

NEW PREPARATION OF α -ALLENIC KETONES

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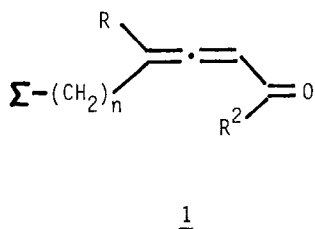
Summary. The ketal aldehyde 2 is the starting material of a two-step synthesis of α -allenic ketones 1 γ -substituted with a functionalized chain.

α -Allenic ketones are versatile building blocks because of the facility with which they give 1,2 or 1,4 -addition with diverse nucleophiles (1) and of their ability to be efficient dienophiles in (4+2) cycloadditions (2). Recently, their conversion into 3(2H) furanones has been reported (3). From the biological point of view, the conjugated α -allenic carbonyls can promote an irreversible inhibition of certain enzymes (4), probably via a Michael attack of a nucleophilic part of it.

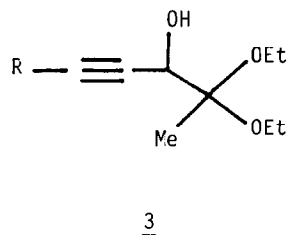
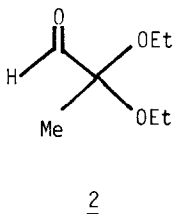
In a program aiming at the synthesis of such inhibitors for the enzymes involved in the metabolism of polyamines (5), we became interested in the preparation of 1,3-functionalized allenic derivatives (6). In this letter we report a new synthesis of γ -substituted α -allenic ketones of general formulae 1.

Known methods leading to α -allenic ketones (7) appeared unsuitable for the synthesis of our compounds. It seemed to us that the ketal-aldehyde 2 could be a good starting material for such purpose : it can be easily prepared from ethyl pyruvate (8) and it possesses an aldehydic group which can be transformed into α -acetylenic alcohols 3. These could be precursors of allenic linkage since many methods for preparing allenic compounds involve a propargylic-allenic transposition of a propargylic alcohol derivative (halide, ester, ether...) (7b,c).

Consequently, 2 was treated with several lithium acetylides leading to alcohols 3 with fairly good yields.



(Σ = functional group)



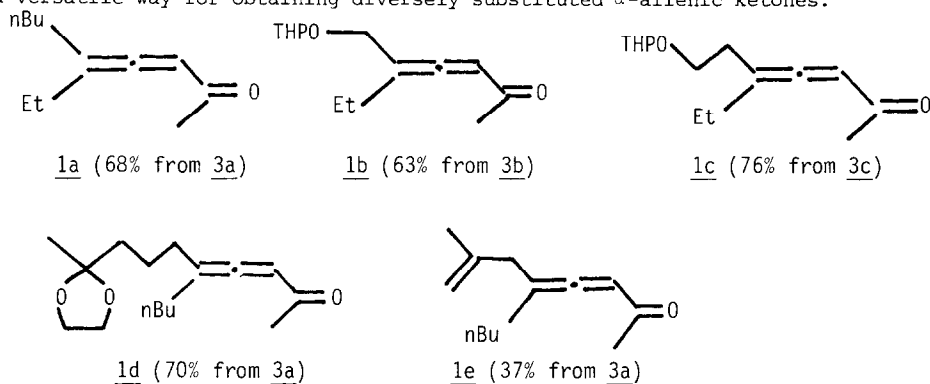
3a R = nBu (83%)

3b R = THPOCH₂- (69%)

3c R = THPOCH₂CH₂- (82%)

Thus, alcohols 3 were quantitatively transformed into their mesylates (mesyl chloride, triethylamine, 0°, in methylene chloride) and allowed to react with a large excess (4 molar equivalents) of an organo-copper species prepared, according to (10), by addition of 4 molar equivalents of cuprous bromide to a Grignard reagent in tetrahydrofuran at -30°. α -Allenic ketals are the only isolated products of that reaction and they are hydrolyzed into allenic ketones 1 during the purification step on silica gel (11).

The following examples are representative of our results which constitute a fast and versatile way for obtaining diversely substituted α -allenic ketones.



The investigation of the synthetic utility of these ketones as well as the determination of their biological activity are currently in progress.

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REFERENCES

1. a) M.BERTRAND and J.LE GRAS, *Bull.Soc.chim.Fr.*, 1962, 2136. b) J.BERLAN, J.P.BATTIONI and K.KOOSHA, *Tetrahedron Letters*, 1976, 3355. c) M.BERTRAND, G.GIL and J.VIALA, *Tetrahedron Letters*, 1977, 1785. d) J.C.CLINET and G.LINSTRUMELLE, *Nouv. J. Chimie*, 1977, 1, 373.
2. a) J.L.GRAS, *J.Chem.Research (S)*, 1982, 300 (M) ; 1982, 3032. b) J.L.GRAS and A.GUERIN, *Tetrahedron Letters*, 1985, 26, 1781.
3. S.WOLFF and W.C.AGOSTA, *Tetrahedron Letters*, 1985, 26, 703.
4. a) D.F.COVEY and C.H.ROBINSON, *J.Amer.Chem.Soc.*, 1976, 98, 5038. b) T.F.TAM, R.W.SPENCER, E.M.THOMAS, J.J.COPP and A.KRANTZ, *J.Amer.Chem.Soc.*, 1984, 106, 6849.
5. A.DOUTHEAU, J.GORE and G.QUASH, *French Pat.N°83-12863* (1983) and *European Pat, N°84-401627* (1984).
6. A.DOUTHEAU, A.SABA, J.GORE and G.QUASH, *Tetrahedron Letters*, 1982, 23, 2461.
7. a) M.HUCHE, *Tetrahedron*, 1980, 36, 331. b) S.R.LANDOR, *The Chemistry of the Allenes*, Academic Press, 1982. c) S.PATAI, *The Chemistry of Ketenes, Allenes and related Compounds*, J.Wiley and Sons, 1980.
8. F.HUET, M.PELLET, A.LECHEVALLIER and J.M.CONIA, *J.Chem.Res.(S)* 1982, 246 (M) 1982, 2528.
 The yield of 2 can be improved by the use of Swern's method (9) in the oxidation step (92%).
9. A.J.MANCUSO, S.H.HUANG and D.SWERN, *J.Org.Chem.*, 1978, 43, 298.
10. P.VERMEER, J.MEIJER and L.BRANDSMA, *Rec.Trav.Chim.*, 1975, 94, 112.
11. The analytical data for ketones 1 as well as alcohols 3 are in accordance with the depicted structures.

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