Reactions of Nitroxides. Part XII [1]. – 2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl Chloroformate – A New Reactive Nitroxyl Radical. A One-pot Synthesis of 2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl *N*,*N*-Dialkyl-carbamates

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The reactive nitroxides 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chloroformate and 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chlorothionoformate were synthesized from 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl and diphosgene (68 %) or thiophosgene (61 %), respectively. The reactions of the chloroformate and chlorothionoformate with lower secondary amines lead to 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl *N*,*N*-dialkylcarbamates (59 – 94 %) and thionocarbamates (35 – 65 %), respectively. Unexpectedly, the same 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl *N*,*N*-dialkylcarbamates were obtained directly in a one-pot reaction of 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl with diphosgene and lower tertiary alkylamines by dealkylation in 32 – 86 % yield. The antifungal activity of the synthesized carbamates and thionocarbamates has been demonstrated.

Key words: Diphosgene, Thiophosgene, Nitroxyl Radicals

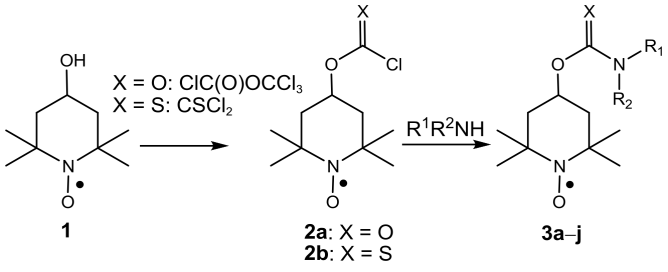
Introduction

In previous papers we described the synthesis and the pesticidal activity of urea, thiourea, and selenourea derivatives bearing either an aryl [2] or a nitroxyl moiety [3, 4]. Aryl iso(chalcogen)cyanates [2] and 4-iso(chalcogen)cyanato-2,2,6,6-tetramethylpiperidin-1-oxyl [3, 4], respectively, were applied as starting materials. Antifungal activity of the synthesized derivatives has been demonstrated.

Analogously to urea derivatives, carbamates are well known as pesticides. Carbaryl (1-naphthyl *N*-methylcarbamate, CAS: [63-25-2] [5, 6]), carbofuran (2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl *N*-methylcarbamate, CAS: [1563-66-2] [6, 7]), propoxur (2-isopropoxyphenyl *N*-methylcarbamate, CAS: [114-26-1] [8]), pirimicarb ([2-(dimethylamino)-5,6-dimethylpyrimidin-4-yl] *N*,*N*-dimethylcarbamate, CAS: [23103-98-2] [9]), and methiocarb (3,5-dimethyl-4-(methylthio)phenyl *N*-methylcarbamate, CAS: [2032-65-7] [10]), are the most prominent examples. The mode of action of carbamate insecticides is very similar to that of the organophosphate insecticides as they inhibit cholinesterase enzymes [11]. Thionocarbamates (C=S instead of C=O) show antifungal activity. The thionocarbamates tolnaftate (naphthiomate, β-naphthyl *N*-methyl-*N*-(3-methylphenyl) thionocarbamate) and tolciclate ((1,2,3,4-tetrahydro-1,4-methanonaphthalen-6-yl) *N*-methyl-*N*-(3-methylphenyl)thionocarbamate) have been proven to block ergosterol biosynthesis (what is in correlation with their antifungal activity [12]) in fungal cells and cell extracts [12, 13]. Moreover, the antifungal activities of D-glucopyranosyl thiocarbamates have been recently reported [14].

A successful synthesis of a reactive chlorothionoformate containing a nitroxyl moiety, namely 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chlorothionoformate (**2b**) [15], prompted us to synthesize its reactive oxygen analog 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chloroformate (**2a**). The application of both reactive nitroxyl radicals, the chloroformate **2a** and the chlorothionoformate **2b**, as the starting materials in reactions with secondary amines, afforded the corresponding *N*,*N*-dialkylcarbamates and *N*,*N*-dialkylthionocarbamates bearing a nitroxyl moiety. The pesticidal activity of these compounds has been evaluated.

