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A high yielding, one-pot synthesis of *O*,*S*-dialkyl dithiocarbonates from alcohols using Mitsunobu's reagent

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Abstract—A novel Mitsunobu-based protocol has been developed for the synthesis of *O*,*S*-dialkyl dithiocarbonates from a variety of primary, secondary and tertiary alcohols using carbon disulfide, in good to excellent yields. This protocol is mild and efficient compared to other reported methods.

O,*S*-Dialkyl dithiocarbonates (xanthates) are a versatile source of radicals,[1] intermediates in the synthesis of thiols,[2] thiocarbonates,[3] alkenes,[4] alkanes,[5] S-activated carbanions[6] and photosensitisers[7] for the polymerization of vinyl monomers. They have also been used in the synthesis of natural products,[8] Claisen rearrangement,[9] and are also important for biological activities.[10] Traditionally, they are prepared from an alcohol in a three-step process.[11] The reaction involves the use of strong bases such as sodium hydride, sodium amide or potassium *t*-butoxide in polar aprotic solvents like DMSO,[12] DMF[13] or diglyme.[14] Phase-transfer catalysis and crown ethers have also been used with strong bases specifically for the preparation of dithiocarbonates from unfunctionalized alcohols.[15] However, most of these methods suffer from limitations such as long reaction times, use of expensive strongly basic reagents, and tedious work-up. Consequently, there is continued interest in developing new and convenient methods for the synthesis of dithiocarbonates using mild reaction conditions. Our group[16] has been engaged over several years on the development of new methodologies for the synthesis of carbamates and dithiocarbamates using cheap and safe reagents like CO_2 and CS_2. Recently we reported[17] the synthesis of carbamates- and dithiocarbamates from the corresponding alcohols using Mitsunobu's reagent. Based on our recent work,[17] we report herein a chemoselective, highly efficient and mild synthesis of *O*,*S*-dialkyl dithiocarbonates of primary, secondary and tertiary alcohols using Mitsunobu's reagent.

Thus we carried out[18] the synthesis of dithiocarbonates by mild thiocarbonation of alcohols with carbon disulfide and an alcohol in the presence of Mitsunobu's reagent.

We assume that the unstable dithiocarbonic acid **1** generated from the alcohol and CS_2 reacts with the Mitsunobu zwitterion **2** formed from Ph_3P and diethyl azodicarboxylate, to furnish the stabilized zwitterionic species **3** which in turn undergoes S-alkylation giving rise to the formation of the dithiocarbonate ester as shown in Scheme 1.

Thus, various alcohols were reacted using Mitsunobu's reagent and carbon disulfide solution in dry dimethylsulfoxide (DMSO) at room temperature for 4–8 h, to afford *O*,*S*-dialkyl dithiocarbonates in good to excellent yields (76–98%) as shown in Table 1. Isomeric *O*,*S*-dialkyl dithiocarbonates were prepared by altering the order of addition of the respective alcohols (Table 1, entries 2 and 18, 10 and 19) We examined several solvents such as *n*-heptane, *n*-hexane, DMSO, DMF and HMPA of which dry DMSO proved to be the most suitable. The overall reaction is shown in Scheme 2.

In conclusion, we have developed a convenient and efficient protocol for the one-pot, four-component coupling of various alcohols with a variety of primary, secondary

