ISSN 1070-4280, Russian Journal of Organic Chemistry, 2018, Vol. 54, No. 4, pp. 668–669. © Pleiades Publishing, Ltd., 2018.
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SHORT COMMUNICATIONS

Mechanochemical Activation of the Reaction of Tetraacetylglycoluril with Some Cyclic Primary Amines. Synthesis of Acetamides

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Received May 10, 2017

Abstract—A new mechanochemical method has been proposed for the synthesis of some acetamides containing a cyclic fragment by reaction of primary cyclic amines with tetraacetylglycoluril.

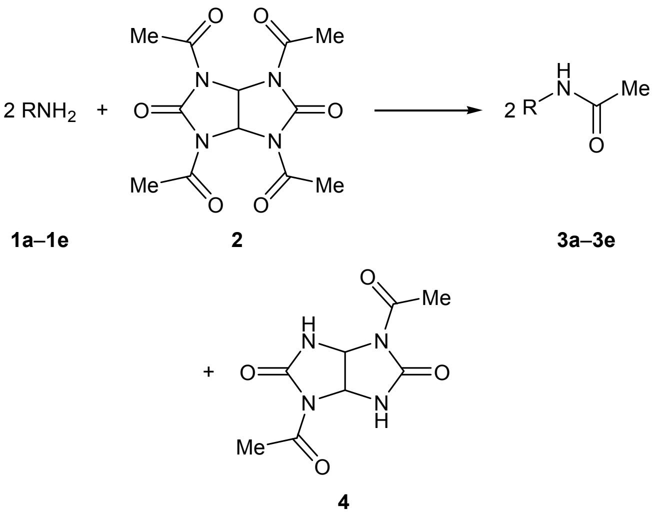
DOI: 10.1134/S1070428018040292

Derivatives of bicyclic bisureas are polyfunctional compounds that have found wide application in various fields of human activity (disinfecting agents, medicines, components of explosives, etc.) [1, 2]. Among these, a particular position is occupied by *N*-acetyl derivatives, some of which are efficient bleaching activators for detergents [3]. The main methods of synthesis of *N*-substituted bicyclic bis-ureas have been reviewed in [4, 5].

There are limited published data on the use of the parent *N*-acetylated bicyclic bisurea, tetraacetylglycoluril **2**, as acetylating agent in the synthesis of proteins [6] and acylamines [7], and these data are scanty and non-systematic. Mechanochemical synthesis provides a convenient method for the preparation of organic compounds [8, 9]. However, the behavior of *N*-acyl derivatives of bicyclic bisureas toward amines under mechanochemical activation has not been studied previously.

Taking into account the above stated, we were the first to accomplish mechanochemical reactions of some primary amines **1a**–**1e** with tetraacetylglycoluril **2**. Simple grinding of a mixture of amine **1a**–**1e** and bisurea **2** in a porcelain mortar for 5 min at room temperature afforded 74–90% of the corresponding acetamides **3a**–**3c** and **3e**; in the synthesis of compound **3d** from 4-aminoantipirine **1d**, the reaction mixture was heated for 1 h at 110°C, and the yield of **3d** was as low as 33%. According to [10], the reaction of **2** with aniline (**1a**) in chloroform at room temperature yields 73% of acetanilide (**3a**) in 90 h; this procedure is less efficient than the mechanochemical synthesis because of long reaction time. Acetamides **3a**–**3d** were also prepared independently by acylation of the corresponding amines with acetic anhydride; the products obtained by the two methods were identical, and their properties were in agreement with published data.

2-Amino-5-chlorobenzhydrol, 5-chloro-2-methylaminobenzhydrol, 5-aminosalicylic acid, anthranilic acid, and 5-aminoquinoline failed to undergo acetylation with glycoluril **2** under mechanochemical activa-



R = Ph (**a**), PhCH$_2$ (**b**), cyclohexyl (**c**), 1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl (**d**), 4-phenyl-4,5-dihydro-1,3-thiazol-2-yl (**e**).