Herein we present a synthesis of the new, reactive nitroxyl radical **2a**, the syntheses of new nitroxyl-substituted *N*,*N*-dialkylcarbamates **3a** – **e** and *N*,*N*-dialkylthionocarbamates **3f** – **j** from secondary amines,



3a: X = O, R^1 = H, R^2 = CH_3
3b: X = O, R^1 = CH_3, R^2 = CH_3
3c: X = O, R^1 = C_2H_5, R^2 = C_2H_5
3d: X = O, R^1 = *n*-C_3H_7, R^2 = *n*-C_3H_7
3e: X = O, R^1 = *n*-C_4H_9, R^2 = *n*-C_4H_9
3f: X = S, R^1 = H, R^2 = CH_3
3g: X = S, R^1 = CH_3, R^2 = CH_3
3h: X = S, R^1 = C_2H_5, R^2 = C_2H_5
3i: X = S, R^1 = *n*-C_3H_7, R^2 = *n*-C_3H_7
3j: X = S, R^1 = *n*-C_4H_9, R^2 = *n*-C4H9

Scheme 1. Synthesis of carbamates **3a** – **e** and thionocarbamates **3f** – **j** ($ClC(O)OCCl_3$ = diphosgene).

and **2a** or **2b**, respectively, as well as the pesticidal evaluation of **3a** – **j**. In addition, we show an alternative, efficient, one-pot synthesis of the *N*,*N*-dialkylcarbamates **3b** – **e** without using secondary amines and chloroformates but 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl (**1**), diphosgene (trichloromethyl chloroformate), and tertiary alkylamines according to the modified version of the von Braun dealkylation method [16 – 18], where chloroformates act as dealkylation agents [19 – 29].

Results and Discussion

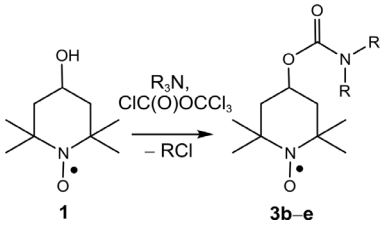
In our previous paper [15], the synthesis of the nitroxyl-substituted chlorothionoformate **2b** from **1** and thiophosgene in the presence of pyridine was reported. The product was obtained in 61 % yield (Scheme 1). The attempts of the analogous synthesis of chloroformate **2a** from **1** and diphosgene in the presence of pyridine afforded the expected chloroformate only in low and irreproducible yield (max. 25 %). However, when tribenzylamine (an amine used in the synthesis of the reactive nitroxyl 4-isocyanato-2,2,6,6-tetramethylpiperidin-1-oxyl [3, 30]) was used instead of pyridine, the expected chloroformate **2a** was successfully obtained in 68 % yield (Scheme 1).

The reactions of chloroformate **2a** and chlorothionoformate **2b** [15] with secondary lower amines afforded the 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl *N*,*N*-dialkylcarbamates **3a** – **e** and the 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl *N*,*N*-dialkylthionocarbamates **3f** – **j** in 59 – 94 % and 35 – 65 % yield, respectively (Scheme 1, Table 1/A).

Unexpectedly, the 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl *N*,*N*-dialkylcarbamates **3b** – **e** were also obtained in a one-pot reaction. If lower trialkylamines are used as bases in the reaction of diphosgene with **1**, a dealkylation of the tertiary amine occurs, and *N*,*N*-dialkylcarbamates **3b** – **e** are obtained in 32 – 86 % yield in a simple, one-pot reaction (Scheme 2, Table 1/B). The dealkylation of the tertiary amine is accompanied by the formation of an alkyl chloride. Its presence in the reaction mixture (*n*-butyl chloride in the synthesis of **3j** from **1**, diphosgene and tributylamine) was confirmed by GC/MS analysis. The identity of **3b** – **e** obtained either from the chloroformate **2a** and dialkylamine or directly from **1**, diphosgene, and trialkylamine was confirmed by the comparison of the corresponding melting points, IR and MS spectra. Analogous attempts to obtain **3g** – **j** directly from **1**, thiophosgene, and trialkylamine failed. Inseparable mixtures of difficult-to-identify products were obtained.

Table 1. *N*,*N*-Dialkylcarbamates **3a** – **e** and *N*,*N*-dialkylthionocarbamates **3f** – **j**; A: from dialkylamines and the respective carbamate **2a** or thionocarbamate **2b**; B: from **1**, diphosgene and trialkylamines.

