An efficient use of microwave-superoxide combination for the synthesis of organic carbamates and dithiocarbamates

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The present report demonstrates an efficient use of microwave-tetraethylammonium superoxide combination under non-aqueous conditions to bring about a mild and safe carbamation/thiocarbamation of amines, using carbon dioxide/carbon disulfide and methyl iodide.

Keywords: Carbamate, dithiocarbamate, superoxide, microwave

Organic carbamates and dithiocarbamates have attracted a great deal of importance due to their interesting chemistry and wide utility. Although a number of methodologies have been developed, the standard preparation of carbamates/dithiocarbamates generally involves the use of toxic and highly reactive phosgene/thiophosgene and its derivatives, thereby posing environmental and safety problems. As a result, considerable effort has been made to develop a phosgene/thiophosgene free route for the preparation of carbamates and thiocarbamates. However, many of these methods suffer from limitations, such as long reaction times, use of expensive and strongly basic reagents, use of volatile solvents, tedious work-up, and low yields.

Prompted by the current use of microwave (MW) irradiation in organic synthesis and due to the interest on superoxide organic chemistry, it was thought worthwhile to explore the role of MW-superoxide combination to achieve an efficient synthesis of carbamates and dithiocarbamates via a three-component coupling of an amine, CO₂/CS₂ and methyl iodide (Schemes I and II).

In order to optimize the yield of products, the effects of various parameters such as molar proportion of the reactants, Watt (160, 320, 480 & 800) and irradiation time were studied in detail using the substrate 1a as reference. Under the optimized MW irradiation [160W], various amines 1a-f underwent smooth coupling with CO₂ in the presence of tetraethylammonium superoxide (Et₄NO₂) in 5 to 7 minutes to afford the incipient carbamate anion. The amines 1a, 1b, 1f and 1g-m, however, underwent reaction with CS₂/Et₄NO₂ under MW at 320W in 3 to 7 minutes to give the dithiocarbamate anion, in dry DMF. Addition of methyl iodide and subsequent quenching with cold brine solution at room temperature readily furnished the methyl ester of carbamate 2 or dithiocarbamate 3 in fairly good yields (Tables I and II). It is important to mention that superoxide alone in the absence of MW was able to achieve the same transformation in considerably longer reaction time (2.5 hr) with 1a. To observe the sole role of MW on the above reactions, some blank experiments under microwave irradiation in the absence of Et₄NO₂ were also carried out resulting in no net reaction. However when MW is coupled with superoxide ion, the rate of reaction is dramatically enhanced, thereby highlighting the significance of MW-superoxide combination. All the products were identified by their physical data, IR and NMR spectra, which were in conformity with their structures.

Experimental Section
IR spectra were recorded on a Jasco FT/IR-5300 spectrophotometer. ¹H NMR was run on a Jeol AL300 FT-NMR spectrometer. The chemical shifts are given in ppm with respect to TMS as internal standard. The TLC spots were detected using iodine chamber. All commercially available chemicals were purchased from Aldrich and Merck. Dry DMF from Aldrich was stored over molecular sieves (4Å) prior to use. Crude products were purified by column chromatography.
General procedure for the preparation of 2a-f/3a-j

To a stirred mixture of potassium superoxide (0.568 g, 8 mmole) and tetraethylammonium bromide (0.840 g, 4 mmole) (weighted under nitrogen atmosphere using an atmosbag) in dry dimethylformamide (15 mL) was bubbled carbon dioxide gas continuously for 15 min, whereas CS$_2$ (0.609 g, 8 mmole) was admitted directly while stirring the mixture for 10 min. The amine (4 mmole) was finally introduced and the contents of the vessel were subjected to microwave irradiation at 160 W and 320 W for CO$_2$ and CS$_2$ containing mixtures respectively in a LG microwave oven for 3-7 min. Methyl iodide was subsequently added and the mixture was shaken thoroughly. The reaction-mixture was poured into a beaker containing brine solution (15 mL) and cold water (15 mL) and then extracted with diethyl ether (3 × 20 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$, filtered and evaporated to give the product 2/3, which was purified by column chromatography.

Phenyl-carbamic acid methyl ester, 2a: $^1$H NMR: δ 3.8 (s, 3H, OCH$_3$), 9.1 (br s, NH), 7.2-7.7 (m, 5H, Ar-H).

(4-Methoxyphenyl)-carbamic acid methyl ester, 2b: $^1$H NMR: δ 3.7 (s, 3H, OCH$_3$), 4.1 (s, 3H, ArOCH$_3$), 9.0 (br s, NH), 6.8 (d, 2H, Ar-H), 7.3 (d, 2H, Ar-H).

