SHORT PAPER

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A one-pot rapid synthesis of dithiocarbamates from alcohols using a polymer supported diethyl dithiocarbamate anion†

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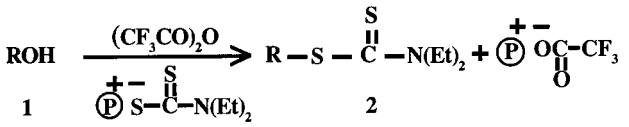
A polymer supported diethyl dithiocarbamate anion reacts with primary and secondary alcohols via their tirfluoracetates giving alkylated diethyl dithiocarbamates in good yields.

Thiocarbamates possess many biological properties, ranging from hypnotic, analgesic and anaesthetic to fungicidal, bactericidal and tuberculostic activity. Amines react with carbon disulfide and alkali metal hydroxides to form salts of dithiocarbamic acids ($RR^1N–CS–S^-Na^+$), which are strongly nucleophilic and react with many electrophiles to give dithiocarbamates.The dithiocarbamoyl moiety was shown to be a very useful synthetic tool[1,2] and a good precursor to thiols and other sulfur functionalities.[3] The traditional preparative methods for the alkylation of dithiocarbamates usually require the interaction of metal dithiocarbamate with an electrophilic substrate such as an alkyl halide or an aryldiazonium salt.[4] However, these methods require either long reaction times or high temperature because of low solubility of metal salts of dithicarbamates in organic solvents. Drastic reaction conditions result in the decomposition of aryldiazoniums salts. As a result of these problems, dithiocarbamates are formed in low yield accompanied by side products. Therefore, there is a need to develop a rapid, clean and high yielding method for alkylation of dithiocarbamates under mild condition.

In this paper we describe a new highly efficient and straightforward method for the alkylation of polymer supported diethyl dithiocarbamate by alcohols via the corresponding trifluoracetates which are not isolated as such. Furthermore, the exceptionally mild conditions that are used may allow its application to sensitive substrate molecules.



a $PhCH_2^-$ **b** $4\text{-}O_2N\text{-}PhCH_2^-$
c $4\text{-}ClPhCH_2^-$ **d** $40BrPhCH_2^-$
e $3,4\text{-methylenedioxy-}C_6H_3CH_2^-$ **f** $PhCH{=}CHCH_2^-$
g $CH_3(CH_2)_{16}CH_2^-$ **h** $HOCH_2(CH_2)_6CH_2^-$
i Menthyl -
1j $(CH_3)_2C.OHCH_2CH{\cdot}CH_3$ **2j** $(CH_3)_2C.O_2CCF_3CH_2CH{\cdot}CH_3$
1k $4\text{-HO }C_6H_4CH_2^-$ **2k** $4\text{-}CF_3\ Co.OC_6H_4CH_2^-$

The success of this transformation may be attributed to the high nucleofugal character of the trifluoracetate moiety in nucleophilic substitution,[5] which resembles that of triflates.[6] Trifluoroacetylation was carried out in almost quantitative yield by treatment of the alcohol with an excess of trifluoracetic anhydride. The reaction was complete in a few minutes a room temperature. The resulting trifluoracetic acid and the excess anhyhdride were evaporated off and the intermediate trifluoracetate was treated *in situ* with polymer supported diethyl dithiocarbamate in acetonitrile at room temperature. Spontaneous reaction took place. The transformation was complete after 5 minutes. The reaction, which was monitored by TLC, leads to the expected diethyl dithiocarbamates in chromatographically and spectroscopically pure state and the yields are good (Table 1).

Our procedure is useful for primary and secondary alcohols. However, when the reaction was attempted with tertiary alcohol (**1j**) and phenol (**1k**), formation of intermediate trifluoracetates proceed in high yields but the subsequent nucleophilic substitution failed and the intermediate ester was recovered unchanged under these specified reaction conditions. A complex mixture of products was obtained under forcing conditions (DMF, 150°C, 10 h). Moreover, the reaction turned out to be chemoselective when secondary and tertiary alcohol functions are present in the same substrate (**1j**). It is also important to note that dihydric alcohol (**1h**), was also smoothly converted into the corresponding dithiocarbamate. Some of the dithiocarbamates are thermally unstable and therefore, they decompose on heating at higher temperatures (**2g,2h, 2j**).