Compound	X	R^1	R^2	Y_A (%)	Y_B (%)	m. p. (°C)
3a	O	H	CH_3	84.6	–	75 – 77
3b	O	CH_3	CH_3	94.3	31.9	106 – 108
3c	O	C_2H_5	C_2H_5	58.6	83.5	66 – 67
3d	O	*n*-C_3H_7	*n*-C_3H_7	72.2	80.3	56 – 57
3e	O	*n*-C_4H_9	*n*-C_4H_9	60.2	85.7	31 – 34
3f	S	H	CH_3	34.8	–	133 – 137
3g	S	CH_3	CH_3	65.2	–	114 – 117
3h	S	C_2H_5	C_2H_5	42.1	–	108 – 110
3i	S	*n*-C_3H_7	*n*-C_3H_7	40.5	–	67 – 70
3j	S	*n*-C_4H_9	*n*-C_4H_9	52.5	–	oil



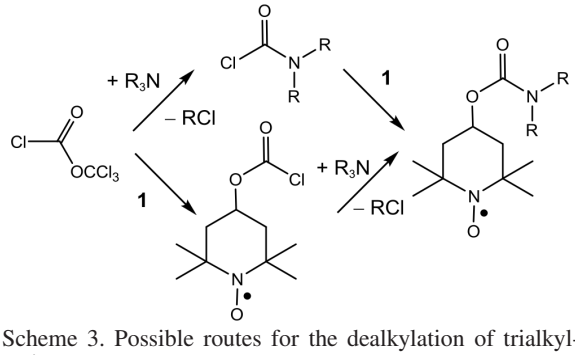
3b: R = CH_3
3c: R = C_2H_5
3d: R = *n*-C_3H_7
3e: R = *n*-C_4H_9

Scheme 2. Synthesis of carbamates **3b** – **e** accompanied by dealkylation of trialkylamines.

The structures of the synthesized *N*,*N*-dialkylcarbamates **3a** – **e** and *N*,*N*-dialkylthionocarbamates **3f** –

Table 2. Antifungal activity of **3a – j**: reduction of the growth of colonies (%).

Compound **3**	X	R^1	R^2	*Alternaria alternata*	*Botrytis cinerea*	*Rhizoctonia solani*	*Phytophtora cactorum*	*Fusarium culmorum*	*Blumeria graminis*
a	O	H	CH_3	61	65	28	35	27	1
b	O	CH_3	CH_3	19	55	58	21	28	0
c	O	C_2H_5	C_2H_5	19	53	64	21	22	0
d	O	*n*-C_3H_7	*n*-C_3H_7	48	35	72	36	44	15
e	O	*n*-C_4H_9	*n*-C_4H_9	58	69	55	43	50	7
f	S	H	CH_3	70	72	28	72	58	6
g	S	CH_3	CH_3	61	66	27	28	22	35
h	S	C_2H_5	C_2H_5	37	0	56	38	28	31
i	S	*n*-C_3H_7	*n*-C_3H_7	76	74	0	79	53	51
j	S	*n*-C_4H_9	*n*-C_4H_9	72	70	25	75	55	31



Scheme 3. Possible routes for the dealkylation of trialkylamines.

j were confirmed by spectroscopic methods (MS, HRMS and IR). Possible alternative routes of the dealkylation of the tertiary amine in the synthesis of **3b – e** are presented in Scheme 3.

The antifungal activities of *N*,*N*-dialkylcarbamates **3a – e** and *N*,*N*-dialkylthionocarbamates **3f – j** were tested. A weak to medium antifungal activity was found (Table 2).