(4-Fluorophenyl)-carbamic acid methyl ester, 2c: $^1$H NMR: δ 3.8 (s, 3H, OCH$_3$), 9.2 (br s, NH), 7.2 (d, 2H, Ar-H), 7.8 (d, 2H, Ar-H).

(4-Chlorophenyl)-carbamic acid methyl ester, 2d: $^1$H NMR: δ 3.7 (s, 3H, OCH$_3$), 9.2 (br s, NH), 7.0 (d, 2H, Ar-H), 7.6 (d, 2H, Ar-H).

(4-Bromophenyl)-carbamic acid methyl ester, 2e: $^1$H NMR: δ 3.6 (s, 3H, OCH$_3$), 9.1 (br s, NH), 6.8 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H).

(4-Nitrophenyl)-carbamic acid methyl ester, 2f: $^1$H NMR: δ 3.9 (s, 3H, OCH$_3$), 9.7 (br s, NH), 7.8 (d, 2H, Ar-H), 8.3 (d, 2H, Ar-H).

Phenyl dithiocarbamic acid methyl ester, 3a: IR (Neat): 648, 1086, 1513, 3390 cm$^{-1}$; $^1$H NMR: δ 3.5 (s, 3H, SCH$_3$), 4.0 (br s, NH), 7.2-7.5 (m, 5H, Ar-H).

Table I — Microwave-Et$_4$NO$_2$ assisted synthesis of carbamates via a three-component coupling of an amine, CO$_2$ and methyl iodide

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4-Methoxyphenyl dithiocarbamic acid methyl ester, 3b: IR (Neat): 658, 1095, 1258, 1498, 3404 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 3.2 (s, 3H, SCH\(_3\)), 4.2 (br s, NH), 6.8 (d, 2H, Ar-H), 7.3 (d, 2H, Ar-H), 3.8 (s, 3H, OCH\(_3\)).

4-Nitrophenyl dithiocarbamic acid methyl ester, 3c: IR (Neat): 659, 1088, 1512, 2927, 3408 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 3.4 (s, 3H, SCH\(_3\)), 4.3 (br s, NH), 7.6 (d, 2H, Ar-H), 8.1 (d, 2H, Ar-H).

4-Methylphenyl dithiocarbamic acid methyl ester, 3d: IR (Neat): 643, 1096, 1502, 1636, 3386 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 3.2 (s, 3H, SCH\(_3\)), 4.2 (br s, NH), 6.9 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 2.3 (s, 3H, CH\(_3\)).
Benzyl dithiocarbamic acid methyl ester, 3e: IR (Neat): 652, 1085, 1474, 3396 cm\(^{-1}\); \(^1\)H NMR: 3.3 (s, 3H, SCH\(_2\)), 2.6 (br, NH), 3.9 (d, CH\(_2\)-Ar), 7.1-7.2 (m, 5H, Ar-H).

Diphenyl dithiocarbamic acid methyl ester, 3f: IR (Neat): 657, 1143, 1516, 1521 cm\(^{-1}\); \(^1\)H NMR: 3.4 (s, 3H, SCH\(_2\)), 7.0-7.5 (m, 10H, Ar-H).

2-(4-Methoxyphenyl)ethyl dithiocarbamic acid methyl ester, 3g: IR (KBr): 662, 1208 cm\(^{-1}\); \(^1\)H NMR: 3.2 (s, 3H, SCH\(_2\)), 1.7-2.1 (m, 6H, 3CH\(_2\)), 3.7 (br, 2H, CH\(_2\)), 4.2 (br, 4H, CH\(_2\)) N), 6.7-7.1 (m, 4H, Ar-H).

Piperidine-1-carbodithioic acid methyl ester, 3h: IR (Neat): 649, 1086, 1217 cm\(^{-1}\); \(^1\)H NMR: 3.4 (s, 3H, SCH\(_2\)), 1.8-2.5 (m, 4H, CH\(_2\)N), 3.6 (t, CH\(_2\)N), 6.7-7.1 (m, 4H, Ar-H).

Pyrrolidine-1-carbodithioic acid methyl ester, 3i: IR (KBr): 662, 1208 cm\(^{-1}\); \(^1\)H NMR: 3.2 (s, 3H, SCH\(_2\)), 1.7-2.1 (m, 6H, SCH\(_2\)), 4.2 (br, 4H, SCH\(_2\)).

**Conclusion**

In conclusion, the combined role of microwave-superoxide has been exploited to achieve a mild and safe approach for the synthesis of organic carbamates/dithiocarbamates under non-aqueous medium employing amines, CO\(_2\)/CS\(_2\) and methyl iodide.

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**References**


