CHEMISTRY LETTERS, pp. 1231-1232, 1983.

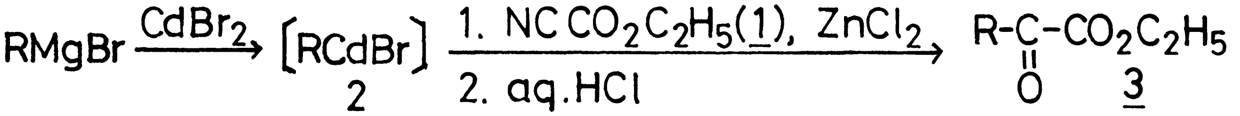
REACTION OF ORGANOCADMIUM REAGENTS WITH ETHYL CYANOFORMATE: PREPARATION OF α-KETO ESTERS

Yasunobu AKIYAMA, Tomomi KAWASAKI, and Masanori SAKAMOTO*
Meiji College of Pharmacy, 1-35-23, Nozawa, Setagaya-ku, Tokyo 154

Organocadmium reagents reacted with the cyano-function of ethyl cyanoformate in the presence of $ZnCl_2$ to afford the corresponding α-keto esters.

Although the addition of organometallic reagents to the cyano-function of ethyl cyanoformate (1) appeared of interest for synthesis of α-keto[1)] and α-dehydroamino esters,[2)] such a reaction has not been known so far. Thus, Grignard reagents and organolithium compounds add to the ester-function of 1 rather than the cyano-function, affording the corresponding tertialy alcohols or ethoxy carbonyl compounds.[3)] Recently, G. P. Axiotis[1b)] has reported that triethoxyacetonitrile as protected form of 1 reacts with organolithium reagents to give α-keto esters. We have now found that organocadmium reagents (2a-e) react with 1 activated by using $ZnCl_2$[4)] to give the corresponding α-keto esters (3a-e).

In typical reaction, the solution of the freshly prepared cyclohexylcadmium bromide (2a)[5)] (30.5 mmol) in dry ether (66ml) was added slowly to the suspension of ethyl cyanoformate (1) (30 mmol) and $ZnCl_2$ (30 mmol) in dry ether (70 ml) at 0°C under argon. After addition, the mixture was stirred for 23 h at room temperature, quenched with 10% HCl aqueous solution (20 ml), and extracted with CH_2Cl_2(70 ml). The extract was concentrated under reduced pressure to give a syrup, from which 66% yield of ethyl α-oxocyclohexaneacetate (3a) was obtained by silica-gel column chromatography (elution with benzene). It was confirmed by direct comparison of its physical and spectral data with those of the sample prepared by the procedure



$$RMgBr \xrightarrow{CdBr_2} \underset{2}{[RCdBr]} \xrightarrow[2.\ aq.HCl]{1.\ NCCO_2C_2H_5(1),\ ZnCl_2} \underset{3}{R-\overset{\displaystyle O}{\underset{}{C}}-CO_2C_2H_5}$$

Table 1. Yields and Physical Data of α-Keto Esters 3a-e

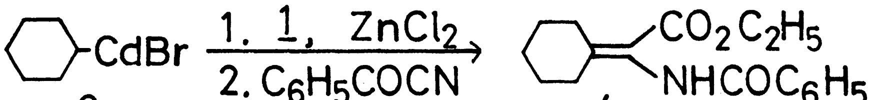
Compd. No.	R	Yield(%)[a)]	Bp(°C)[mmHg]	Lit.	$\nu_{max}^{CHCl_3}$ cm^{-1}	Mp(°C) of 2,4-DNP[b)]
3a	c-C_6H_{11}	66	132-135[22]	132[20][1d)]	1720	167-168
3b	c-C_5H_9	44	102-105[17]	——	1720	153-154
3c	s-C_4H_9	57	98-100[17]	——	1725	109-110
3d	i-C_3H_7	24	105-110[14][c)]	62[11][1e)]	1740	179-179.5
3e	C_6H_5	31	127-130[5]	100-103[1][1c)]	1740, 1695	155-156

a) Isolated yield after purification by distillation. b) 2,4-Dinitrophenylhydrazone of 3; all 2,4-DNP gave satisfactory elemental analysis. c) Bath temperature are provided.

