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A SIMPLE ACCESS TO α,ß-DIKETOESTERS

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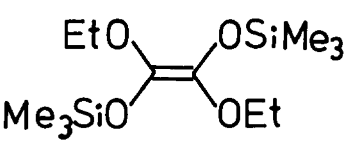
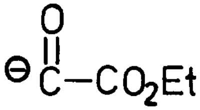
Abstract: Carboxylic acid chlorides react with 1,2-diethoxy-1,2-bis(trimethylsiloxy)ethylene in the presence of catalytic amounts of $ZnCl_2$ to produce regiospecifically protected α,ß-diketoesters.

Vicinal tricarbonyl compounds continue to be of interest because they can be used synthetically in a variety of ways1). Recently, several new synthetic routes to α,ß-diketoesters ($R\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}CO_2R$) were reported2,3), notably the Wasserman procedure according to which ß-ketoesters are transformed into the α-enamino derivatives by $(MeO)_2CHNMe_2$ followed by ozonolysis or cleavage by singlet oxygen2). We wish to describe a different approach based on the acylation of 1,2-diethoxy-1,2-bis(trimethylsiloxy)ethylene (1), which can be viewed as a synthetic equivalent of the unknown anion 24,5). 1 is readily prepared by reacting oxalic acid ester with Na/K in the presence of chlorotrimethylsilane6).



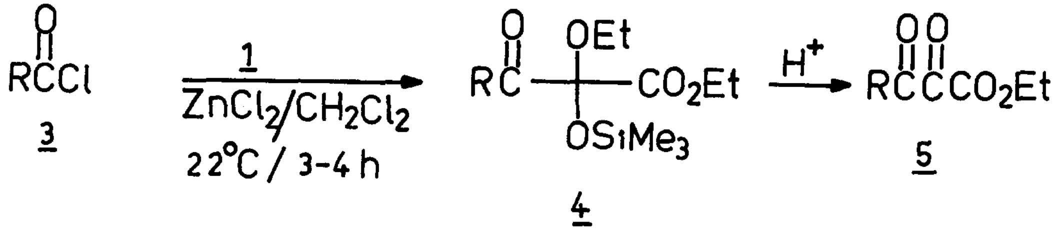
1



$$^{\ominus}\overset{O}{\overset{\|}{C}}-CO_2Et$$

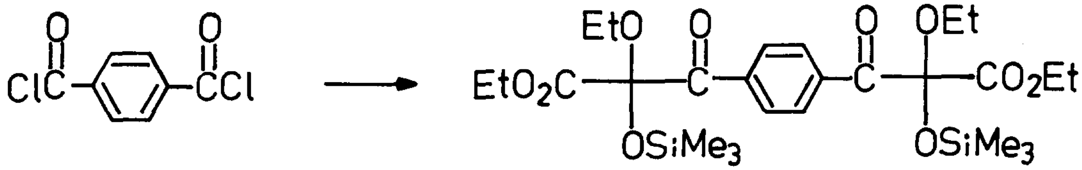
2

The reaction of acid chlorides 3 with 1 in the presence of catalytic amounts of $ZnCl_2$ in CH_2Cl_2 affords excellent yields of 4, which are the regiospecifically protected derivatives of the corresponding α,ß-diketoesters 5[7,8].



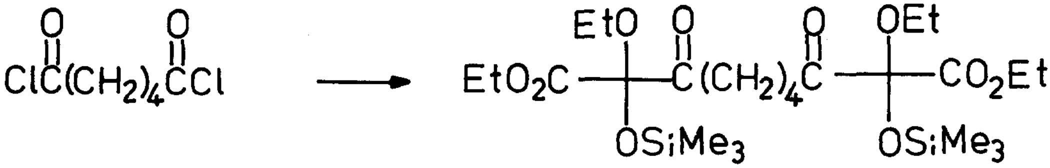
a) R = C_6H_5 (82%)
b) R = o-Me-C_6H_4 (91%)
c) R = CH_3 (72%)
d) R = $CHMe_2$ (93%)
e) R = CMe_3 (88%)

Dichlorides were found to react analogously using two equivalents of 1, although longer reaction times are required (12 - 24 h):



6

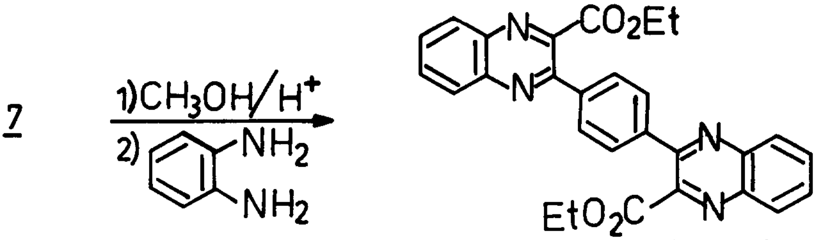
7 (88%)



8

9 (85 %)

Desilylation using methanol containing aqueous 2N HCl affords the vicinal tricarbonyl compounds (as a mixture of partially hydrated species)[9]. The synthetic utility of the present methodology is illustrated by the preparation of the novel quinoxaline 10[7]:



10 (72%)

Compounds of the type 4, 7 and 9 are likely to be convenient precursors of other heterocycles. In summary, the $ZnCl_2$ mediated acylation of 1 represents a mild and simple synthesis of regiospecifically protected α,ß-diketoesters which can be used for further transformations[10].

