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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[1-7]. 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[8] and its derivatives[9], thereby posing environmental and safety problems. As a result, considerable effort has been made to develop a phosgene/thiophosgene free route[10] 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[11].

Prompted by the current use of microwave (MW) irradiation in organic synthesis[12] and due to the interest on superoxide organic chemistry[13], 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, CO_2/CS_2 and methyl iodide (**Schemes I** and **II**).

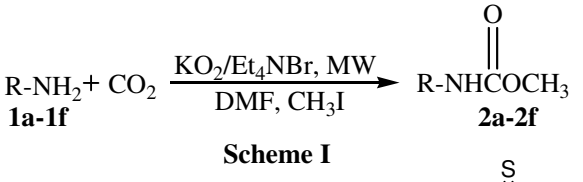
In order to optimize the yield of products, the effects of various parameters such as molar proportion of the reactants, Watt (160, 320, 480, 640 & 800) and irradiation time were studied in detail using the substrate **1a** as reference. Under the optimized MW irradiation [160W], various amines **1a-f** underwent smooth coupling with CO_2 in the presence of tetraethylammonium superoxide (Et_4NO_2) in 5 to 7 minutes to afford the incipient carbamate anion. The amines **1a, 1b, 1f** and **1g-m**, however, underwent reaction with CS_2/Et_4NO_2 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 Et_4NO_2 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

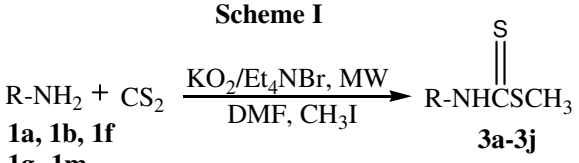
IR spectra were recorded on a Jasco FT/IR-5300 spectrophotometer. ^{1}H NMR was run on a Jeol AL300 FT-NMR spectrometer. The chemical shifts are given in ppm with respect to TMS as internal standard. The TLC spots were detected using iodine chamber. All commercially available chemicals were purchased 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 **1** (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_2SO_4, filtered and evaporated to give the product **2/3**, which was purified by column chromatography.



Scheme I



Scheme II

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_4NO_2 assisted synthesis of carbamates *via* a three-component coupling of an amine, CO_2 and methyl iodide

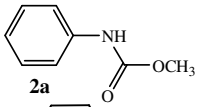
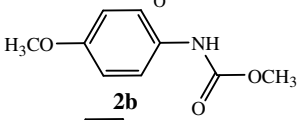
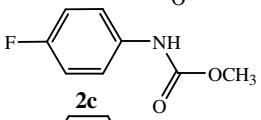
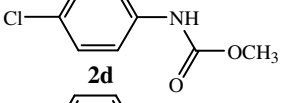
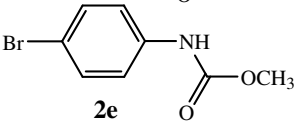
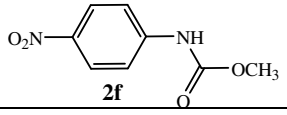
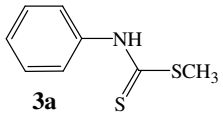
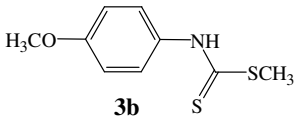
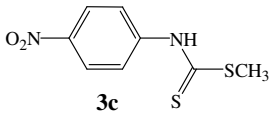
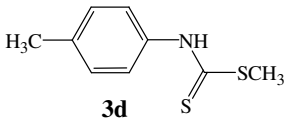
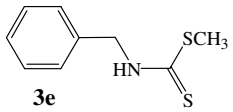
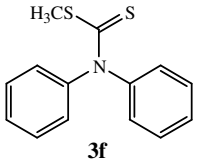
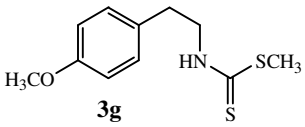
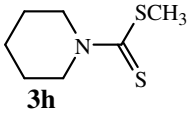
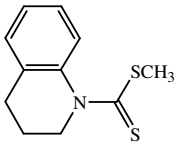
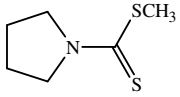
Entry	Substrate	Product	Time(min)	Conversion (%)
1	Aniline **1a**	 **2a**	5	95.5
2	*p*-Anisidine **1b**	 **2b**	6.5	90.2
3	*p*-Fluoroaniline **1c**	 **2c**	6	93.7
4	*p*-Chloroaniline **1d**	 **2d**	6.5	91
5	*p*-Bromoaniline **1e**	 **2e**	7	91.9
6	*p*-Nitroaniline **1f**	 **2f**	5	77.5

Table II — Microwave-Et_4NO_2 assisted synthesis of dithiocarbamates *via* a three-component coupling of an amine, CS_2 and methyl iodide

Entry	Substrate	Product	Time(min)	Conversion (%)
1	Aniline **1a**	 **3a**	4	85
2	*p*-Anisidine **1b**	 **3b**	7	78
3	*p*-Nitroaniline **1f**	 **3c**	5	65
4	*p*-Toluidine **1g**	 **3d**	6	72
5	Benzylamine **1h**	 **3e**	5	67
6	Diphenylamine **1i**	 **3f**	4	76
7	2-(-4-Methoxy phenyl) ethylamine **1j**	 **3g**	6	63
8	Piperidine **1k**	 **3h**	3	90
9	1,2,3,4-Tetrahydroquinoline **1l**	 **3i**	3	89
10	Pyrrolidine **1m**	 **3j**	3	83

4-Methoxyphenyl dithiocarbamic acid methyl ester, 3b: IR (Neat): 658, 1095, 1258, 1498, 3404 cm^{-1}; ^1H NMR: δ 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}; ^1H NMR: δ 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}; ^1H NMR: δ 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}; ^1H NMR: δ 3.3 (s, 3H, SCH_3), 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}; ^1H NMR: δ 3.4 (s, 3H, SCH_3), 7.0-7.5 (m, 10H, Ar-H).

[2-(4-Methoxyphenyl)ethyl] dithicarbamic acid methyl ester, 3g: IR (Neat): 649, 1086, 1210, 1477, 3386 cm^{-1}; ^1H NMR: δ 3.4 (s, 3H, SCH_3), 2.4 (br, NH), 2.9-3.1 (m, 2H, CH_2NH), 3.6 (t, CH_2-Ar), 3.9 (s, 3H, OCH_3), 6.7 (d, 2H, Ar-H), 7.1 (d, 2H, Ar-H).

Piperidine-1-carbodithioic acid methyl ester, 3h: IR (KBr): 662, 1208 cm^{-1}; ^1H NMR: δ 3.2 (s, 3H, SCH_3), 1.7-2.1 (m, 6H, $3CH_2$), 4.2 (br, 4H, CH_2N).

1,2,3,4-Tetrahydroquinoline-1-carbodithioic acid methyl ester, 3i: IR (Neat): 648, 1215, 1587 cm^{-1}; ^1H NMR: δ 3.4 (s, 3H, SCH_3), 1.8-2.5 (m, 4H, $2CH_2$), 3.7 (br, 2H, CH_2N), 6.7-7.1 (m, 4H, Ar-H).

Pyrrolidine-1-carbodithioic acid methyl ester, 3j: IR (Neat): 670, 1217 cm^{-1}; ^1H NMR: δ 3.2 (s, 3H, SCH_3), 1.8-2.0 (m, 4H, $2CH_2$), 3.8 (br, 4H, CH_2N).

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.

Acknowledgement

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