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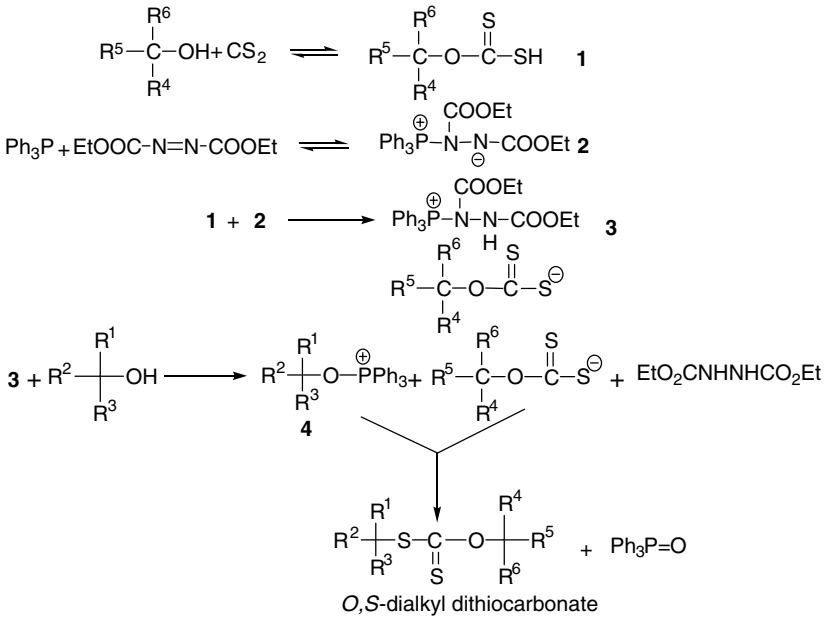
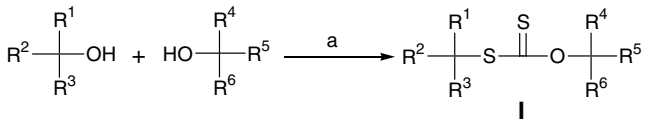


Scheme 1. Proposed mechanism of formation of the dithiocarbonates.

Table 1. Conversion of alcohols into dithiocarbonates of general formula **I**[a]

Entry	R^1	R^2	R^3	R^4	R^5	R^6	Time (h)	Yields (%)
1	Phenyl	H	H	Phenyl	H	H	5	92
2[b]	2-Phenethyl	H	H	*n*-Hexyl	H	H	4	97
3	2-Phenethyl	H	H	*n*-Propyl	*n*-Propyl	H	5	86
4	*n*-Propyl	H	H	*n*-Octyl	H	H	5	93
5	*i*-Amyl	H	H	Cyclohexyl	H	H	6	85
6	*n*-Butyl	H	H	*n*-Butyl	H	H	5	82
7	2-Naphthyloxyethyl	H	H	Phenyl	H	H	6	85
8	2-Naphthyloxyethyl	H	H	4-Methoxyphenyl	H	H	5	83
9	*n*-Butyl	*n*-Butyl	H	*n*-Octyl	H	H	6	84
10[b]	*n*-Butyl	*n*-Butyl	*n*-Butyl	*n*-Dodecyl	H	H	7	76
11	*n*-Hexyl	H	H	Phenyl	H	H	6	80
12	*n*-Heptyl	H	H	Benzyl	H	H	5	83
13	*n*-Octyl	H	H	3-Methoxybenzyl	H	H	5	89
14	*n*-Heptyl	H	H	*n*-Dodecyl	H	H	4	98
15	*n*-Pentyl	Methyl	H	Cyclohexyl	H	H	6	90
16	2-Naphthyloxyethyl	H	H	*n*-Butyl	*n*-Butyl	*n*-Butyl	8	76
17	3-(2-Naphthyloxy)prop-1-yl	H	H	*n*-Octyl	H	H	5	93
18[b]	*n*-Hexyl	H	H	2-Phenethyl	H	H	4	96
19[b]	*n*-Dodecyl	H	H	*n*-Butyl	*n*-Butyl	*n*-Butyl	7	77

[a] All the products were characterized by IR, NMR and mass spectral data.
[b] Entries 2 and 18 and entries 10 and 19 are isomeric products.



Scheme 2. Reagents and conditions: (a) dry DMSO, DEAD/Ph_3P, CS_2, rt, 4–8 h.

and tertiary alcohols via a Mitsunobu zwitterion. This reaction generates the corresponding *O*,*S*-dialkyl dithiocarbonates in high yields. Furthermore, this method exhibits substrate versatility, mild reaction conditions and experimental convenience. This synthetic protocol is believed to offer a more general method for the formation of C–S bonds, essential in numerous organic syntheses.

