A Facile Method of Synthesis of α-Acetylenic Ketones

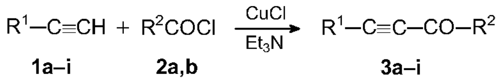
Sophia I. Shergina, Ivan E. Sokolov and Alevtina S. Zanina*

Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. Fax: +7 3832 352350

Copper(I) chloride catalysed acylation of a variety of terminal acetylenes with acyl chlorides is a convenient method of synthesising α-acetylenic ketones.

Acetylenic ketones are versatile intermediates in organic synthesis and can be used for preparing aminovinylketones[1] and heterocyclic compounds such as pyrimidinones,[2] quinolines[3] and pyrazoles.[4] The main methods for the preparation of α-acetylenic ketones are based on organometallic synthesis,[5] but their application in a preparative-scale procedure is limited. A catalytic method for the synthesis of α-ethynylketones was first described by Tohda *et al.*[6] They used complex catalyst CuI and $PdCl_2(PPh_3)_2$ with Et_3N as a solvent, which greatly limited the application of this method. In contrast to ref. 6, we have reported on the use of copper(I) compounds and their chelates as catalytic agents and aprotic solvents in the reaction of terminal acetylenes with acyl chlorides.[7,8]

The present paper is concerned with the application of copper(I) chloride as an active catalyst for the acylation of n-, isoalkyl- and cycloalkenylacetylenes with acyl chlorides.



$$R^1{-}C{\equiv}CH + R^2COCl \xrightarrow[Et_3N]{CuCl} R^1{-}C{\equiv}C{-}CO{-}R^2$$

1a–i **2a,b** **3a–i**

The reaction was carried out in benzene involving one or two equivalents of Et_3N.[†]

All new compounds described in this paper were fully characterized by complete spectral and analytical data. From Table 1 it is evident that alkylacetylenes **1a–c** are less active in this reaction than **1f–i**. This can be attributed to the lower solubility of intermediate-forming acetylenides in the reaction mixture. This is confirmed by our data on the acylation of unsubstituted acetylene. In spite of a wide variety of experimental conditions we failed to obtain the acylation product. The starting acetylenic compounds **1a–e** were prepared by the methods given in ref. 9 and **1f,g** by the methods in ref. 10.

In conclusion, we consider that the present method is the most useful and convenient alternative of the existing ones.[11] The main advantages are the following: there is no need to use sodamide or metallic acetylenides; the reaction is very simple to perform; and the reaction conditions are mild and the yields of α-acetylenic ketones are good.

Table 1 Synthesis of ketones **3a–i** $R^1{-}C{\equiv}C{-}CO{-}R^2$.

3	R^1	R^2	Conditions Time/h;	*T*/°C	B.p./°C (mmHg)	Yield (%)[a]
a	Bu^n	Bu^t	10	50	78(6)	80
b	n-C_5H_{11}	Pr^i	10	55	82.5(3)	63
c	n-C_5H_{11}	Bu^t	10	55	129(30)	65
d	Cyclohexenyl-1	Bu^t	2.5	45	104.5(2)	69
e	Cyclopentenyl-1	Bu^t	2	60	93.5(2.5)	77
f	$Me_3CC(OMe)Me$	Pr^i	1	50	140(30)	81
g	$Me_2CHCH_2C(OMe)Me$	Pr^i	1.5	50	142(27)	92
h	$Me_3CC(OMe)Me$	Bu^t	1	50	118–120(15)	85
i	$Me_2CHCH_2C(OMe)Me$	Bu^t	1.5	50	118–120(13)	65

[a] All yields refer to the distilled product.

References

1 A. S. Zanina, A. A. Kirchanov, S. I. Shergina, I. E. Sokolov and V. I. Kostrovski, *Zh. Org. Khim.*, 1982, **18**, 772 [*J. Org. Chem. USSR (Engl. Transl.)*, 1982, **18**, 670].

2 S. S. Sabri, A. Q. Hussein and F. H. Al-Haijar, *J. Chem. Eng. Data*, 1985, **30**, 512.

3 M. S. Sinsky and R. J. Bass, *J. Heterocycl. Chem.*, 1984, **21**, 759.

4 H. B. Shivarama, U. K. Venkatramana and K. R. Sridhar, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 3409.

5 J. Mathiew and J. Weill-Raynal, *Introduction of an α-Functional Carbon Chain*, G. Thieme, Stuttgart, 1979, vol. III, p. 494.

6 Y. Tohda, K. Sonogashira and N. Hagihara, *Synthesis*, 1977, 777.

7 A. S. Zanina, S. I. Shergina, I. E. Sokolov and I. L. Kotljarevski, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 1158 (in Russian).

8 A. S. Zanina, S. I. Shergina, I. E. Sokolov and I. L. Kotljarevski, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, 855 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1986, 777).

9 L. Brandsma, *Preparative Acetylenic Chemistry*, Elsevier, Amsterdam, 1971, pp. 49, 137.

10 I. E. Sokolov and I. L. Kotljarevski, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 202 (in Russian).

11 G. Giacomelli, K. Rosini, A.-M. Caporusso and F. Palla, *J. Org. Chem.*, 1983, **48**, 4887.

Received: Moscow, 4th August 1994;
Cambridge, 13th September 1994; Com. 4/04836I

[†] A typical reaction procedure is as follows: pivaloyl chloride **2a** (0.2 mol) was added to a mixture of CuCl (0.02 mol), Et_3N (0.2 mol) and acetylenes **1d** (0.2 mol) in 100 ml benzene under a N_2 atmosphere. The resulting reaction mixture was additionally stirred for 2.5 h at 45 °C. The reaction was monitored using GLC and was complete when the peak of the starting reagent **1d** disappeared. After being cooled, the reaction mixture was treated with water (50 ml) and was extracted with diethyl ether (200 ml). The combined organic layers were washed with dilute (6 M) HCl (50 ml) and water (3 × 50 ml) and were then dried (Na_2SO_4). After filtration, solvents were removed under reduced pressure and the crude product was purified by distillation to give ketone **3d** (69%). A variety of acetylenic ketones were prepared in good yields by this simple procedure (data are given in Table 1).