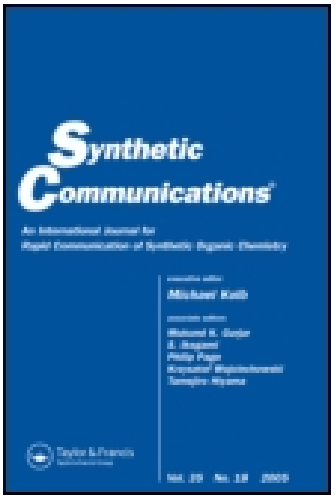


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Convenient Synthesis of Cerpegin

Aida Avetisyan [a] & Lousine Karapetyan [a]

[a] Department of Chemistry , Yerevan State University , Yerevan, Armenia

Published online: 05 Aug 2010.

To cite this article: Aida Avetisyan & Lousine Karapetyan (2010) Convenient Synthesis of Cerpegin, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:17, 2607-2609, DOI: 10.1080/00397910903296037

To link to this article: http://dx.doi.org/10.1080/00397910903296037

Synthetic Communications®, 40: 2607–2609, 2010

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903296037

Taylor & Francis
Taylor & Francis Group

CONVENIENT SYNTHESIS OF CERPEGIN

Aida Avetisyan and Lousine Karapetyan
Department of Chemistry, Yerevan State University, Yerevan, Armenia

A convenient procedure for the preparation of cerpegin is described.

Keywords: Cerpegin; dihydrofuranone; dimethylformamiddimethylacetal

The alkaloid from *Ceropegia juncea* Roxb., cerpegin, is a rare, naturally occurring pyridine. Cerpegin structure was elucidated as 1,1,5-trimethylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (**3**).[1] *Ceropegia juncea* is reported to be a tranquilizing, anti-inflammatory, analgesic, and antiulcer Indian plant.[2] Because of the application of cerpegin, its preparation has been the subject of detailed studies.[3–9]

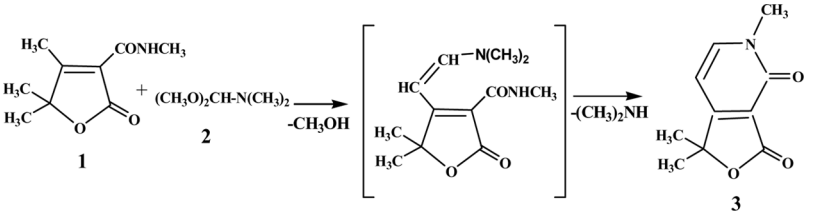
In an extension of our synthetic studies on chemically and biologically interesting cerpegin, we report here a convenient synthesis of cerpegin starting from 3-(N-methyl)carbamoyl-4,5,5-trimethyl-2,5-dihydrofuran-2-one (**1**).[10]

1,1,5-Trimethylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (cerpegin, **3**) was prepared by the reaction of 3-(N-methyl)carbamoyl-4,5,5-trimethyl-2,5-dihydrofuran-2-one (**1**) with N,N-dimethylformamiddimethylacetal (**2**). A mixture of **1** (1 equiv.) and **2** (1.1 equiv.) in absolute benzene was boiled for 35 h, producing **3** with 89% yield. The formation of cerpegin (**3**) occurs via the methyl group of compound **1** condensation with N,N-dimethylformamiddimethylacetal (**2**) followed by cyclization of the intermediate enamine with dimethylamine evolution.

Received June 12, 2009.

The chemical science community of Armenia has carried heavy loss with the passing of Prof. Aida Avetisyan on October 19, 2009. Professor Avetisyan was an extraordinary person, and all her life was devoted to the service of chemical science and its teaching in the walls of the Yerevan State University. She forever has connected scientific activity with the chemistry of heterocyclic compounds containing oxygen, nitrogen, and sulfur atoms. Professor Avetisyan has brought a significant contribution to education and professional training of many students and young specialists. Professor Avetisyan's students, colleagues, and friends will remember for a long time her image—an image of the multitalented scientist and teacher.

Address correspondence to Lousine Karapetyan, Department of Chemistry, Yerevan State University, 1 A. Manoukyan Str., 0025 Yerevan, Armenia. E-mail: lousine_karapetyan@yahoo.com



EXPERIMENTAL

The melting point was determined by the open capillary method. Infrared (IR) spectra were recorded on a Specord 751 R spectrometer in mineral oil; NMR spectra were recorded on a Varian Mercury 300 instrument (at 300 MHz for ^{1}H CMR and 75, 46 MHz for ^{13}C NMR) using tetramethylsilane (TMS) as internal standard. Mass spectra were obtained on a Nermag Riber R10–10H with 70-eV electron impact ionization. The purity of the synthesized compound was controlled by means of thin-layer chromatography (TLC) on Silufol UV-254 plates; the eluent acetone/benzene ratio was 1:2, developed by iodine vapors.

