

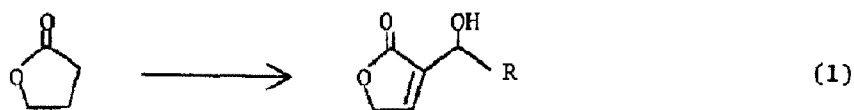
A NEW APPROACH TO SULFENYLATED ENOLATES

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ABSTRACT:

Bissulfonylation followed by monodesulfonylation with a Grignard reagent cleanly provides magnesium enolates of α -phenylthiocarbonyl compounds for aldol condensation.

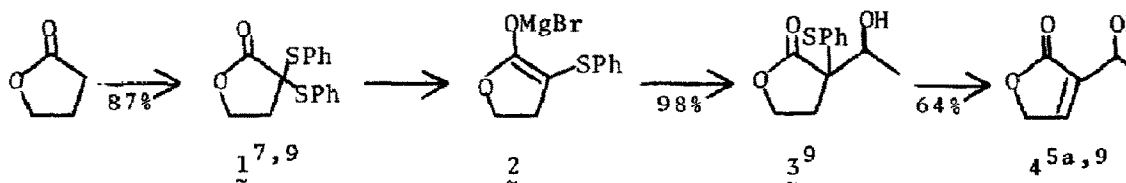
In conjunction with our investigation into a total synthesis of allamandin^{1,2} we required the transformation outlined in eq 1. We envisioned reaction of the enolate of a sulfonylated lactone³ with an aldehyde followed by oxidation to the



sulfoxide and thermolysis to the olefin. Aldol reactions of the sulfonylated enolates have previously been noted for their tendency for reversibility.⁴ Indeed attempts to execute such a scheme using typical conditions to generate the enolate of the sulfonylated lactone with lithium dialkylamide bases followed by quenching with an aldehyde (with or without the addition of zinc or magnesium salts) led to equivocal results. In this letter we wish to report a new generation of magnesium enolates of sulfonylated carbonyl partners and their exploitation for the transformation outlined in eq 1.⁵

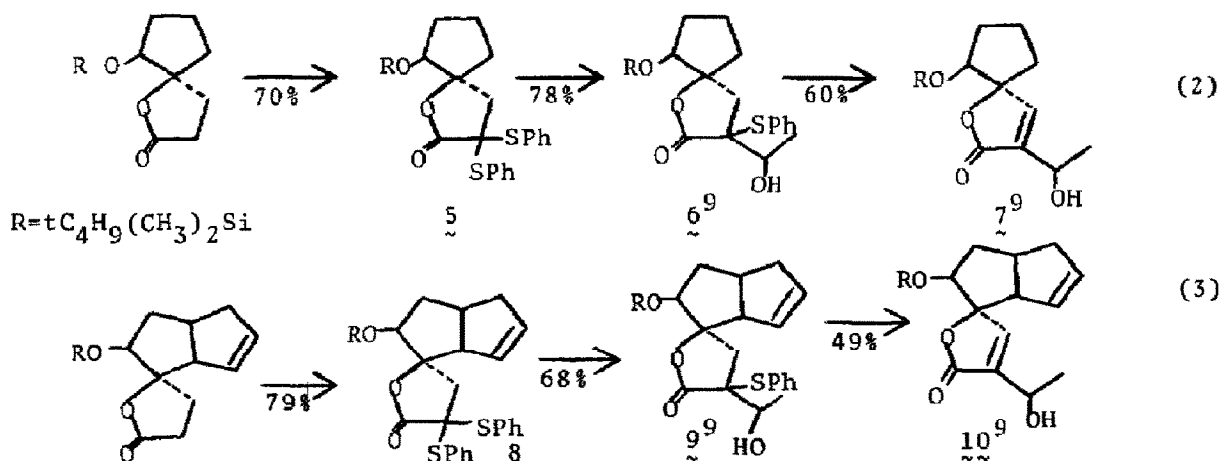
Bissulfonylation of γ -butyrolactone^{3,6-8} [$\text{LiN}(\text{C}_2\text{H}_5)_2$, 2 eq PhSSO_2Ph , THF, -78°] gave cleanly 1 (δ 4.1, t, 2H, $J=6\text{Hz}$; δ 2.4, t, 2H, $J=6\text{Hz}$, ir 1780cm^{-1}). Addition of ethylmagnesium bromide in ether to a -10° solution of 1 in THF gave a suspension of the magnesium enolate 2.¹⁰ Distilling in excess acetaldehyde at -10° led to a clear solution. Work-up gave a virtually quantitative yield of the aldol adduct 3 as a 2:1 diastereomeric ratio [determined by methyl doublets ($J=6.5\text{Hz}$) at δ 1.3 and 1.2]. Oxidation (MCPBA, CH_2Cl_2 , -78°) followed immediately by thermolysis in refluxing carbon tetrachloride³ (CaCO_3) gave the desired α -hydroxyalkyl