of L. M. Weinstock.[1c)] In a similar manner, other organocadmium bromides (2b-e) reacted with 1 to give the corresponding α-keto esters (3b-e) in moderate yields, respectively. The results are shown in Table 1. In contrast, phenylmagnesium bromide reacted with 1 in the presence of ZnCl$_2$ to obtain 13% yield of 3e, together with several unknown products. The result is explained that 1 activated by ZnCl$_2$ as acid-base complex tends to be decomposed by action of a strong base such as Grignard reagent compared with organocadmium reagent (2).[6)]

In the absence of ZnCl$_2$, the reaction of 2e with 1 gave a mixture of 3e and ethyl benzoate in 17% yield and in a ratio of ca. 3:2,[7)] whereas one of Grignard reagents affords tertialy alcohols.[3)] The differences between the reactivities of 2 and Grignard reagents towards 1 is explained by the tendency that soft nucleophiles such as mercaptanes add to the cyano-function of 1,[8)] while hard nucleophiles such as amines to the ester-function.[9)] Indeed, organocadmium reagents (2) is softer than Grignard reagents,[10)] and attacked at the carbon of the cyano-function to give 3.

Furthermore, instead of hydrolysis, the reaction mixture obtained from activated 1 and 2a was allowed to treat with benzoyl cyanide for 6 h at room temperature to give ethyl 1-(N-benzoylamino)-1-cyclohexylideneacetate (4) in 20% yield. The structure was decided by direct comparison of its physical and spectral data with those of the sample prepared by the procedure of C. Shin.[2c)]



2a

4

References

1) a) E. D. Thorsett, *Tetrahedron Lett.*, 1982, 1875; b) G. P. Axiotis, *ibid.*, 1981, 1509; c) L. M. Weinstock, R. B. Currie, and A. V. Lovell, *Synth. Commun.*, 11, 943 (1981); d) E. Adlerova, P. Vejdekova, and M. Protiva, *Collect. Czech. Chem. Commun.*, 29, 97 (1964); e) W. Boureault, *C. R. Acad. Sci.*, 132, 417 (1901); see also references therein.

2) a) For a review, see C. Shin, *Yuki Gosei Kagaku Kyokai Shi*, 37, 830 (1979); b) L. Somekh and A. Shanzer, *J. Org. Chem.*, 48, 907 (1983); c) C. Shin, K. Sato, A. Ohtsuka, K. Mikami, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, 46, 3876 (1975).

3) H. Finger and R. Gaul, *J. Prakt. Chem.*, 111, 54 (1925); P. Bruylants, *Bull. Soc. Chim. Belg.*, 1924, 529.

4) Selective activation of the cyano-function of 1 with ZnCl$_2$ is shown in the reaction of active methylene compounds, T. Iimori, Y. Nii, T. Izawa, S. Kobayashi and M. Ohno, *Tetrahedron Lett.*, 1979, 2525.

5) P. R. Jones, P. D. Sherman, and K. Schwarzenberg, *J. Organomet. Chem.*, 10, 521 (1967); H. Gilman and J. F. Nelson, *Recl. Trav. Chim. Pays-Bas*, 55, 518 (1936).

6) P. R. Jones and P. J. Desio, *Chem. Rev.*, 78, 491 (1978).

7) Determined by nuclear magnetic resonance spectroscopy.

8) G. Statzinger, *Justus Liebigs Ann. Chem.*, 1978, 473.

9) L. A. Carpino, *J.* Am. Chem. Soc., 82, 2725 (1960).

10) T. -L. Ho, "Hard and Soft Acids and Bases Principle in Organic Chemistry," Academic Press, New york, San Francisco, London (1977).

(Received June 1, 1983)