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Unexpected Reaction of Oximinoacetoacetate with Amines: A Novel Synthesis of Carbamates

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Unexpected Reaction of Oximinoacetoacetate with Amines: A Novel Synthesis of Carbamates

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Abstract: The synthesis of alkyl carbamates by a solvent-free reaction of oximinoacetoacetate and amine at 130°C is reported. A preliminary mechanism to this unexpected reaction is also given.

Keywords: Carbamate synthesis, keto-enol tautomerization, oxime

Carbamates are compounds of growing interest because of their unique applications in the field of pharmaceuticals[1,2] as drug intermediates, in the agrochemical industry[3–5] as herbicides, fungicides, and pesticides, and in the polymer industry in the synthesis of polyurethane and dendrimers.[6,7] Organic carbamates have also played an important role in the area of synthetic organic chemistry, primarily as versatile building blocks or as efficient protecting groups.[8,9]

Carbamate syntheses have been accomplished by several methods including carbonization of amines or imines by chloroformate[10,11] or organic acids in the presence of azides[12,13] and organic carbonate under solvent-free conditions,[14,15] and finally by metal-mediated reductive acylation of nitriles[16] or oxime carbonates.[17]

In an ongoing work studying the use of 2-oximinoacetoacetate **1** as a building block in the synthesis of pyrrole derivatives as precursors of porphyrin macromolecules,[18,19] we found that when equimolar amounts

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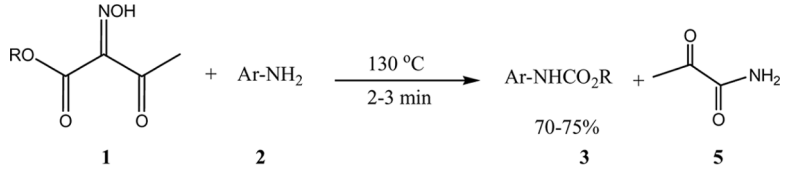
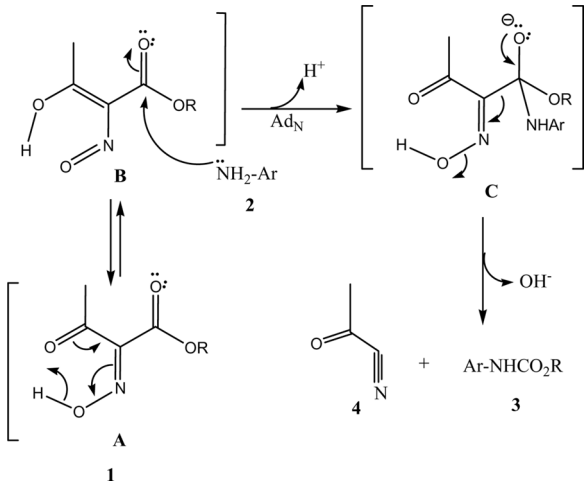


Scheme 1. a, R = Et, Ar = 2-C_5H_4N; b, R = Me, Ar = 2-C_5H_4N; c, R = Et, Ar = 2-(4-CH_3-C_5H_3N); d, R = Me, Ar = 2-(4-CH_3-C_5H_3N); e, R = Et, Ar = 4-C_6H_4-CH_3; f, R = Me, Ar = 4-C_6H_4-CH_3; g, R = Et, Ar = 2-C_6H_4-CH_3; h, R = Me, Ar = 2-C_6H_4-CH_3; i, R = Et, Ar = 2-C_6H_4-OCH_3; j, R = Me, Ar = 2-C_6H_4-OCH_3; k, R = Et, Ar = 4-C_6H_4-OCH_3; and l, R = Me, Ar = 4-C_6H_4-OCH_3.

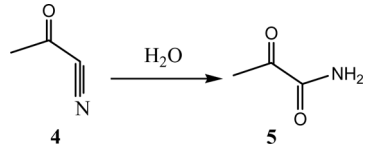
of oxime **1** and primary aromatic amine **2** were heated in a preheated oil bath at 130 °C for 2–3 min, alkyl carbamate **3** was obtained in moderate yield (70–75%) (Scheme 1).

The structure of the product was fully delineated by spectroscopic tools and in some cases by comparing the physical and spectroscopic data with those of an authentic sample of previously reported carbamates.