γ -butenolide [ir 3600, 3500, 1760 cm^{-1} ; nmr δ 7.25 (1H, m, $J=1.3\text{Hz}$), 4.8 (2H, 4.68 (1H, m), 2.9 (1H, b_s), 1.4 (3H, d, $J=7\text{Hz}$).



The Grignard reagent served as a nucleophile towards sulfur, not the carbonyl group, to give a clean mixture of the magnesium enolate contaminated only by ethylphenylsulfide. This method differs from conventional approaches in that no amine base is present; therefore, the system lacks a coordinating reagent to reduce the Lewis acidity of the chelating metal.

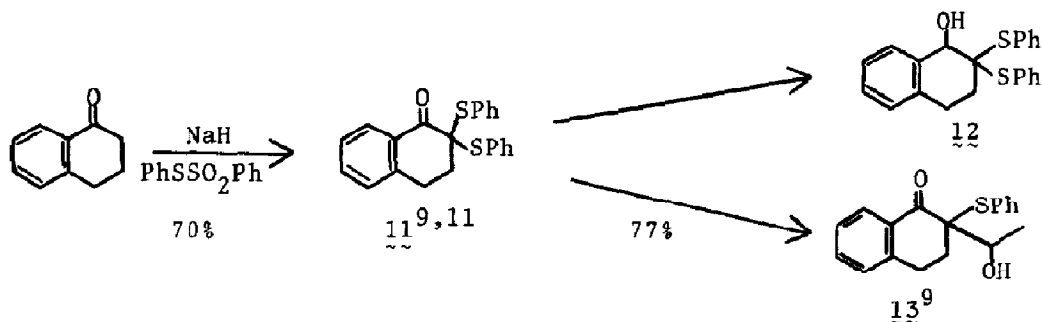
The success of this approach is illustrated by the examples in eq 2-3. Formation of 5 and 8 lithium diisopropylamide was employed. Aldol condensation proceeded smoothly under the above conditions; whereas, attempts to synthesize 6 via conventional routes failed. Nmr suggests that 6 is a 1:1 diastereomeric



mixture (two methyl doublets at δ 1.3 and 1.2, $J=6\text{Hz}$). That the center bearing the hydroxyl group rather than that bearing sulfur is the source of the stereoheterogeneity is suggested by the fact that the elimination product 7 remains 1:1 diastereomeric mixture (two doublets at δ 7.28 and 7.20, $J=1.5\text{Hz}$ for the ν proton and δ 1.55 and 1.50, $J=6.6\text{Hz}$ for the methyl group). On the other hand,

9 was a 6:1 diastereomeric mixture from which the major isomer was separated, mp 119-121°. Thus, good diastereoselectivity can be seen with these magnesium enolates. Dehydrosulfenylation of this isomer generated a homogeneous butenolide 10 [ir 1750cm^{-1} ; nmr δ 7.0, 1H, d, $J=1.5\text{Hz}$; 4.7, 1H, q. d., $J=7, 1.5\text{Hz}$; 4.1, 1H, dd, $J=11, 7\text{Hz}$; 1.5, 3H, d, $J=7\text{Hz}$].

We explored the extension of this chemoselective method to enolates of β -ketosulfides in which the competition for attack at the carbonyl group versus the



sulfide would be even more severe. In this case, bissulfenylation proceeded smoothly with sodium hydride in THF at r.t.^{3,6,8} Reaction of 11 with ethylmagnesium bromide led only to the reduction product 12 and use of methylmagnesium bromide gave 13 in only 10% yield. However, use of methylmagnesium bromide and 5 mol% of cuprous bromide-dimethylsulfide followed by acetaldehyde led to the aldol product 13 in good yield as a 3.5:1 diastereomeric mixture [two doublets, $J=7\text{Hz}$, at δ 1.3 and δ 1.05]. Thus, it appears that this method represents a general and convenient approach to enolates of α -phenylthiocarbonyl compounds free of complicating agents.¹²

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