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THE USE OF DITHIOESTERS AS ACYL ANION EQUIVALENTS. DOUBLE HOMOLOGATION OF THE "$\overset{\ominus}{C}H_2-\overset{\ominus}{C}=O$" SYNTHON.

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The concept of "umpolung" has had a dramatic effect upon synthetic methodology since its initial introduction by Corey and Seebach in 1965.[1] Since that time, there has been considerable activity aimed at devising and utilizing reagents wherein this reverse polarity allows C-C bond formation hitherto inaccessible. The great majority of umpolung reagents employed for this purpose involve sulfur compounds acting as masked acyl anions.[2] We now report that readily available dithioesters,[3] 1, known to undergo thiophilic addition[4] with Grignard reagents, furnish magnesiodithio acetals 2 which react with a variety of electrophilic reagents (E) leading to the dithioketals 3. The latter are simply masked carbonyl derivatives which may be released to 4 with mercuric chloride or other standard procedures. A representative number of examples are provided in Table 1. An extensive study[4] on the carbophilic and thiophilic addition of Grignard reagents to dithioesters has been reported, however, except for the addition of reactive halides (MeI, crotyl bromide) and water to 3, no survey of the synthetic potential was described. A recent paper has

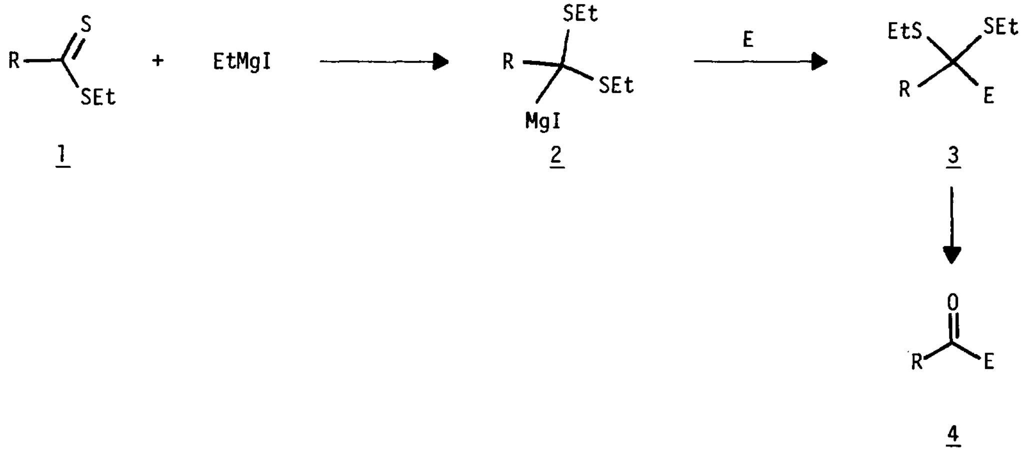
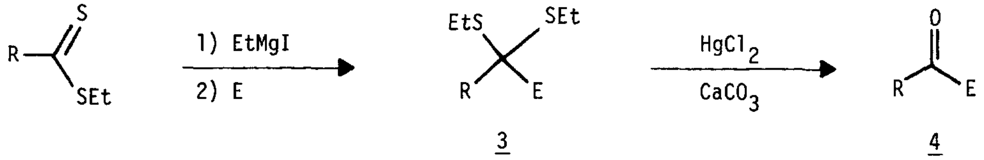
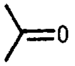
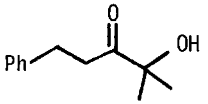
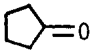
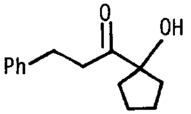
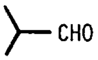
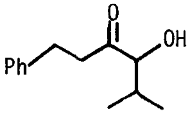
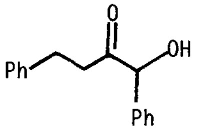
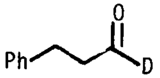
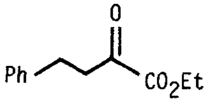


TABLE 1



R	E	% 3[a,c]	4 (%)[a,d,e]	
$PhCH_2CH_2$		70		(79)
"		51		(58)
"		58		(90)
"	PhCHO	55		(61)
"	D_2O	95		(65)
"	$ClCO_2Et$	60[d]		(18)
n-C_3H_7	$ClCO_2Et$	70[d]	b	
"	CO_2	80	b	

