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# ONE-STEP STEREOSPECIFIC CONVERSION OF ALCOHOLS INTO DITHIOCARBAMATES : A SMOOTH PATHWAY FOR THE INTRODUCTION OF A SULPHUR FUNCTIONALITY[1]

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Summary: Functionnally diverse dithiocarbamates were prepared from the corresponding alcohols in a mild high-yielding one-pot synthesis involving unexpensive ziram (zinc N,N-dimethyldithio carbamate) in a stereospecific Mitsunobu type procedure.

The dithiocarbamoyl moiety was shown to be a very useful synthetic tool[2,3] and a good precursor to thiols and other sulphur functionalities[4]. Traditional preparative methods for dithiocarbamates usually require the interaction of a dithiocarbamate anion with an electrophilic substrate such as an alkyl halide or an aryldiazonium salt[5].

Taking advantage of recent results[6] dealing with the reactivity of zinc salts in the Mitsunobu reaction, we have developed a very mild and efficient procedure for the conversion of functionnally diverse alcohols into the corresponding N,N-dimethyldithiocarbamates[7]. Various primary dithiocarbamates prepared according to the present method are listed in Table I. Moreover, miscellaneous chiral secondary alcohols were submitted to the same reaction in order to ascertain the epimerization of the activated carbon that is associated with the Mitsunobu mechanism[6] ( Table II ).

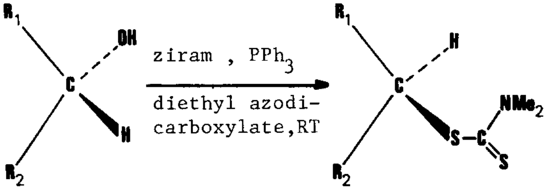


Table I : Primary dithiocarbamates ($R_1$= H)

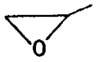
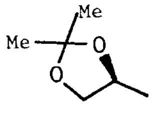
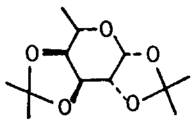
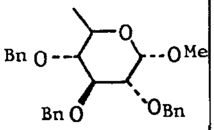
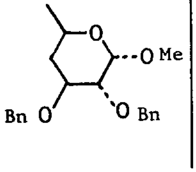
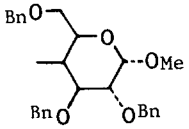
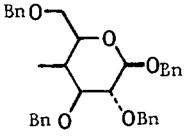
| $R_2$ | yield | $\alpha_D^{20}$(c,$CHCl_3$) | ref. | $R_2$ | yield | $\alpha_D^{20}$(c,$CHCl_3$) | ref. |
|---|---|---|---|---|---|---|---|
| Ph | 92% | - | 8 | (E) PhCH=CH- | 95% | - | 8,9 |
| $Br(CH_2)_5$- | 89% | - | - |  | 85% | - | 10 |
|  | 87% | -9.2°(3.41) | 10 |  | 92% | -27°(1.43)<br>(mp.124-5°C) | 11 |
|  | 90% | +37°(1.26)<br>(mp.105-6°C) | 12 |  | 91% | +62.5°(2.42) | 13 |

Table II : Chiral secondary dithiocarbamates

| $R_1$, $R_2$ | yield | $\alpha_D^{20}$(*c*,$CHCl_3$) | ref. |
|---|---|---|---|
| Me , COOEt | 80% | +70.5°(3.82) | 14 |
| 3-neomenthyl | 86% | +32.5°(2.37)<br>(mp.90-1°C) | 6 |
| 3-α -cholesteryl | 87% | -11.5°(2.04)<br>(mp.161-2°C) | 8 |

| $R_1$, $R_2$ | yield | $\alpha_D^{20}$(*c*,$CHCl_3$) | ref. |
|---|---|---|---|
|  | 78% | +71°(3.71) | 15 |
|  | 81% | +6°(4.14) | 16 |

$^1$H Nmr(300 MHz) data together with optical rotation measurements bring full confirmation of the stereospecificity in this nucleophilic inversion[14]. Such zinc salt-mediated stereospecific functionalizations of various types are currently under investigation.

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## References and Notes

1. Part of this work is accepted for presentation at the 12th International Symposium on the Organic Chemistry of Sulfur, Nijmegen (Holland),30th june-4th july 1986.
2. T.Hayashi and H.Midorikawa, Synthesis, 100 (1984).
3. T.Hayashi, I.Hori and T.Oishi, J.Am.Chem.Soc., 105, 2909 (1983) and ref. cited therein.
4. J.L.Wardell, in "The Chemistry of the Thiol Group" by S.Patai, John Wiley and sons, 1974 p.519.
5. W.Walter and K.D.Bode, Angew.Chem.Int.Ed., 6, 281 (1967).
6. P.Rollin, Synthetic Commun., 16, 611 (1986) and ref. cited therein.
7. In a typical experiment, diethyl azodicarboxylate (DEAD, 2mmol) was added dropwise at 0°C to a stirred dry toluene suspension containing the alcohol (1 mmol), triphenylphosphine (2 mmol) and ziram (0.75 mmol ; 1.5 equiv.); after the reaction was complete, purification was effected by direct silicagel column chromatography. For lower solubility substrates, THF could advantageously replace toluene.
   All new compounds gave consistent IR, MS and Nmr data.
8. K.Hojo, H.Yoshino and T.Mukaiyama, Chemistry Letters, 437 (1977).
9. Substitution took place exclusively at C-1 of (E)-cinnamyl alcohol and no regio-isomeric dithiocarbamate ($S_N2'$) was detected.
10. Commercially available racemic glycidol and (+)-2(S),3-O-isopropylideneglycerol were used as precursors.
11. The synthesis of glycosyl dithiocarbamates was pioneered by Professor S.Tejima's group; see for instance S.Tejima and S.Ishiguro, Chem.Pharm.Bull., 15, 255 (1967).
12. Hydroxyl precursor synthesized according to A.Liptak, I.Jodal and P.Nanasi, Carbohydrate Res., 44, 1 (1975).
13. (cf.ref.12) J.M.Lancelin, Doct.Thesis, Orléans, 1985.
14. G.Nachmias, Ann.Chim.(Paris), 7, 584 (1952). The conversion of (-)-(S)-ethyl lactate to the corresponding (+)-(R)-dithiocarbamate was ascertained by examination of the known correlated carboxylic acid : A.Fredga and A.Bjorn, Arkiv Kemi, 23, 91 (1964).
15. (cf.ref.12) P.J.Garegg and H.Hultberg, Carbohydrate Res., 93, C 10 (1981).
16. (cf.ref.12) J.M.Petit and P.Sinaÿ, Carbohydrate Res., 64, 9 (1978).

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