Acknowledgement: This work was supported by the Fonds der Chemischen Industrie.

References:

1) M.B. Rubin, Chem. Rev. 75, 177 (1975).

2) H.H. Wasserman, W.T. Han, Tetrahedron Lett. 25, 3743 (1984); and ref. cited therein.

3) K. Schank, C. Lick, Synthesis 1983, 392; see also M.M. Yousif, S. Sacki, M. Hamana, Heterocycles 15, 1083 (1981); A. Schönberg, E. Singer, Tetrahedron 34, 1285 (1978).

4) We have previously used 1 to affect aldol and Michael additions as well as α-tert-alkylations to produce α-ketoesters: M.T. Reetz, H. Heimbach, K. Schwellnus, Tetrahedron Lett. 25, 511 (1984).

5) For previous examples of synthetic equivalents of 2, see the following reviews: O.W. Lever, Jr., Tetrahedron 32, 1943 (1976); T.A. Hase, J.K. Koskimies, Aldrichimica Acta 15, 35 (1982); see also ref.[8] below.

6) Y.N. Kuo, F. Chen, C. Ainsworth, J.J. Bloomfield, J.Chem.Soc., Chem.Commun. 1971, 136. Compound 1 (E/Z mixture) is easy to handle and can be stored for months at room temperature.

7) Suk-Hun Kyung, Dissertation, Universität Marburg 1985.

8) Tetramethoxyethylene has been shown to react with benzoylchloride at 120-140°C (16 h) to produce the methoxy analog of 4b in 67% yield: R.W. Hoffmann, J. Schneider, Chem.Ber. 99, 1900 (1966).

9) Vicinal tricarbonyl compounds are known to be hygroscopic. The hydrated form can be converted into the tricarbonyl form using standard procedures[1,7]; see also T. Kawetami, S. Hibino, S. Takano, J.Chem.Soc., Perkin Trans. I 1972, 391; T. Yamazaki, T. Oohama, T. Doinchi, T. Takizawa, Chem. Pharm. Bull. 20, 238 (1972).

10) Typical procedure. Synthesis of 4a: In a 100 ml round bottom flask with a nitrogen inlet about 100 mg of anhydrous $ZnCl_2$ is heated under vacuum with a bunsen burner until the substance melts. After cooling to room temperature, 30 ml of dry CH_2Cl_2 and 10 mmol of a carboxylic acid chloride are added. The mixture is stirred and 10 mmol of 1 added dropwise at room temperature over a period of about 20 min. After stirring for 3-4 h, the solvent is stripped off and the residue kugelrohr distilled (150°C/1 torr) to yield 2.66 g (82%) of 4a. For $C_{16}H_{24}O_5Si$ calc. C 59.23, H 7.46; found C 58.63, H 7.22. ^1H-NMR ($CDCl_3$, TMS ext.) δ = 0.17 (s, 9H), 1.13 (t, 3H), 1.25 (t, 3H), 3.63 - 3.73 (m, 2H), 4.15 - 4.22 (m, 2H), 7.38 - 8.21 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ = 1.3, 13.7, 15.1, 59.9, 61.7, 99.4, 128.0, 130.0, 133.2, 168.3, 192.5.

Dichlorides 6 and 8 require longer reaction times (12 - 24 h). Oxalic acid dichloride reacts with 1 to form the corresponding product in 89% yield, although a correct elemental analysis could not be obtained[7]. In contrast, 7 and 9 can be isolated in analytically pure form by kugelrohr distillation (200°C/0.4 torr). Typical desilylation is achieved by stirring the acylation products (~10 mmol) with methanol (20 ml) containing 0.5 ml of 2N HCl for a few hours followed by evaporation of the solvent[7]. Compound 8 (m.p. 199°C)[7] is prepared using the standard quinoxaline synthesis based on o-phenylenediamine/H^+ (see ref.[1,7] as well as G.B. Barlin, "The Pyrazines" in The Chemistry of Heterocyclic Compounds, Vol. 41, Wiley, N.Y. 1982).

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