1,1,5-Trimethylfuro[3,4-c]pyridine-3,4(1H,5H)-dione (Cerpegin, 3)

A mixture of 1 g (0.01 mol) of 3-(N-methyl)carbamoyl-4,5,5-trimethyl-2,5-dihydrofuran-2-one (**1**) and 1.5 mL (0.011 mol) N,N-dimethylformamiddimethylacetal (**2**) in absolute benzene was boiled for 35 h until dimethylamine evolution had ceased. The evolved dimethylamine was absorbed with hydrochloric acid (35%). After removal of the solvent, water was poured on the crystalline residue, and the formed precipitate was filtered off and washed with water. The product was obtained as pale yellow needles (CH_2Cl_2-EtOH) in 89% yield, mp: 268–270 °C (mp 268–270 °C[1]). IR, γ_{max}, cm^{-1}: 1760 (C=O), 1670 (C=O), 1630 (C=C), 1620 (C=C). ^{1}H NMR (DMSO-d_6/CCl_4: 1/3) δ_H: 1.48 s (6H, $2CH_3$), 3.4 s (3H, NCH_3), 4.9 d (1H, $^{3}J = 4.9$, CCH=CHN), 5.65 d (1H, $^{3}J = 4.9$, CCH=CHN). ^{13}C NMR (DMSO-d_6/CCl_4: 1/3) δ_C: 24.18 ($2CH_3$), 37.75 (N-CH_3), 82.51, 98.38, 112.17, 145.96, 157.90, 166.88, 170.86. MS (70 eV) m/z: 193 [M$^+$] (34.58), 178 [M-CH_3]$^+$ (100), 150 [M-CH_3CO]$^+$ (4.79), 136 (3.65),108 (12.87), 79 (5.79), 42 (49.67). Found (%): C, 62.36; H, 5.95; N, 7.49. $C_{10}H_{11}NO_3$(193.20) calculated (%): C, 62.17; H, 5.74; N, 7.25.

This easy and convenient synthesis provides an example of an efficient route to furo[3,4-c]pyridine-3,4(1H,5H)-dione and provides a potential route to the cerpegin analogs.

REFERENCES

1. Adibatti, N. A.; Thirugnanasambantham, P.; Kulothundan, C.; Viswanathan, S.; Kameswaran, L.; Balakrishna, K.; Sukumar, E. A pyridine alkaloid from *Ceropegia juncea*. *Photochemistry* **1991**, *30*, 2449–2450.
2. Sivakumar, K.; Eswaramurthy, S.; Sabramanian, K.; Natarajan, S. Structure of cerpegin, a new alkaloid. *Acta. Crystallogr.* **1990**, *C46*, 839–841.

3. Guillier, F.; Nivoliers, F.; Bourguignon, J.; Dupas, G.; Marsais, F.; Godard, A.; Quéguiner, G. Metalation of π-deficient heterocycles: A facile synthesis of cerpegin. *Tetrahedron Lett.* **1992**, *33*, 7355–7356.
4. Kelly, T. R.; Walsh, J. J. The synthesis of cerpegin. *J. Org. Chem.* **1992**, *57*, 6657–6658.
5. Maisuo, K.; Arase, T. Synthesis of a pyridone alkaloid, cerpegin. *Chem. Pharm. Bull.* **1995**, *43*, 2091–2094.
6. Hong, H.; Comins, D. L. A three-step synthesis of cerpegin. *J. Org. Chem.* **1996**, *61*, 391–392.
7. Villemin, D.; Liao, L. One-pot, three-step synthesis of cerpegin. *Tetrahedron Lett.* **1996**, *37*, 8733–8734.
8. Matsuo, K.; Kobayashi, M.; Sugimoto, K. Alternative synthesis of a pyridon alkaloid, cerpegin. *Heterocycles* **1997**, *45*(6), 1191–1195.
9. Lazaar, J.; Hoarau, C.; Mongin, F.; Trécourt, F.; Godard, A.; Quéguiner, G.; Marsais, F. One-pot, four-step synthesis of cerpegin. *Tetrahedron Lett.* **2005**, *46*, 3811–3813.
10. Avetissyan, A.; Karapetyan, L. The synthesis of new 2-iminoderivatives of 2,5-dihydrofurans and their chemical transformations. *Synth. Commun.* **2009**, *39*(1), 7–19.