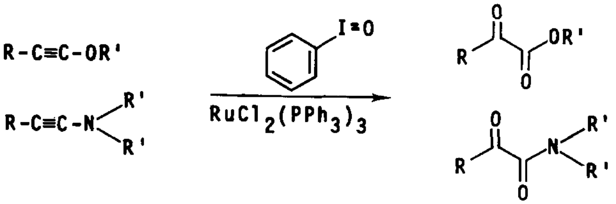
Tetrahedron Letters,Vol.23,No.36,pp 3661-3664,1982
Printed in Great Britain
0040-4039/82/363661-04$03.00/0

Ru-CATALYZED OXIDATION OF SUBSTITUTED ACETYLENES TO α-KETO ESTERS AND α-KETO AMIDES WITH IODOSYLBENZENE

Paul Müller* and José Godoy,
Département de Chimie Organique, Université de Genève,
1211 Genève 4, Switzerland

Summary. Oxidation of alkynyl ethers and -amines with iodosylbenzene in presence of Ru-catalysts affords α-keto esters and α-keto amides in 44-84% yield. These conversions can also be effected with RuO_4.

Oxidations based on iodosylbenzene are of current interest in connection with model studies for peroxidases and cytochrome P-450.[1] Preparative applications in catalytic and uncatalyzed systems have been reported with PhIO,[2] but also $PhIO_2$.[3] We have previously found that PhIO in conjunction with Ru-catalysts is an efficient reagent for conversion of alcohols to aldehydes, ketones or carboxylic acids.[2a] Disubstituted acetylenes are converted to α-diketones in yields of 65-86%, while terminal acetylenes are cleaved to carboxylic acids.[4] We have applied the combination of PhIO/Ru-catalyst to 1-alkynyl ethers and 1-alkynyl amines to obtain the corresponding α-keto esters and amides in fair to excellent yield, depending on the substituents present in the substrate:



The results are summarized in Tables 1 and 2.

Table 1. Oxidation of 1-alkynyl ethers[5] with $PhIO/RuCl_2(PPh_3)_3$[a]

Substrate	R	R'	Isolated yield[b]	Remark[8]
1	H	C_2H_5	-	decomposition
2	CH_3	C_2H_5	67%[c]	
3	*iso*-C_3H_7	CH_3	60%	64% with RuO_4[10]
4	*n*-C_6H_{13}	CH_3	59%	
5	*n*-C_4H_9	*iso*-C_3H_7	60%	
6	C_6H_5	C_2H_5	70%	1 mmol scale (30 min)

[a] Conditions: 10 mmol of substrate, 2.6 equiv. of PhIO, 1% catalyst, 15 min at RT. [b] by chromatography on SiO_2 with pentane (PhI) followed by CH_2Cl_2. [c] by distillation.

Table 2. Oxidation of 1-alkynyl amines[11] with $PhIO/RuCl_2(PPh_3)_3$[a]

Substrate	R	R'	Isolated yield	Remark[8]
7	CH_3	C_2H_5	-	decomposition
8	*iso*-C_3H_7	CH_3	44%	5 mmol scale
9	C_6H_5	CH_3	84%	71% with RuO_4[10]
10	C_6H_5	C_2H_5	76%	

[a] Same conditions as above, but 1.5 h reaction time.

In a typical experiment 96 mg of catalyst ($RuCl_2(PPh_3)_3$) in 25 ml of CH_2Cl_2 were added to PhIO (5.72 g, 26 mmol) suspended in 50 ml of CH_2Cl_2. Dimethyl(phenylethynyl)amine (1.45 g, 10 mmol) in 25 ml of CH_2Cl_2 was added at once. An exothermic reaction started immediately. After 1.5 h stirring excess PhIO was filtered, the solvent evaporated and the product was purified by column chromatography. Iodobenzene was eluted with CH_2Cl_2, the product, *N,N*-dimethyl-2-*oxo*-benzylamide (1.49 g, 84%) with ether.

No reaction occurs without catalyst; for example, 2 was recovered unchanged after exposure to 3 eq. of PhIO during 3 h. The α-keto esters and amides, once formed, are stable towards $PhIO/RuCl_2(PPh_3)_3$: ethyl pyruvate was not degraded under the reaction conditions during 12 h. Oxidation proceeds also with other Ru-catalysts such as $Ru_3(CO)_{12}$, $RuCl_2(CO)_2(PPh_3)_2$, ruthenocene in CH_2Cl_2 and $RuCl_3$ aq. (in acetone). The recently published variation of the catalytic RuO_4 procedure[10] was applied to 3 and 9 and gave comparable results as PhIO. However, with respect to other substrates, our system differs significantly from RuO_4. It is inert towards alkenes, simple arenes and ethers, but reacts with sulfides to yield sulfoxides and sulfones.[14]

With respect to this latter reaction, it is comparable to PhIO/TPPFe(III)Cl[1d] or $PhIO_2$ combined with Lewis acid catalysts.[3b]

To our knowledge the literature concerning oxidation of 1-alkynyl ethers and amines is very limited. α-Keto esters have been isolated in good yield from ozonolysis[15] or oxidation with $OsO_4/KClO_3$[16] of 1-alkynyl ethers and by ozonolysis of bromoacetylenes.[17] Only one observation dealing with conversion of an 1-alkynyl amine to a α-keto amide by means of singlet oxygen has been reported.[18] The present procedure is simple and convenient. The only limitation encountered so far occurred with ethoxyacetylene (1) and *N*,*N*-diethylpropinylamine (7) which underwent decomposition rather than oxidation under the reaction conditions.

