Tetrahedron Letters No. 46, pp 4379 - 4382, 1971. Pergamon Press. Printed in Great Britain.

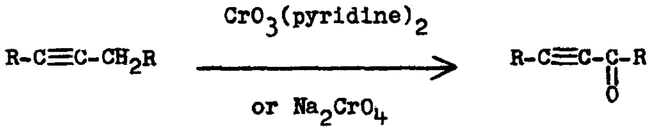
PREPARATION OF CONJUGATED ACETYLENIC KETONES BY OXIDATION OF ALKYNES WITH CHROMIUM TRIOXIDE-PYRIDINE COMPLEX OR SODIUM CHROMATE

James E. Shaw and James J. Sherry

Department of Chemistry, Moorhead State College
Moorhead, Minnesota 56560, U.S.A.

(Received in USA 8 September 1971; received in UK for publication 11 October 1971)

We wish to report a new method for the synthesis of conjugated acetylenic ketones which provides these compounds in a single step from readily available alkynes by oxidation with chromium trioxide-pyridine complex or anhydrous sodium chromate. These oxidizing agents have been previously used for the allylic oxidation of olefins.[1,2]



$$R\text{-}C\equiv C\text{-}CH_2R \xrightarrow[\text{or } Na_2CrO_4]{CrO_3(\text{pyridine})_2} R\text{-}C\equiv C\text{-}\underset{\underset{O}{\|}}{C}\text{-}R$$

In a typical case oxidation of 0.015 moles of 4-octyne with 0.225 moles of isolated chromium trioxide-pyridine complex[3] in 450 ml of methylene chloride at room temperature for 24 hours with stirring under nitrogen provided a 42% yield of 4-octyn-3-one.[4,5] The infrared spectrum (neat) of the ketone showed strong bands at 2215 ($C\equiv C$) and 1675 ($C{=}O$) cm^{-1}. The nmr spectrum (CCl_4) had three-proton triplets at τ 8.94 and 8.89, a two-proton sextuplet at 8.36, a two-proton triplet at 7.63, and a two-proton quartet at 7.51 ($J = \sim 7$ Hz in all cases). It was determined by gas chromatography that 4-octyn-3-one was the only product in the reaction other than a considerable amount of unreacted 4-octyne. Similarly, oxidation of 0.060 moles of 4-octyne with 0.120 moles of anhydrous sodium chromate in 200 ml of acetic acid and 120 ml of acetic anhydride at 40-45° for two days provided 4-octyn-3-one in 19% yield along with a large amount of unreacted 4-octyne.[6]

Several other alkynes were oxidized with chromium trioxide-pyridine complex and sodium chromate using conditions similar to those described for 4-octyne, and the results are shown in the following Table.[5]

Table

Alkyne	Product	% Yield[a] using $CrO_3(pyridine)_2$	% Yield[a] using Na_2CrO_4
4-octyne	4-octyn-3-one	42	19
5-decyne	5-decyn-4-one	46[b]	20
1-phenyl-1-butyne	4-phenyl-3-butyn-2-one	40	17
2-decyne	2-decyn-4-one	31	18
1-decyne	1-decyn-3-one	0	0

[a] All yields were determined by glpc (SE-30) unless otherwise noted.
[b] In this case ten mole equivalents of the complex were used, and the yield was based on product isolated by column chromatography on alumina.

In each case the only product other than unreacted starting material was the conjugated acetylenic ketone which had the triple bond located in its original position. The fact that 2-decyne gave only 2-decyn-4-one (three-proton singlet at τ 8.01 and a two-proton triplet at 7.57, $J = 7$ Hz) shows that a methyl group on a triple bond is not readily oxidized. This can be explained by the fact that attack at the methylene position would give a more stable free radical (or carbonium ion) as a possible intermediate[7] than would attack at the methyl. Alkynes with terminal triple bonds such as 1-decyne and 5-phenyl-1-pentyne did not react with chromium trioxide-pyridine complex or sodium chromate under the conditions employed, and large amounts of starting material were recovered. The reason for the unreactivity of the terminal alkynes is not apparent at this time.

In each of the crude oxidation products considerable amounts of starting material were present, and the yields would be much higher if they were based only on alkyne consumed. Although optimum reaction conditions have not been determined, it was observed in the sodium chromate runs that an increased number of mole equivalents of oxidizing agent and/or higher temperatures did not increase the yields of ketone. Since most of the alkyne was consumed under these conditions, cleavage of the triple bond may have occurred to give acids which were lost in the basic work-up.[6] Although the use of chromium trioxide-pyridine complex gives higher yields, it must be noted that the sodium chromate method has the advantages that the oxidizing agent is more readily available and large amounts of alkyne can be handled at one time since only two mole equivalents of oxidizing agent are used instead of 15.[8]

ACKNOWLEDGEMENT: We wish to thank the Minnesota State College Board for financial support.

FOOTNOTES AND REFERENCES

1. C. W. Marshall, R. E. Ray, I. Laos, and B. Riegel, *J. Am. Chem. Soc.*, **79**, 6308 (1957); N. W. Atwater, *ibid.*, **83**, 3071 (1961); W. G. Dauben and A. C. Ashcraft, *ibid.*, **85**, 3673 (1963).
2. W. G. Dauben, M. Lorber, and D. S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969).
3. The complex was prepared by the method of Dauben and co-workers (ref 2). It was observed that if the complex was made directly in the methylene chloride (R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970)), the yields were not as good.
4. The work-up for the alkyne oxidations with chromium trioxide-pyridine complex was similar to that used by Dauben and co-workers (ref 2) and involved extraction with ether and repeated washings with saturated sodium bicarbonate, 5% hydrochloric acid, and water.

5. The products after purification by preparative glpc (SE-30 column) gave the expected infrared and nmr spectra and gave physical constants in agreement with those reported in the literature. In the case of 2-decyn-4-one the melting point and nmr spectrum of the 2,4-dinitrophenylhydrazine derivative were the same as those reported (G. Martin, Compt. Rend., 245, 1933 (1957); M. L. Filleux-Blanchard and G. Martin, Bull. Soc. Chim. Fr., 2618 (1968)) but the refractive index of the ketone was $n_D^{23.5°}$ 1.4486 instead of $n_D^{20°}$ 1.4600.
6. The work-up for the sodium chromate runs consisted of pouring the reaction mixture into three times its volume of water and then extracting twice with a 1:1 solution of ether and petroleum ether. The organic phase was then washed several times with water and saturated sodium bicarbonate before drying and evaporating under reduced pressure.
7. K. B. Wiberg, "Oxidation in Organic Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 105-109; K. B. Wiberg and S. D. Nielson, J. Org. Chem., 29, 3353 (1964).
8. For other recent methods for preparing acetylenic ketones and aldehydes see: G. Zweifel and N. L. Polston, J. Am. Chem. Soc., 92, 4068 (1970); A. Vallet and R. Romanet, Bull. Soc. Chim. Fr., 3616 (1970); J. F. Normant and M. Bourgain, Tetrahedron Letters, 2659 (1970).