Experimental Section

2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl (**1**) was synthesized by oxidation of 2,2,6,6-tetramethyl-4-piperidinol with 30 % hydrogen peroxide (77 %, m. p. 71 – 73 °C) according to lit. [31 – 33]. Thiophosgene was manufactured in the Institute of Industrial Organic Chemistry. Diphosgene (trichloromethyl chloroformate) was purchased from Aldrich. The experiments were performed in a 25 mL round-bottom flask, equipped with a magnetical stirrer. The *N*,*N*-dialkylcarbamates **3a – e** and *N*,*N*-dialkylthionocarbamates **3f – j** were obtained as red crystals (except **3j**). TLC control and column chromatography were carried out on silica gel Merck Alurollen 5562, Alufolien 5554 and Merck 1.09385.1000 (0.040 – 0.063 mm, 230 – 400 mesh), respectively. The following abbreviations for mobile phases are used throughout the text: HA9 = hexane:ethyl acetate 9:1, BA9, BA95 = benzene:ethyl acetate 9:1, 95:5, respectively, BM9, BM95 = benzene:methanol 9:1, 95:5, respectively, CA9 = carbon tetrachloride:ethyl acetate 9:1. Visualization of TLC plates: UV 254 and/or iodine vapor. MS [EI, 70 eV, *m/z*, int. (%)] data were recorded using AMD 604 and Agilent Technologies 5975 B mass spectrometers. HR MS (EI) data were recorded using an AMD 604 mass spectrometer. MS and HR MS (ESI, positive ions, CH_3OH as a solvent) were recorded using a Micromass LCT apparatus. IR (ν in cm^{-1}) data were recorded using a FT/IR Jasco 420 spectrophotometer. The methods for assessing antifungal activity involving both *in vitro* and *in vivo* tests were identical to those previously published [3].

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl chloroformate (**2a**)*

Tribenzylamine (1.722 g, 6 mmol) in benzene (18 mL) was added to the solution of 4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxyl (**1**, 0.344 g, 2 mmol) in benzene (5 mL). The solution of trichloromethyl chloroformate (diphosgene, 0.396 g, 2 mmol, 245 μL) in benzene (4 mL) was added with a syringe at r. t. The reaction mixture was stirred at r. t. for 24 h, and the progress of the reaction was monitored by TLC (HA9, BA9, BM9). The second portion of diphosgene (0.198 g, 1 mmol, 125 μL) in benzene (2 mL) was added at r. t. with a syringe. After the reaction had been completed (approximately after additional 1 – 2 h, TLC monitoring), the precipitate (2.07 g) was filtered off, and the filtrate was concentrated under reduced pressure. The red residue was subjected to column chromatography (HA9 as a mobile phase). Red crystals of **2a** were obtained (0.3183 g, 68 %). M. p. 58 – 60 °C. – MS (EI, 70 eV): *m/z* (%) = 236 (10), 234 (29) $[M]^+$, 155 (17), 154 (21), 147 (9), 140 (12), 139 (37), 124 (69), 109 (100), 82 (13), 81 (17), 69 (33), 68 (15), 67 (26), 63 (13), 55 (24), 41 (40). – HRMS ((+)-EI): *m/z* = 234.0891 (calcd. 234.0897 for $C_{10}H_{17}NO_3Cl$, $[M]^+$). – HRMS ((+)-ESI): *m/z* = 253.1297 (calcd. 253.1290 for $C_{11}H_{20}NO_4Na$, $[M^*+Na]^+$) [34]. – IR (KBr pellet): ν = 1763 (C=O), 1166 cm^{-1}.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl chlorothionoformate (**2b**)* [15]

Thiophosgene (1.55 mL, 2.33 g, 20.3 mmol) was added with a syringe to benzene (16.5 mL). A solution of 2,2,6,6-tetramethyl-4-hydroxypiperidin-1-oxyl (0.861 g, 5 mmol) and pyridine (0.85 mL, 10.5 mmol) in benzene (8 mL) was added dropwise to the thiophosgene solution at 18 – 20 °C. The reaction mixture was stirred for 20 min at ambient temperature. The precipitate was filtered off and washed with benzene (2 – 5 mL). Benzene was evaporated under reduced pressure. The crystalline residue (1.284 g) was recrystallized from hexane (7 mL) to give **2b** (0.7604 g, 61 %). M. p. 78 – 84 °C. – R_f: 0.24 (HA9), 0.55 (CA9), 0.61 (BA9), 0.77 (BM9). – MS (EI, 70 eV): *m/z* (%) = 252 (3), 250 (10) $[M]^+$, 155 (22), 154 (10), 140 (8), 139 (11), 124 (66), 109 (77), 100 (19), 98 (18), 95 (8), 83 (28), 82 (33), 81 (25), 79 (18), 74 (14), 69 (80), 67 (39), 60 (14), 56 (53), 55 (81), 53 (13), 44 (26), 43 (19), 42 (100), 40 (24). – IR (KBr pellet): ν = 2976, 1308, 1270, 1243, 1017 cm^{-1} [15].

