Azas, N., and Vanelle, P., *Eur. J. Med. Chem*., 2012, vol. 54, p. 75. https://doi.org/10.1016/j.ejmech.2012.04.029
15. Musiol, R., Jampilek, J., Kralova, K., Richardson, D.R., Kalinowski, D., Podeszwa, B., Finster, J., Niedbala, H., Palka, A., and Polanski, J., *Bioorg. Med. Chem*., 2007, vol. 15, p. 1280. https://doi.org/10.1016/j.bmc.2006.11.020
16. Albert, A. and Magrath, D., *Biochem. J*., 1947, vol. 41, p. 534. https://doi.org/10.1042/bj0410534
17. Kormendy, K., Kovacs, T., Szulagyi, J., Ruff, F., and Kovesdi, J., *Acta Chim. Acad. Sci. Hung*., 1981, vol. 108, p. 167.
18. Clavier, S., Rist, Ø., Hansen, S., Gerlach, L.O., Högberg, T., and Bergman, J., *Org. Biomol. Chem*., 2003, vol. 1, p. 4248. https://doi.org/10.1039/B307399H