HETEROCYCLES, Vol 15, No 1, 1981

A NEW SYNTHESIS OF 3(2H)-FURANONES FROM KETONES

Tamejiro Hiyama,* Masaki Shinoda, Hiroyuki Saimoto, and Hitosi Nozaki
Department of Industrial Chemistry, Kyoto University, Yoshida, Kyoto 606, Japan

Ketones are allowed to react with the lithium salt of propynal diethyl acetal and the resulting adducts are treated with sulfuric acid-methanol (1:1) to give the title compounds.

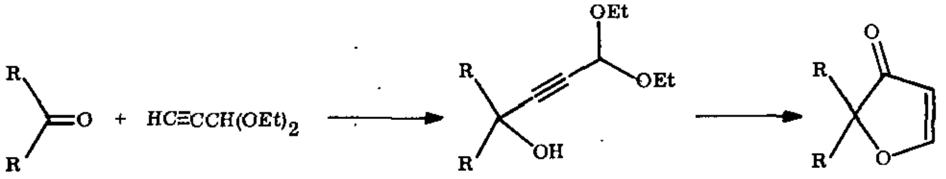
We wish to report a facile two-step procedure for the synthesis of 3(2H)-furanones[1,2,3] based on the acid-catalyzed ring closure of propynal diethyl acetal adduct of ketones.

Ketone I was allowed to react with the carbanion of propynal diethyl acetal (II) to give the adduct III which was in turn dissolved in methanol and treated with sulfuric acid at 0°C. Both hydration of the triple bond and deacetalization took place spontaneously to yield 3(2H)-furanone IV having characteristic spectral properties (IR: two strong absorptions near 1700 and 1560 cm^{-1}, PMR: two doublets around δ 5.4 and 8.1). The results are given in the order of ketone, III (% yield), and IV (% yield): acetone, IIIa (64), IVa (98); cyclohexanone, IIIb (99), IVb (67, 59[4]); cyclododecanone, IIIc (79), IVc (70). Thus, the new method is applicable to both acyclic and cyclic ketones. The adduct of II and heptanal, however, gave a complex mixture of products under the above cyclization condition.

Formation of 3(2H)-furanone from III is remarkable in respect that the propargylic tertiary hydroxyl group in III stands against dehydration in contrast to the acid-catalyzed cyclopentenone synthesis from propargyl alcohol dianion adduct of ketones.[5] Thus, the intermediate Va or Vb should be responsible for the III ⟶ IV transformation according to the Baldwin's rule[6] (5-exo-trig, allowed).[7]

Following experimental procedure for IVc is typical: To a THF (10 ml) solution of II (0.96 g, 7.5 mmol) was added butyllithium hexane solution (1.85 M, 7.5 mmol) at -78°C. After 10 min cyclododecanone (0.91 g, 5.0 mmol) dissolved in THF (7 ml) was added in 15 min. Stirring at -78°C for 1 h and at r.t. for 30 min followed by work-up and column chromatography (silica gel, hexane-ether 5:1) gave IIIc (1.22 g, 79% yield).

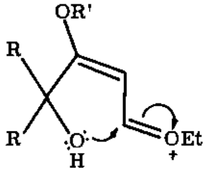
The adduct IIIc (0.22 g, 0.71 mmol) was dissolved in methanol (1.0 ml) and cooled at 0°C. To this solution was added 98% sulfuric acid (1.0 ml) dropwise over 10 min. After the addition was completed, the reaction mixture was stirred for 30 min and worked up. Preparative TLC purification (silica gel, hexane-



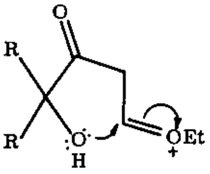
I II III IV

a: R = Me, b: R,R = -(CH$_2$)$_5$-, c: R,R = -(CH$_2$)$_{11}$-

ether 1:1, R_f 0.33–0.47) gave IVc (0.117 g, 70% yield), mp 81.0–81.5°C (hexane), IR (Nujol): 1709, 1684, 1567 cm^{-1}, PMR (CCl_4): δ 5.43 (d, J = 2.7 Hz), 8.04 (d, J = 2.7 Hz), MS: m/e 236 (M^+), Found: C, 75.92; H, 10.23%.



Va



Vb

R' = H or Me (or $COCF_3$)

REFERENCES AND NOTES

1. Biologically active natural products having a 3(2H)-furanone moiety: (a) bullatenone: W. Parker, R. A. Raphael, and D. I. Wilkinson, J. Chem. Soc., **1958**, 3871; A. Takeda, S. Tsuboi, and T. Sakai, Chem. Lett., **1973**, 425. (b) jatrophone: S. M. Kupchan, C. W. Sigel, M. J. Matz, C. J. Gilmore, and R. F. Bryan, J. Am. Chem. Soc., **98**, 2295 (1976). (c) a metabolite of stremphylium radicinum: J. F. Grove, J. Chem. Soc. C, **1971**, 2261. (d) a flavor component of pineapple: D. W. Henry and R. M. Silverstein, J. Org. Chem., **31**, 2391 (1966).
2. Application of 3(2H)-furanone for synthesis: (a) R. Noyori, Y. Hayakawa, S. Makino, N. Hayakawa, and H. Takaya, J. Am. Chem. Soc., **95**, 4103 (1973). (b) Z. Lysenko, F. Ricciardi, J. E. Semple, P. C. Wang, and M. M. Joullie, Tetrahedron Lett., **1978**, 2679. (c) S. W. Baldwin and J. M. Wilkinson, ibid., **1979**, 2657. (d) A. B. Smith, III and P. J. Jerris, Synth. Comm., **8**, 421 (1978); Tetrahedron Lett., **1980**, 711. (e) A. B. Smith, III and R. M. Scarborough, Jr., ibid., **1978**, 4193.
3. Methods for 3(2H)-furanone synthesis: (a) C. Venturello and R. D'Aloisio, Synthesis, **1977**, 754. (b) P. K. Gupta, J. G. Ll. Jones, and E. Caspi, J. Org. Chem., **40**, 1420 (1975). (c) P. Margaretha, Tetrahedron Lett., **1971**, 4891. (d) F. Sher, J. L. Isidor, H. R. Taneda, and R. M. Carlson, ibid., **1973**, 577. (e) B. K. Carpenter, K. E. Clemens, E. A. Schmidt, and H. M. R. Hoffmann, J. Am. Chem. Soc., **94**, 6213 (1972). (f) H. M. R. Hoffmann, K. E. Clemens, E. A. Schmidt, and R. H. Smithers, ibid., **94**, 3201 (1972). (g) M. A. Barrow, A. C. Richards, R. H. Smithers, and H. M. R. Hoffmann, Tetrahedron Lett., **1972**, 3101.
4. Trifluoroacetic acid (r.t.) was used for the cyclization in place of H_2SO_4-MeOH.
5. T. Hiyama, M. Shinoda, and H. Nozaki, J. Am. Chem. Soc., **101**, 1599 (1979); idem, Tetrahedron Lett., **1979**, 3529.
6. (a) J. Baldwin, J. Chem. Soc. Chem. Comm., **1976**, 734. (b) J. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman, and R. C. Thomas, ibid., **1976**, 736. (c) J. Baldwin in "Further Perspectives in Organic Chemistry," Ciba Foundation Symposium 53, Elsevier, Amsterdam, 1978, p 85.

7. This work was financially assisted by the Ministry of Education, Science and Culture, Japanese Government (Grant-in-aid No 475665). We are indebted to Professor M. Schlosser for helpful discussions on the occasion of the international cooperative research program supported by JSPS.

Received, 4th July, 1980