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18. *Typical experimental procedure: O,S-Dibenzyl dithiocarbonate* (entry 1): Benzyl alcohol (1 ml, 9 mmol) and CS_2 (4 ml, in excess) were dissolved in dry DMSO (35 ml). To the reaction mixture triphenylphosphine (2.2 g, 9 mmol) was added and then diethyl azodicarboxylate (1.33 ml, 9 mmol) was added slowly in 2–3 small portions. Next, benzyl alcohol (1 ml, 9 mmol) was added. The reaction was stirred until completion (5 h) as checked by TLC. The reaction mixture was then poured into distilled water (50 ml) and extracted with ethyl acetate thrice. The organic layer was separated and dried over anhydrous sodium sulfate and then concentrated to obtain *O,S*-dibenzyl dithiocarbonate as an oil (2.33 g, 92%). IR (neat): 1085, 1190, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 4.28$ (s, 2H, PhCH_2S), 5.52 (s, 2H, PhCH_2O), 7.20–7.40 (m, 10H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 38.2$ (PhCH_2S), 74.5 (PhCH_2O), 127.4, 127.9, 128.5, 128.7, 140.10, 142.20 (aromatic region), 172.2 (*C*=S) ppm; Mass: *m/e* (%) = 274 (91), 197 (39), 105 (42), 91 (100); Analysis: $C_{15}H_{14}OS_2$, Calcd C, 65.66; H, 5.14; S, 23.37. Found: C, 65.89; H, 5.02; S, 23.55.

O,S-n-Heptyl-3-phenylpropyl dithiocarbonate (entry 2): Oil, IR (neat): 1088, 1194, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.93$–0.96 (*t*, 3H, $J = 6.9$ Hz, CH_3 of *n*-hexyl), 1.29–1.48 (m, 8H of CH_2 of *n*-hexyl), 2.26–2.30 (m, 2H, PhCH_2CH_2CH$_2$), 2.56–2.59 (t, 2H, $J = 6.3$ Hz, PhCH_2), 2.90–2.93 (*t*, 2H, $J = 6.5$ Hz, PhCH$_2$CH$_2CH_2$–S), 3.64–3.69 (t, 2H, $J = 7.1$ Hz, OCH_2), 7.08–7.25 (m, 5H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.5$, 23.2, 26.8, 30.5, 32.5 (*C*–S), 33.9, 34.5, 68.3 (O–CH_2), 125.8, 128.3, 128.8, 139.2, 172 (C=S) ppm; Mass: *m/e* (%) = 296 (84), 197 (38), 99 (54), 85 (63), 71 (45), 43 (100); Analysis: $C_{16}H_{24}OS_2$, Calcd C, 64.81; H, 8.16; S, 21.63. Found: C, 65.12; H, 7.93; S, 21.25.

O,S-1-Propylbutyl-3-phenylpropyl dithiocarbonate (entry 3): Oil, IR (neat): 1090, 1199, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.94$–0.97 (t, 6H, $J = 6.5$ Hz, CH_3), 1.32–1.36 (m, 4H, CH_2CH_3), 1.43–1.46 (m, 4H, O–CH–CH_2), 2.27–2.30 (m, 4H, PhCH$_2CH_2CH_2$), 2.54–2.57 (t, 2H, $J = 6.4$ Hz, PhCH_2), 2.85–2.87 (t, 2H, $J = 6.6$ Hz, PhCH$_2$CH$_2$– CH_2–S), 3.20–3.24 (m, 1H, O–*CH*), 7.08–7.25 (m, 5H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 14.3$, 17.2, 32.7 (S–CH_2), 34.2, 35.6, 72.3 (O–*CH*), 126.4, 128.2, 128.8, 138.8, 172.5 (C=S) ppm; Mass, *m/e* (%) = 310 (85), 197 (41), 99 (53), 105 (44), 91 (100%); Analysis: $C_{17}H_{26}OS_2$, Calcd C, 65.75; H, 8.44; S, 20.65. Found: C, 65.33; H, 8.59; S, 20.99.