Table 1. Conditions of synthesis, yields, melting points, and ^{1}H NMR data of compounds **3a**–**3e**

Initial amine	Reaction time, min	Temperature, °C	Product (yield, %)	mp, °C	^{1}H NMR spectrum, δ_{NH}, ppm
Aniline (**1a**)	5	25	**3a** (74)	116–117	7.94
Benzylamine (**1b**)	5	5	**3b** (81)	60–62	7.78
Cyclohexylamine (**1c**)	5	25	**3c** (79)	103–105	5.98
4-Aminoantipyrine (**1d**)	60	110	**3d** (33)	197–201	9.09
4-Phenyl-4,5-dihydro-1,3-thiazol-2-amine (**1e**)	20	150	**3e** (90)	206–208	12.24

tion. In these cases, compound **2** was converted to diacetylglycoluril **4**, as reported previously for the reaction of **2** with diamines [11]. The reaction of diacetylglycoluril **4** with aniline under mechanochemical activation gave only traces of acetanilide **(3a)**.

The reaction of **2** with benzylamine (**1b**) was accompanied by vigorous evolution of heat, so that it was necessary to cool the reaction mixture to 5°C (Table 1); obviously, this is related to the high basicity of amine **1b** compared to other amines. Poor solubility of diacetylglycoluril **4** provides an additional advantage to the mechanochemical procedure of synthesis of acetamides **3a**–**3d** which can be readily extracted with an appropriate solvent. Diacetylglycoluril **4** isolated from the reaction mixture can be used to regenerate tetraacetyl derivative **2** according to [12], and the latter can be reused.

Acetylanilide (3a). A mixture of 2 mL (22 mmol) of aniline (**1a**) and 1.55 g (5 mmol) of tetraacetylglycoluril **2** was ground in a porcelain mortar for 5 min at 25°C. The mixture was treated with 25 mL of ethanol, the undissolved material was filtered off, and the filtrate was evaporated to give 1 g (74%) of **3a**.

Acetamides **3b**–**3e** were synthesized in a similar way; the reaction temperatures, times, and yields are given in Table 1.

The ^{1}H NMR spectra were recorded on a Bruker Avance III HD spectrometer at 400 MHz using DMSO-d_6 as solvent and tetramethylsilane as internal standard. The progress of reactions was monitored by TLC on Silufol UV-254 plates (eluent ethanol–benzene, 1:4), following the disappearance of the initial amine; spots were visualized by treatment with Ehrlich's reagent.

REFERENCES

1. Bakibaev, A.A., Yagovkin, A.Yu., and Vostretsov, S.N., *Russ. Chem. Rev.*, 1998, vol. 67, p. 295.
2. Petersen, H., *Synthesis*, 1973, p. 243.
3. Zavel'skaya, V.D. and Zamchuk, Z.S., *Prikladnaya khimiya: Obzornaya informatsiya* (Applied Chemistry. Review Data), Moscow: NIITEKhIM, 1988, p. 1.
4. Bakibaev, A.A., Yagovkin, A.Yu., and Korol'kova, S.M., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2000, vol. 43, no. 3, p. 43.
5. Kravchenko, A.N. and Chikunov, I.E., *Russ. Chem. Rev.*, 2006, vol. 75, p. 191.
6. Kuhling, D., *Justus Liebigs Ann. Chem.*, 1973, p. 263.
7. Hase, Ch. and Kuhling, D., *Justus Liebigs Ann. Chem.*, 1975, p. 95.
8. Wang, G.W., *Chem. Soc. Rev.*, 2013, vol. 42, p. 7668.
9. James, S.L. and Friscic, T., *Chem. Soc. Rev.*, 2013, vol. 42, p. 7494.
10. Kuhling, D. and Hase, Ch., FRG Patent Appl. no. 2220690, 1973.
11. Vladimir, M.S.A. and Sindelar, V., *Tetrahedron*, 2011, vol. 67, p. 8937.
12. Bakibaev, A.A., Mamaeva, E.A., Yanovskii, V.A., Bystritskii, E.L., and Yagovkin, A.Yu., *Preparativnye metody sinteza azotsoderzhashchikh soedinenii na osnove mochevin* (Preparative Methods of Synthesis of Nitrogen-Containing Compounds on the Basis of Ureas), Tomsk: Agraf-Press, 2007, p. 124.