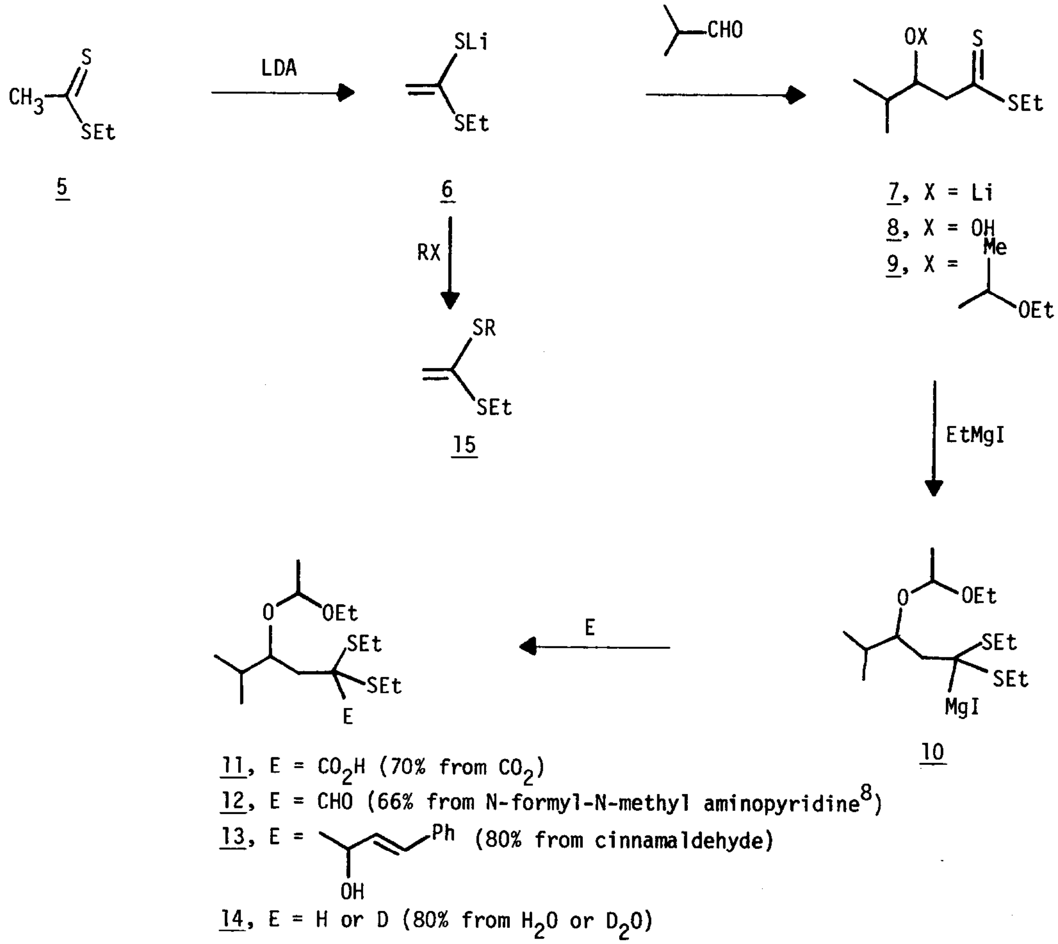
a) All yields are for isolated, pure, material obtained from preparative layer chromatography (*silica gel, 5-15% ethylacetate-hexane*). *Structures are consistent with all* spectral *and* elemental analyses. Since all reactions were carried out on 1-3 mmol scale and most experiments performed only once, the yields have not been examined for optimization; b) Hydrolysis not performed; c) Reactions performed in THF at -20° using 2.0 equiv EtMgI. Completion of the thiophilic addition

TABLE 1 - Footnotes (Continued)

was determined by tlc (SiO_2-hexane) and usually took 2-5 hr. Addition of the electrophile (2.0 equiv) at -20° was followed by tlc (SiO_2, 5% EtOAc-hexane) and usually was complete within 5 hr; d) Obtained by adding magnesio dithioacetal solution to the chloroformate at -78° and warmed to -20° for 2 hr; e) Hydrolysis performed with $HgCl_2$-$CaCO_3$ buffer; E. J. Corey and B. W. Erickson, *J. Org. Chem.*, 36, 3553 (1971).

described the synthetic potential of carbophilic addition of allylic Grignards to dithioesters leading to β,γ-unsaturated ketones.[5]

The current work was extended to a double-electrophilic homologation by employing the simple derivative, ethyl dithioacetate 5. Metallation of dithioesters is well known to give the thioenolate 6 and subsequent introduction of alkyl halides give ketene dithioacetals (15).[6] However, reaction of 6 with carbonyl compounds (THF, -78°) gave adducts 7, which upon quenching led to



11, E = CO_2H (70% from CO_2)

12, E = CHO (66% from N-formyl-N-methyl aminopyridine[8])

13, E = (80% from cinnamaldehyde)

14, E = H or D (80% from H_2O or D_2O)

β-hydroxy dithio esters **8** in excellent yields ($\sim$90%).[7] To continue the process of homologation, the hydroxyl group was transformed to its ethoxy ethyl ether **9** (*p*-TsOH, excess ethyl vinyl ether, 25°, 25 min) and treated with ethylmagnesium iodide (2.0 eq, THF, -20°, 5 hr) to produce the magnesio-dithioacetal **10**. A series of electrophiles was added (-20°) to furnish the elaborated thioketals **11**-**14**. In this fashion, the conversion of **5** to **11**-**14** is tantamount to the double homologation of the E_1,E_2-synthon "$\overset{\ominus}{\mathrm{C}}\mathrm{H}_2-\overset{\ominus}{\mathrm{C}}=\mathrm{O}$", a species conspicuously absent from Seebach's review.[2]

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