Experimental

IR spectra were recorded on KBr pellets using a Bomem MB-104 spectrometer and ^1H NMR were recorded on 300 MHz (AC 300 F instrument) with TMS as an internal standard.

General procedure for the preparation of polymer-supported diethyl dithiocarbamate: To a solution of sodium N,N-diethyl dithiocarbamate (50 mmol in 100 ml water), was added Amberlite IRA-400-Cl (10 g) and stirred for 1 h. The resin was filtered and washed with distilled water, alcohol and ether. The resin was dried under vacuum at 40°C for 2h. The capacity of the resin was determined by either titration or UV method and it was found 1 mmol / g of the dry resin.

A typical procedure: To a solution of benzyl alcohol (5 mmol) in dichloromethane (10 ml) was added tirfluroacetic anhydride (5 mmol) (10 mmol for dihydroxylic compounds). The reaction mixture was stirred for 15 minutes at room temperature. The trifluoracetic acid formed, along with the solvent is then evaporated off and the residue was diluted with acetonitrile (10 ml) which was treated with diethyl dithiocarbamate supported resin (6 g, 6 mmol). The reaction mixture was stirred for 5 minutes at 25°C. After completion of the reaction, the resin was filtered off and washed with dichloromethane (2 × 10 ml). Then, removal of the solvent under reduced pressure gave benzyl diethyl dithiocarbamate (84%) in almost pure form.

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Table 1 Synthesis of diethyl dithiocarbamates from alcohols