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N-alkylcarbamates and 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl N-alkylthionocarbamates **3a**, **3b**, **3f**, and **3g**; general procedure*

The solution of pre-cooled methylamine or dimethylamine (∼ 40 – 60 mmol) in benzene (∼ 5 mL) was added dropwise to a chilled solution of 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chloroformate (**2a**) or 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl chlorothionoformate (**2b**) (1 mmol) in benzene (5 – 10 mL). The reaction mixture, protected from humidity, was stirred for 1 h in an ice-water bath and for 24 h at r. t. After the reaction had been completed, the reaction mixture was concentrated and filtered under reduced pressure, and the precipitate was washed with a small amount of benzene. The filtrate was concentrated under reduced pressure. The residue (0.2 – 0.3 g) was purified by column chromatography using BM95 (**3a**, **3f**) or BA95 (**3b**, **3g**) as a mobile phase to give the expected products **3a** (85 %), **3b** (94 %), **3f** (35 %) or **3g** (65 %) as red crystals.

3a: M. p. 75 – 77 °C. – MS (EI, 70 eV): *m/z* (%) = 229 (13) $[M]^+$, 154 (18), 139 (12), 124 (86), 109 (100). – HRMS ((+)-EI): *m/z* = 229.1547 (calcd. 229.1552 for $C_{11}H_{21}N_2O_3$, $[M]^+$). – IR (KBr pellet): ν = 3319, 1710 (C=O), 1687, 1544, 1267, 1137 cm^{-1}.

3b: M. p. 106 – 108 °C. – MS (EI, 70 eV): *m/z* (%) = 243 (9) $[M]^+$, 213 (3), 154 (26), 139 (12), 124 (71), 109 (100), 90 (24), 82 (17), 81 (13), 72 (57). – HRMS ((+)-EI): *m/z* = 243.1720 (calcd. 243.1709 for $C_{12}H_{23}N_2O_3$, $[M]^+$). – IR (KBr pellet): ν = 1703 (C=O), 1194 cm^{-1}.

3f: M. p. 133 – 137 °C. – MS (EI, 70 eV): *m/z* (%) = 245 (7) $[M]^+$, 154 (47), 140 (8), 139 (11), 124 (72), 109 (100). – HRMS ((+)-EI): *m/z* = 245.1319 (calcd. 245.1324 for $C_{11}H_{21}N_2O_2S$, $[M]^+$). – IR (film): ν = 3384, 1540, 1218, 1127 cm^{-1}.

3g: M. p. 114 – 117 °C. – MS (EI, 70 eV): *m/z* (%) = 259 (14) $[M]^+$, 154 (100), 140 (9), 139 (7), 124 (78), 109 (96), 106 (27), 88 (22), 82 (11), 81 (13), 72 (34), 69 (17), 68 (8), 67 (20), 56 (16), 55 (21), 41 (29). – HRMS ((+)-EI): *m/z* = 259.1471 (calcd. 259.1480 for $C_{12}H_{23}N_2O_2S$, $[M]^+$). – IR (KBr pellet): ν = 1534, 1282, 1196, 1144 cm^{-1}.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N,N-diethylcarbamate (**3c**) and 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl N,N-diethylthionocarbamate (**3h**); general procedure*

A chilled solution of diethylamine (∼ 30 mmol) in benzene (∼ 5 mL) was added dropwise to a chilled solution of chloroformate **2a** or chlorothionoformate **2b** (1 mmol) in benzene (5 – 10 mL). The reaction mixture, protected from humidity, was stirred for 1 h in an ice-water bath and for 24 h at r. t. The reaction mixture was filtered under reduced pressure, and the precipitate was washed with a small amount of benzene. The filtrate was evaporated to dryness under reduced pressure. The residue was purified by column chromatography [HA9 (**3c**), BA95 (**3h**)] to give the expected products **3c** (59 %) or **3h** (42 %) as red crystals.