The synthesis of α-ketoesters and -amides is of interest for asymmetric synthesis of α-amino acids[19] and for design of certain enzyme inhibitors.[20] In view of its simplicity our approach should be competitive to procedures described in the literature.[21]

Acknowledgment. This work was supported by the *Swiss National Science Foundation* (grant No 2.420-0.79).

REFERENCES AND NOTES

1) (a) J.T. Groves & W.J. Kruper, Jr., J. Am. Chem. Soc. 101, 7613 (1979); (b) J.T. Groves, W.J. Kruper, Jr., & R.C. Haushalter, *ibid.* 102, 6375 (1980); (c) J.T. Groves, R.C. Haushalter, M. Nakamura, T.E. Nemo & B.J. Evans, *ibid.* 103, 2884 (1981); (d) W. Ando, R. Tajima & T. Takata, Tetrahedron Letters 23, 1685 (1982).

2) (a) P. Müller & J. Godoy, Tetrahedron Letters 22, 2361 (1981); (b) R.M. Moriarty, S.C. Gupta, H. Hu, D.R. Berenschot & K.B. White, J. Am. Chem. Soc. 103, 686 (1981); R.M. Moriarty, H. Hu & S.C. Gupta, Tetrahedron Letters 22, 1283 (1981).

3) (a) D.H.R. Barton, J.W. Morzycki & W.B. Motherwell, J. Chem. Soc., Chem. Commun. 1981, 1044; (b) D.H.R. Barton, C.R.A. Godfrey, J.W. Morzycki, W.B. Motherwell & A. Stobie, Tetrahedron Letters 23, 957 (1982).

4) P. Müller & J. Godoy, Helv. Chim. Acta 64, 2531 (1981).

5) The alkynyl ethers 1 and 2 were obtained from ethylvinyl and ethyl-1-propenyl ether using the procedure of Arens,[6] while 3, 4 and 5 (b.p. 57^{0}/12 Torr) were accessible from the corresponding 1-alkoxy-1-chloroalkanes *via* bromination-dehydrobromination[7] and 6 from 1-ethoxy-2-iodoacetylene *via* coupling with a phenylcopper(I) reagent.[9]

6) J.F. Arens, Rec. Trav. Chim. Pays-Bas 74, 271 (1955).

7) J.R. Nooi & J.F. Arens, Rec. Trav. Chim. Pays-Bas 78, 284 (1959).

8) All products reported exhibited satisfactory IR, ^{1}H-NMR and mass spectral data.

9) W. Verboom, H. Westmijze, H.J.T. Bos & P. Vermeer, Tetrahedron Letters 1978, 1441.

10) H.J. Carlsen, T. Katsuki, V.S. Martin & K.B. Sharpless, J. Org. Chem. 46, 3936 (1981).

11) Ynamine 7 was purchased from Fluka. 8 (b.p. 52°/60 Torr) was synthesized from ether 3[12] while 9 and 10 were prepared from 1-chloro-2-phenylacetylene.[13]

12) P.P. Montijn, E. Harryvan & L. Brandsma, Rec. Trav. Chim. Pays-Bas 83, 1211 (1964).

13) H.G. Viehe & M. Reinstein, Angew. Chem. Int. Ed. 3, 506 (1964); Chemistry of Acetylenes, H.G. Viehe, Ed., Marcel Dekker, New York, N.Y., 1969, Chap. 12.

14) P. Müller & J. Godoy, unpublished results.

15) W.W. Wisaksono & J.F. Arens, Rec. Trav. Chim. Pays-Bas 80, 846 (1961).

16) L. Bassignani, A. Brandt, V. Caciagli & L. Re, J. Org. Chem. 43 4245 (1978).

17) S. Cacchi, L. Caglioti & P. Zappelli, J. Org. Chem. 38, 3653 (1973).

18) C.S. Foote & J.W.-P. Lin, Tetrahedron Letters 1968, 3267.

19) E.J. Corey, R.J. McCaully & H.S. Sachdev, J. Am. Chem. Soc. 92, 2476 (1970); E.J. Corey, H.S. Sachdev, J.Z. Gougoutas & W. Saenger, *ibid.* 92, 2488 (1970); B.W. Bycroft & G.R. Lee, J. Chem. Soc., Chem. Commun. 1975, 988.

20) A.A. Patchett, E. Harris, E.W. Tristram, M.J. Wyvratt *et al.*, Nature 288, 280 (1980).

21) E.L. Eliel & A.A. Hartmann, J. Org. Chem. 37, 505 (1972); L.M. Weinstock, R.B. Currie & A.V. Lovell, Synth. Commun. 11, 943 (1981); J.P. Schaefer & E.J. Corey, J. Org. Chem. 24, 1825 (1959); P. Cou ot & C. Legris, Synthesis 1975, 118; G.P. Axiotis, Tetrahedron Letters 22, 1509 (1981); E.D. Thorsett, *ibid.* 23, 1875 (1982); K. Ogura, N. Katoh, I. Yoshimura & G. Tsuchihashi, *ibid.* 1978, 375; G.A. Russell & G.J. Mikol, J. Am. Chem. Soc. 88, 5498 (1966); P.A. Manis & M.W. Rathke, J. Org. Chem. 45, 4952 (1980); E. Zbiral & E. Werner, Tetrahedron Letters 1966, 2001.

(Received in Germany 2 June 1982)