Tetrahedron Letters,Vol.23,No.34,pp 3511-3512,1982 0040-4039/82/343511-02$03.00/0
Printed in Great Britain

A ONE-STEP SYNTHESIS OF 2-PHENYLTHIO-2-BUTEN-4-OLIDES.

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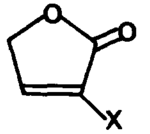
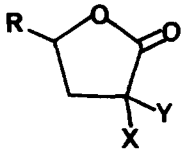
Abstract : The title compounds are prepared by the reaction of an α-acetoxy aldehyde with ethyl phenylthioacetate.

Interest in 2-buten-4-olides stems from their existence in nature[1] and their use as synthetic intermediates[2]. Several Michael additions on compounds **1** and **2** have been reported[3-6] with nucleophiles such as ethyl acetoacetate, organocuprates, ethyl malonate, cyclohexanone, etc.



1 X= SPh
2 X= SOPh

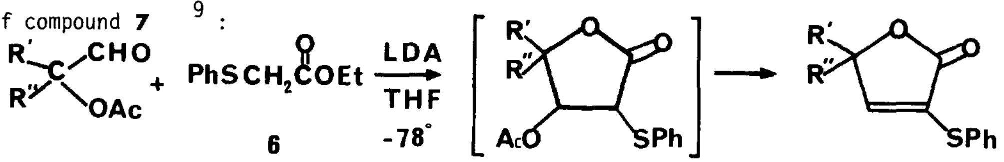


3 X=SPh , Y=H
4 X=SOPh, Y=OAc

R= H, CH$_3$

The described methods of synthesis of compounds **1** and **2** [4,5,7] involve several steps sequences : synthesis of the α-phenylthio-γ-butyrolactone **3** , Pummerer rearrangement with acetic anhydride giving **4** , followed by HOAc elimination and some elimination of phenylsulfenic acid, for instance[5,7].

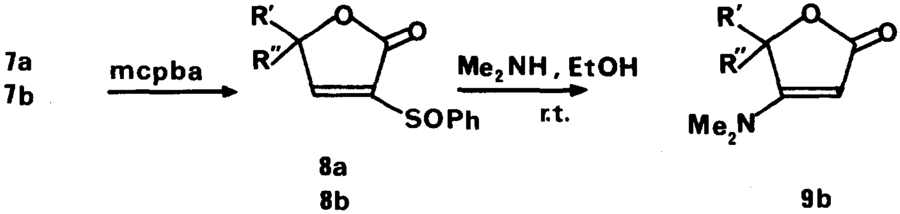
Our interest in the synthesis of β-hydroxy- and β-acetoxy-α-methylene-γ-butyrolactones[8] and a need for 3-dimethylamino-2-buten-4-olide **9** led us to develop a simple one-step synthesis of compound **7** [9] :



5a R'=R''= CH$_3$
5b R'=R''= $-(CH_2)_5-$

7a
7b

The α-acetoxyaldehydes **5** were obtained[8] from aldehydes with an α-hydrogen. The ethyl α-phenylthioacetate[10] anion obtained with LDA in THF was reacted on aldehyde **5** and hydrolyzed at -78°. Lactone **7** was obtained directly (70% yield). The desired 3-dimethylaminobutenolide **9** was subsequently prepared by oxidation of sulfide **7** into sulfoxide **8** [11], (> 90% yield) followed by reaction with dimethylamine in ethanol[12] (60 % yield) :



REFERENCES AND NOTES.