3c: M. p. 66 – 67 °C. – MS (EI, 70 eV): *m/z* (%) = 271 (8) $[M]^+$, 241 (3), 185 (3), 154 (38), 139 (17), 124 (98), 118 (55), 109 (100), 100 (51), 83 (5), 82 (20), 81 (11), 69 (20), 68 (10), 67 (10), 55 (14), 41 (19). – HRMS ((+)-ESI): *m/z* = 294.1921 (calcd. 294.1919 for $C_{14}H_{27}N_2O_3Na$[M+Na]$^+$). – IR (KBr pellet): ν = 1693 (C=O), 1426, 1379, 1279, 1173, 1063 cm^{-1}.

3h: M. p. 108 – 110 °C. – MS (EI, 70 eV): *m/z* (%) = 287 (13) $[M]^+$, 154 (87), 139 (15), 124 (62), 109 (100), 100 (27). – HRMS ((+)-EI): *m/z* = 287.1785 (calcd. 287.1793 for $C_{14}H_{27}N_2O_2S$, $[M]^+$). – IR (KBr pellet): ν = 1517, 1243, 1172 cm^{-1}.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N,N-dialkylcarbamates and 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl N,N-dialkylthionocarbamates **3d**, **3e**, **3i**, and **3j**; general procedure*

A chilled solution of dipropylamine or dibutylamine (∼ 30 mmol) in benzene (∼ 5 mL) was added dropwise to a chilled solution of chloroformate **2a** or chlorothionoformate **2b** (1 mmol) in benzene (5 – 10 mL). The reaction mixture, protected from humidity, was stirred for 1 h in an ice-water bath and for 24 h at r. t. The reaction mixture was filtered under reduced pressure, and the precipitate was washed with a small amount of benzene. The filtrate was washed with 1 M hydrochloric acid (15 mL), concentrated sodium bicarbonate solution (15 mL), and with water (15 mL). The solution was dried over anhydrous magnesium sulfate. After filtration, the filtrate was evaporated to dryness under reduced pressure. The residue (0.3 – 0.45 g) was purified with column chromatography [HA9 (**3d**, **3e**), BA95 (**3e**, **3i**, **3j**)] to give the expected products **3d** (72 %), **3e** (60 %), **3i** (41 %) as red crystals and **3j** (53 %) as a red oil.

3d: M. p. 56 – 57 °C. – MS (EI, 70 eV): *m/z* (%) = 299 (30) $[M]^+$, 269 (6), 213 (8), 155 (16), 154 (51), 146 (93), 140 (14), 139 (18), 128 (26), 124 (100), 109 (54). – HRMS ((+)-EI): *m/z* = 299.2346 (calcd. 299.2335 for $C_{16}H_{31}N_2O_3[M]^+$). – IR (KBr pellet): ν = 1697 (C=O), 1426, 1241, 1168 cm^{-1}.

3e: M. p. 31 – 34 °C. – MS (EI, 70 eV): *m/z* (%) = 327 (8) $[M]^+$, 174 (69), 156 (17), 155 (10), 154 (33), 140 (12), 139 (13), 124 (100), 109 (53). – HRMS ((+)-EI): *m/z* = 327.2663 (calcd. 327.2648 for $C_{18}H_{35}N_2O_3$, $[M]^+$). – IR (KBr pellet): ν = 1696 (C=O), 1475, 1422, 1224, 1166, 1079 cm^{-1}.

3i: M. p. 67 – 70 °C. – MS (EI, 70 eV): *m/z* (%) = 315 (7) $[M]^+$, 162 (84), 154 (64), 140 (9), 139 (10), 128 (13), 124 (100), 109 (67). – HRMS ((+)-EI): *m/z* = 315.2113 (calcd. 315.2106 for $C_{16}H_{31}N_2O_2S$, $[M]^+$). – IR (KBr pellet): ν = 1515, 1226, 1171 cm^{-1}.

