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Short Note

Synthesis of 1-[(2-Oxonaphthalen-1(2*H*)-ylidene)methyl]urea

Jiehua Xu, Anjun Chen and Qingjian Liu*

College of Chemistry, Chemical Engineering and Materials Science
Engineering Research Center of Pesticide and Medicine Intermediate Clean Production
Ministry of Education, Shandong Normal University, Jinan 250014, P. R. China

* Author to whom correspondence should be addressed; E-mail: liuqj@sdnu.edu.cn

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Abstract: An unexpected product, 1-[(2-oxonaphthalen-1(2*H*)-ylidene)methyl]urea **4** of the condensation reaction of 2-hydroxy-1-naphthaldehyde with or without ethyl benzoylacetate and urea under hydrochloric acid-catalyzed and solvent-free conditions is reported.

Keywords: 1-[(2-Oxonaphthalen-1(2*H*)-ylidene)methyl]urea; Condensation reaction Solvent-free conditions

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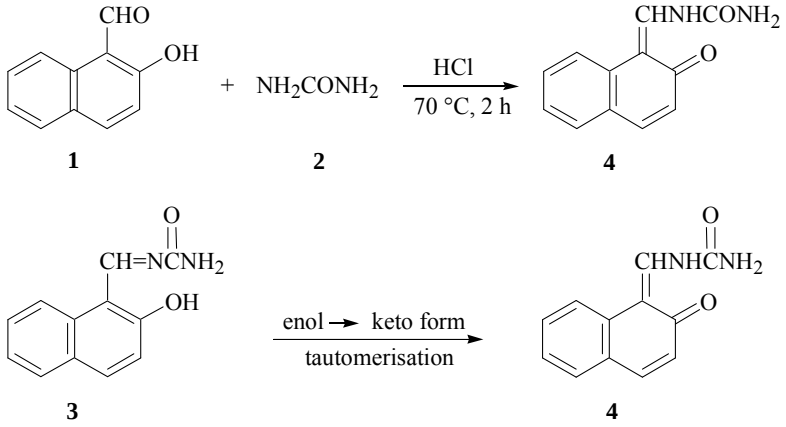
Dihydropyrimidinones (DHPMs) have attracted considerable interest due to the promising biological and pharmacological properties as calcium channel blockers, antihypertensive agents, and anticancer drugs associated with this heterocyclic scaffold.[1,2] Thus, the synthesis of such a heterocyclic nucleus is of considerable importance, and quite a number of synthetic modifications based on the Biginelli three-component condensation reaction of aldehyde, β-ketoester, and urea have been developed.[3]

In continuation of our green chemistry programme towards the synthesis of DHPM heterocyclic compounds, we found an unexpected product, namely 1-[(2-oxonaphthalen-1(2*H*)-ylidene)methyl]urea **4** of the Biginelli reaction of 2-hydroxy-1-naphthaldehyde with ethyl benzoylacetate and urea under hydrochloric acid-catalyzed and solvent-free conditions (Scheme 1).



Scheme 1

In comparative experiments, reactions of 2-hydroxy-1-naphthaldehyde **1** and urea **2** with or without ethyl benzoylacetate under hydrochloric-acid-catalyzed and solvent or solvent-free conditions afforded **4** as the only product. With ethyl or methyl acetoacetate, however, **4** turned out to be a minor product besides the major product of the Biginelli reaction.

It may be rationalized that **4** is the tautomer of **3** that resulted from dehydration condensation reaction of 2-hydroxy-1-naphthaldehyde and urea.

This novel reaction may find application in the synthesis of naphthalenylmethylureas which may be bioactively interesting substances.

Experimental procedure

Method A

A mixture of 2-hydroxy-1-naphthaldehyde **1** (0.86 g, 5 mmol), ethyl benzoylacetate (1.06 g, 5.5 mmol), urea **2** (0.33 g, 5.5 mmol), and hydrochloric acid (2 drops) was heated at 70˚C for 2 h. Upon cooling, ethyl acetate-petroleum (1:1, v/v) was added and a yellow precipitate was obtained, then filtered and recrystallized from ethanol to afford the title compound **4** as yellow crystals, 0.65 g, yield 60.7%, m.p. 179.3-180.8 ˚C.

Structural Characterization

^{1}H NMR (Bruker Avance 300 MHz, DMSO-d_6): δ_H 13.22 (d, J = 10.5 Hz, 1 H, N-H), 9.01 (d, J = 10.5 Hz, 1 H, N-H), 7.97 (d, J = 8.2 Hz, 2 H), 7.81 (d, J = 9.6 Hz, 1 H, Ar-H-4), 7.63 (d, J = 7.6 Hz, 1 H), 7.50-6.58 (m, 3 H), 6.60 (d, J = 9.6 Hz, 1 H, Ar-H-3) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 184.0, 154.3, 147.1, 141.9, 134.5, 129.9, 129.6, 126.9, 126.7, 124.9, 119.9, 108.3 ppm. IR (Bruker Tensor 27, KBr): ν_{max} 3426 (N-H), 1741 (C=O), 1620 (N-C=O), 1584 cm^{-1}. MS (Agilent 5973N MSD, EI, 70 eV): m/z (%) 214 (M^+, 44), 170 (100), 115 (50). Elemental Anal. (Perkin Elmer PE 2400 II HONS) calcd for $C_{12}H_{10}N_2O_2$: C 67.28, H 4.71, N 13.08; found: C 67.26, H 4.60, N 13.04.

Method B

A mixture of 2-hydroxy-1-naphthaldehyde **1** (0.86 g, 5 mmol), urea **2** (0.33 g, 5.5 mmol), and hydrochloric acid (2 drops) was heated at 100˚C for 1 h. Upon cooling, ethyl acetate-petroleum (1:1, v/v) was added and a yellow precipitate was obtained, then filtered and recrystallized from ethanol to give rise to **4** as yellow crystals, 0.49 g, yield 45.5%, m.p. 179.2-180.5 ˚C.

Moreover, other conditions such as solvent-free catalyzed with ammonium chloride and in ethanol catalyzed with hydrochloric acid have also been investigated and **4** was also obtained.

References

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