1. P.G. Marshall in Rodd's *Chemistry of Carbon Compounds*, 2nd Ed., vol. II, part D, S. Coffey editor, Elsevier, New York, 1970, p. 369, E. Demole, D. Berthet, *Helv.Chim. Acta*, 55, 1866 (1972)
2. E.J. Corey, C.U. Kim, R.H.K. Chen, M. Takeda, *J. Amer. Chem. Soc.*, 94, 4395 (1972), R.E. Damon, R.H. Schlessinger, *Tetrahedron Letters*, 4551 (1975) ; H. Kosugi, S. Shiguchi, R. Sekita, H. Uda, *Bull. Soc. Chem. Japan*, 49, 520 (1976).
3. R.N. Gandhi, J.S.E. Holker, M.J. Wright, *J. Chem. Research (S)*, 384 (1981)
4. K. Iwai, H. Kosugi, H. Uda, *Chem. Letters*, 1237-1240 (1974) ; 981-982 (1975)
5. K. Iwai, H. Kosugi, H. Uda, M. Kawai, *Bull. Soc. Chem. Japan*, 50, 242-247 (1977)
6. M. Watanabe, K. Shirai, T. Kumanoto, *Chem. Letters*, 855-858 (1975)
7. H.J. Monteiro, A.L. Gemal, *Synthesis*, 437-438 (1975)
8. J.P. Corbet, C. Benezra, *J. Org. Chem.*, 46, 1141-1147 (1981) ; P. Barbier, C. Benezra *J. Org. Chem.*, submitted.
9. Sulfides **7**a were prepared in the following way : at -78°C was generated LDA (0.023 mol) thioether **6** (0.023 mol) was added 25 mn later in THF (90 mL) and the mixture was stirred for 30 mn. The α-acetoxyaldehyde **5** ($R=R'=CH_3$ or $R=R'=-(CH_2)_5-$, 0.024 mol) in THF (10 mL) was then added to the reaction mixture which was stirred for 1h at -78°C. Hydrolysis of the reaction mixture with NH_4Cl (saturated solution) and extracted (70% isolated yield). Compound **7**a mp 71-72° : ^1H NMR ($CDCl_3$) : 1.43 (s, 6H), 6.55 (s, 1H) 7.30-7.70 (m, 5H) : IR ($CHCl_3$) 1750, 1770, 1600 cm^{-1}, MS 220 ($M^{+\cdot}$) Anal. Calcd for $C_{12}H_{12}O_2S$: C 65.45 H 5.45 S 14.55. Fd C 65.21 H 5.51 S 14.15 ; Compound **7**b : mp 89-90° ; ^1H NMR ($CDCl_3$) : 1.62 (br,s 10H), 6.62 (s, 1H), 7.30-7.60 (m, 5H) ; IR ($CHCl_3$) : 1755, 1590, MS 260 ($M^{+\cdot}$). Anal. Calcd for $C_{15}H_{16}O_2S$: C 69.23, H 6.15, S 12.31. Fd C 69.08 H 6.18 S 12.25.
10. K. Iwai, H. Kosugi, A. Miyazakin, H. Uda, *Synthetic Communications*, 6, 357-363 (1976).
11. Sulfoxides **8** were obtained from sulfides **7** by oxidation with m-chloroperbenzoic acid. Compound **8**a : mp 88-89° ; ^1H NMR ($CDCl_3$) : 1.44, 1.56 (2s, 6H), 7.94 (s, 1H), 7.40-8.30 (m, 5H) ; IR ($CHCl_3$) : 1760 ; MS 236 ($M^{+\cdot}$). Anal. Calcd for $C_{12}H_{12}O_3S$: C 61.02 H 5.08 Fd C 59.77 H 5.05.Sulfoxide **8**b mp 133-134° ; ^1H NMR ($CDCl_3$) : 1.40-1.90 (m, 10H), 7.40-7.95 (m, 5H), 8.03 (s, 1H), IR ($CHCl_3$) : 1760, MS 276 ($M^{+\cdot}$). Anal. Calcd for $C_{15}H_{16}O_3S$: S 11.59 , Fd S 11.52
12. Sulfoxides **8**b (1.45 mmol) in ethanol (10 mL) was treated with an excess Me_2NH (14.5 mmol) at rt for a week. The solvent was removed under vacuum and the crude was chromatographed on a silica gel column. Elution with ether-ethanol 95:5 gave enamine **9**b (0.90 mmol, 60% yield). Enamine **9**b : mp 98-99°, ^1H NMR ($CDCl_3$) : 1.60-2.0 8(m, 10H), 3.04 (s, 6H) , 4.46 (s, 1H) ; IR ($CHCl_3$) : 1725, 1710, 1600, MS 195 ($M^{+\cdot}$). Anal. Calcd for $C_{11}H_{17}NO_2$: C 67.69, H 8.72, N 7.18. Fd : C 67.68, H 8.73, N 7.24.

(Received in UK 22 June 1982)