3j: MS (EI, 70 eV): *m/z* (%) = 343 (5) $[M]^+$, 190 (95), 154 (58), 140 (10), 139 (9), 124 (100), 109 (50), 57 (34), 55 (20). – HRMS ((+)-EI): *m/z* = 343.2426 (calcd. 343.2419 for $C_{18}H_{35}N_2O_2S$, $[M]^+$). – IR (KBr pellet): ν = 2959, 1505, 1460, 1425, 1376, 1211, 1164, 1037 cm^{-1}.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N,N-dimethylcarbamate (**3b**) (dealkylation of trimethylamine)*

A solution of pre-cooled trimethylamine (0.9 g, 15 mmol, 1.5 mL) in benzene (6 mL) was added to a chilled solution of **1** (0.344 g, 2 mmol) in benzene (5 mL). A solution of trichloromethyl chloroformate (diphosgene, 0.279 g, 1.41 mmol, 170 mL) in benzene (2 mL) was added with a syringe. Fumes were observed, the temperature rose to 40 °C, and the reaction mixture became cloudy. The mixture was stirred for 24 h at r. t., and the progress of the reaction was monitored by TLC (HA9, BA9, BM9). A copious amount of a precipitate was formed. The second portion of trichloromethyl chloroformate (diphosgene, 0.139 g, 0.70 mmol, 85 mL) in benzene (1.5 mL) was added. After the reaction had been completed (disappearance of the starting compound **1**, TLC monitoring), the precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The residue (0.519 g) was subjected to column chromatography (mobile phase: hexane : HA9) to give **3b** (0.155 g, 32 %). M. p. 106 – 108 °C.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N,N-diethylcarbamate (**3c**) (dealkylation of triethylamine)*

A solution of triethylamine (1.54 g, 15.3 mmol, 2.1 – 2.2 mL) in benzene (6 mL) was added to **1** (0.344 g, 2 mmol) in benzene (5 mL). A solution of trichloromethyl chloroformate (diphosgene, 0.279 g, 1.41 mmol, 170 mL) in benzene (2 mL) was added with a syringe. Fumes were observed, the temperature rose to 40 °C, and the reaction mixture became cloudy. The reagents were stirred for 24 h at r. t., the progress of the reaction being monitored by TLC (mobile phase: HA9, BA9, BM9). The second portion of diphosgene (0.139 g, 0.70 mmol, 85 μL) in benzene (1.5 mL) was added. After the reaction had been completed (disappearance of **1**, TLC monitoring) the precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The residue (0.78 g) was subjected to column chromatography (mobile phase: HA9) to give **3c** (0.453 g, 84 %). M. p. 66 – 67 °C.

*2,2,6,6-Tetramethyl-1-oxyl-4-piperidyl N,N-dipropylcarbamate (**3d**) and 2,2,6,6-tetramethyl-1-oxyl-4-piperidyl N,N-dibutylcarbamate (**3e**); general procedure (dealkylation of tripropylamine or tributylamine)*

A solution of tripropylamine (2.188 g, 15.3 mmol, 2.9 mL) or tributylamine (2.83 g, 15.3 mmol, 3.6 mL) in benzene (6 mL) was added to **1** (0.344 g, 2 mmol) in benzene (5 mL). A solution of diphosgene (0.279 g, 1.41 mmol, 170 mL) in benzene (2 mL) was added with a syringe. Fumes were observed, the temperature rose to 40 °C, and the reaction mixture became cloudy. The reagents, protected from humidity, were stirred for 24 h at r. t., the progress of the reaction being monitored by TLC (mobile phase: HA9, BA9, BM9). The second portion of diphosgene (0.139 g, 0.70 mmol, 85 μL) in benzene (1.5 mL) was added. The completion of the reaction (disappearance of **1**) was monitored by TLC. If a precipitate was present (the reaction with tripropylamine), the reaction mixture was filtered under reduced pressure, and the precipitate was washed with a small amount of benzene. The benzene filtrate was washed with equal volumes of 1 M hydrochloric acid, concentrated sodium bicarbonate solution, and water. The solution was dried ($MgSO_4$), filtered, and the filtrate was evaporated to dryness under reduced pressure. In the case of the lack of a precipitate (reaction with tributylamine) the reaction mixture was directly extracted, washed, dried and evaporated. The residue (**3d**: 2.28 g, **3e**: 1.05 g) was purified by column chromatography (mobile phase: HA9, **3d**: a crude product was dissolved while hot) to give **3d** (0.480 g, 80.3 %) or **3e** (0.560 g, 86 %). **3d**: M. p. 56 – 57 °C. **3e**: M. p. 31 – 34 °C.

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[34] Because the ESI-MS spectrum of **2a** was recorded from a methanol solution, instead of the spectrum of **2a** (M = 234) the spectrum of the respective -O-C(O)OCH_3 compound (M = 230) is obtained.