O,S-n-Nonyl-1-butylpentyl dithiocarbonate (entry 9): Oil, IR (neat): 1092, 1193,1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.91$–0.93 (*t*, 9H, $J = 6.6$ Hz, CH_3), 1.29–1.33 (m, 20H, CH_2 of chain), 1.50–1.52 (t, 2H, $J = 7.2$ Hz OCH$_2CH_2$ of nonyl group), 1.92–1.94 (m, 4H, SCHCH_2), 2.52–2.54 (m, 1H, S*CH*), 3.54–3.56 (t, 2H, $J = 7.1$ Hz, OCH_2); ^{13}C NMR (100 MHz, $CDCl_3$), $\delta = 14.0$, 23.1, 26.3, 28.9, 29.8, 30.0, 30.3, 36.2, 40.6 (*CH*–S), 67.7 (CH_2O), 172.4 (*C*=S) ppm; Mass, *m/e* (%) = 346 (89), 219 (44), 127 (75), 109 (52), 57 (82), 43 (91); Analysis: $C_{19}H_{38}OS_2$, Calcd C, 65.83; H, 11.05; S, 18.50. Found: C, 65.53; H, 11.20; S, 18.66.

O,S-n-Dodecy1-1,1,-dibutylpentyl dithiocarbonate (entry 10): mp = 64 °C, IR (KBr): 1075, 1183, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$–0.91 (t, 12H, J= 6.9 Hz, CH_3), 1.29–1.33 (m, 30H, $J = 6.8$ Hz, CH_2 of chain), 1.48–1.51 (*t*, 2H, J= 6.7 Hz, OCH$_2CH_2$ of dodecyl group), 1.88–1.90 (m, 6H, S–C–CH_2), 3.51–3.53 (t, 2H, $J = 7.2$ Hz, OCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 14.0$, 23.1, 26.3, 28.9, 29.8, 30.0, 30.3, 36.2, 40.3 (*C*-S), 67.8 (CH_2O), 172.6 (*C*=S) ppm; Mass, *m/e* (%) = 444 (91), 275 (49), 183 (52), 169 (65), 127 (76), 109 (54), 57 (77), 43 (100) Analysis: $C_{26}H_{52}OS_2$ Calcd C, 70.20; H, 11.78; S, 14.40. Found: C, 70.53; H, 11.44; S, 14.31.

O,S-n-Octy1-3(2-naphthyloxy-propyl) dithiocarbonate (entry 16): mp = 110 °C, IR (KBr): 1078, 1187, 1229 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.92$–0.94 (t, 3H, $J = 6.4$ Hz, CH_3), 1.29–1.33 (m, 10H, $J = 6.7$ Hz, CH_2), 1.48–1.50 (m, 2H, $J = 7.0$ Hz, OCH$_2CH_2$), 2.37–2.39 (m, 2H, $J = 6.5$ Hz, O–CH$_2CH_2$CH$_2$–S), 2.88–2.90 (t, 2H, $J = 6.5$ Hz, SCH_2), 3.53–3.55 (t, 2H, $J = 7.2$ Hz, OCH$_2$), 7.04–7.78 (m, 7H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 14.1$, 23.2, 26.3, 28.5, 29.9, 30.5, 32.6, 67.8 (O–CH_2 of *n*-octyl), 71.2 (naphthyl–O–CH_2), 105.8, 118.8, 123.7, 126.4, 127.7, 129.3, 129.5, 134.6, 157.7 (aromatic), 172.5 (*C*=S) ppm; Mass, *m/e* (%) = 390 (95), 277 (44), 185 (62), 127(69), 113 (65), 57(73), 43 (100); Analysis: $C_{22}H_{30}O_2S_2$, Calcd C, 67.65; H, 7.74; S, 16.42. Found: C, 67.29; H, 7.92; S, 16.61.