A preliminarily and plausible explanation can be given, which is depicted in Scheme 2. Oxime **1** as α-keto oxime undergoes keto-enol tautomerization via intramolecular 1,5-hydrogen migration[20] to form enol-tautomer **B**. Therefore, a nucleophilic addition (Ad_N) of amine **2** at the carbonyl of the ester affords intermediate **C**. The latter intermediate rearranges and undergoes a thermal degradation via reformation of carbonyl group and OH^- removal to afford the final carbamate product **3** and 2-oxopropionitrile **4**.



Scheme 2.



4 5

Scheme 3.

Compound **4** was not detected or isolated, but 2-oxopropionamide (pyruovamide) **5** was detected by gas chromatography–mass spectrometry (GC-MS) in the final reaction mixture. Compound **5** is the hydrolysis product of 2-oxopropionitrile **4** (Scheme 3).

Other mechanistic pathways, such as Beckmann-like rearrangement of oxime **1** followed by Ad_N of amine that then follows the same sequence as mentioned previously, cannot be ruled out. Therefore, further studies are currently under way.

In conclusion, a new method for carbamate synthesis was reported. The simple reaction conditions (solvent-free and catalyst-free), coupled with the availability of the starting material, give this method the advantage over other reported methods.

EXPERIMENTAL

General

Melting points are uncorrected. NMR spectra were recorded on Bruker WM 300 and DRX 500 spectrometers (300 MHz and 500 MHz for ^{1}H, 75 and 125 MHz Infrared, for ^{13}C) using tetramethylsilane (TMS) as internal standard and the deuterated solvent as lock. Infrared (IR) spectra were obtained using a Perkin-Elmer 983 spectrophotometer. Electron impact ionisation–mass spectrometry (EIMS) and electron spray ionization (ESI) were performed on a Varian AMD 604 instrument using 70-eV ionization energy. All the chromatographic separations were performed using Grade 3 neutral alumina 70 to 230-mesh silica gel. Oxime 1 was prepared following the literature procedure,[21] and all the data of the synthesized carbamates were checked either with the previously reported or commercially available samples.[22]

Typical Procedure for Carbamate 3

Equimolar amounts of oxime **1** and primary aromatic amine **2** (5 mmol each) were mixed properly in a round-bottomed flask equipped with a

reflux condenser. The reaction mixture was heated in a preheated oil bath at 130°C for 2–3 min. A very vigorous reaction was noticed (use caution). The flask was removed from the oil bath and cooled to room temperature. The product was obtained and purified either by crystallization or column chromatography.

Ethyl N-(2-Pyridyl)-carbamate 3a[10]

Off-white crystals from ethanol, mp 105–106°C; IR (KBr) (cm^{-1}): 3346 (NH), 1710 (CO); ^1H NMR ($CDCl_3$): δ (ppm) 1.36 (t, 3H, CH_3 ethyl), 4.28 (q, 2H, CH_2 ethyl), 6.95 (m, 1H), 7.69 (m, 1H), 8.05 (d, 1H), 8.45 (m, 1H), 9.73 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 14.6 (CH_3), 61.3 (CH_2), 112.5, 118.4, 138.5, 147.6, 152.5 (ring carbons), 153.7 (CO); ms: m/z (%): 166 (M^+) (62), 121 (17), 107 (22), 94 (100), 78 (35).

Carbamate 3c

Recrystallized from ethanol, mp 127–128°C; IR (KBr) (cm^{-1}): 3345 (NH), 1712 (CO); ^1H NMR ($CDCl_3$): δ (ppm) 1.26 (t, 3H, CH_3 ethyl), 2.64 (s, 3H, CH_3), 4.27 (q, 2H, CH_2 ethyl), 6.81 (s, 1H), 7.91 (d, 1H), 8.22 (d, 1H), 9.95 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ (ppm) 13.9 (CH_3), 18.4 (CH_3), 61.5, 110.1, 118.2, 140.3, 149.9, 152.4, 153.7; ms: m/z (%): 180 (M^+) (62), 135 (17), 108 (22), 92 (100), 81 (35). Calcd. for $C_9H_{12}N_2O_2$; C, 60.01; H, 6.66; N, 15.55. Found: C, 59.78; H, 6.74; N, 15.54%.

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