Product	m.p./b.p. (C)	Yield (%)	Mol. formula	Found C	(Calcd) H	(%) N	S	Cl/Br/F	ν_{max}/cm^{-1} (Kbr/Neat)	δ ($CHCl_3$, TMS)
2a	229/760 mm	84	$C_{12}H_{17}NS_2$	60.18 (60.25	7.17 7.11	5.91 5.85	26.86 26.77	— —)	799, 1500, 1600, 2933, 3015	1.28 (m, 6H, 2 × CH_2**CH_3**), 3.73 (q, 2H, **CH_2**CH_3), 4.06 (q, 2H, **CH_2**CH_3), 4.58 (s, 2H, **CH_2**–Ar), 7.25 (m, 5H, Ar–H)
2b	74–76	76	$C_{12}H_{16}N_2O_2S_2$	50.81 (50.70	5.71 5.63	9.77 9.85	22.61 22.52	— —)	799, 1240, 1347 1510, 1595, 2933, 3010.	1.28 (t, 6H, 2 × CH_2**CH_3**), 3.73 (q, 2H, **CH_2**CH_3), 4.02 (q, 2H, **CH_2**CH_3), 4.52 (s, 2H **CH_2**–Ar), 7.58 (d, 2H, Ar–H), 8.17 (d, 2H, Ar–H)
2c	223/760 mm	80	$C_{12}H_{16}NS_2Cl$	52.68 (52.74	5.91 5.86	5.18 5.12	23.51 23.44	13.07 13.00)	798, 1225, 1485 1580, 2985, 3005	1.29 (t, 6H, 2 × CH_2**CH_3**), 3.77 (q, 2H, **CH_2**CH_3), 4.12 (q, 2H, **CH_2**CH_3), 4.54 (s, 2H, CH_2–Ar), 7.61 9d, 2H, Ar–H), 8.05 (d, 2H, Ar–H)
2d	69–71	78	$C_{12}H_{16}NS_2Br$	45.21 (45.28	5.11 5.03	4.51 4.40	20.02 20.12	25.21 25.15)	794, 1235 1485, 1585, 2980, 3010	1.26 (t, 6H, 2 × CH_2**CH_3**), 3.58 (q, 2H, **CH_2**CH_3), 4.02 (q, 2H, **CH_2**CH_3), 4.62 (s, 2H, CH_2–Ar), 7.26 (d, 2H, Ar–H), 7.46 (d, 2H, Ar–H)
2e	49	74	$C_{13}H_{17}NO_2S_2$	55.41 (55.32	5.91 6.02	4.84 4.96	22.71 22.69	— —)	799, 909, 1200, 1265, 1490, 1690, 2933, 3010	1.25 (t, 6H, 2 × CH_2**CH_3**), 3.70 (q, 2H, **CH_2**CH_3), 4.10 (q, 2H, **CH_2**CH_3), 4.65 (s, 2H, CH_2–Ar), 5.88 (s, 2H, OCH_2O), 7.6 (m, 3H, Ar–H)
2f	Oil	70	$C_{14}H_{19}Ns_2$	63.32 (63.32	7.21 7.21	5.19 5.19	24.21 24.21	— —)	669, 914, 969 1225, 1340, 1490, 1660, 2980, 3028	1.30 (t, 6H, 2 × CH_2**CH_3**), 3.72 (q, 2H, **CH_2**CH_3), 4.13 (q, 2H, **CH_2**CH_3), 4.27 (d, 2H, CH_2S), 5.85 (m, 1H,=**CH**CH_2, 6.50 (d, 1H, =**CH**Ar), 7.5 (m, 5H, Ar–H)
2g	236–240/ 760mm (decomp.)	83	$C_{23}H_{47}NS_2$	68.91 (68.82	11.81 11.72	3.38 3.49	16.04 15.96	— —)	729, 774, 854 1215, 1350, 1465, 2847, 2927	1.16 (t, 6H, 2 × CH_3), 1.26 (m, 35H, $CH_3CH_2)_{16}$, 3.74 (q, 4H, 2 × NCH_2), 4.34 (t, 2H, Ch_2S)
2h	252/760mm (decomp.)	78	$C_{18}H_{36}N_2S_4$	53.03 (52.94	8.77 8.82	6.81 6.86	32.43 31.37	— —)	734, 768, 1220, 1345, 1465, 2820, 2947	1.27 (t, 12H 4 × CH_2**CH_3**), 3.58 (q, 8H, 4 × **CH_2**-CH_3), 4.15 (m, 12H, $(CH_2)_6$), 4.50 (t, 4H × SCH_2)
2i	215/760mm	78	$C_{23}H_{45}NOS_2$	66.61 (66.50	10.91 10.84	3.28 3.37	15.51 15.42	— —)	740, 850, 960 1030, 1110, 1155, 1230, 1345, 1375, 1450, 1610, 2940, 3350	0.81 (d, 3H, CH_3), 1.30 (t, 6H, 2 × CH_2CH_3), 1.40–1.80 (m, 10H), 1.9–2.2 (m, 16H), 2.5–2.8 (m, 3H), 3.8 (q, 2H, **CH_2**CH_3), 4.15 (1, 2H, **CH_2**CH_3), 5.5 (m, 2H)
2j	241/760mm (decomp.)	81	$C_{13}H_{22}NOS_2F_3$	47.58 (47.42	6.78 6.69	4.18 4.26	19.51 19.45	17.41 1733)	830, 950, 1020 1180, 1220, 1340, 2880, 3400	1.25 (s, 3H), 1.27 (s, 3H), 1.30 (t, 6H), 1.39 (d, 3H), 1.76 (dd, 1H), 2.06 (dd, 1H), 2.12 (br, 1H), 3.12 (m, 1H), 3.76 (1, 2H), 4.08 (q, 2H)
2k	94	87	$C_{14}H_{16}NO_2S_2F_2$	47.77 (47.86	4.63 4.55	4.08 3.98	18.14 18.23	16.28 16.33)	760, 810, 920 1020, 1140, 1225, 1740, 2840	1.31 (t, 6H, 2 × CH_2**CH_3**), 3.78 (q, 2H, **CH_2**CH_3), 4.15 (q, **CH_2**CH_3), 4.65 (s, 2H, CH_2Ar), 7.8 (d, 2H, Ar–H), 7.92 (d, 2H, Ar–H(