Reaction of Ketene Silyl Acetals with Diazonium Salts: a Novel α-Amino Acid Ester Synthesis

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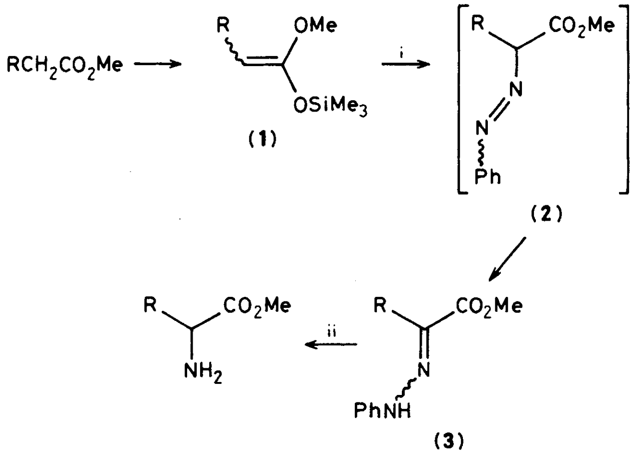
The reaction of ketene silyl acetals with arenediazonium tetrafluoroborate gave α-hydrazono and α-azo esters, which were easily hydrogenated to α-amino esters.

There is considerable interest in the use of organosilicon compounds in organic synthesis. In particular, silyl enol ethers and ketene silyl acetals have been widely used as nucleophilic synthons for ketones, aldehydes, and esters in order to functionalize these carbonyl compounds at the α-position.[1—3] During our research on novel synthetic methods for α-amino acids (or α-keto acid derivatives as the straightforward precursors for α-amino acids),[4—6] we examined the reactivity of silicon enolates with arenediazonium salts as potential amino cation equivalents. Preliminary experiments on the reaction between silyl enol ethers and arenediazonium salts have revealed that arenediazonium salts act as aryl cation equivalents; the reaction proceeds with nitrogen evolution to afford α-arylated ketones in high yields.[7] In striking contrast, however, we have now observed that the diazonium salts react with ketene silyl acetals without liberating nitrogen to give α-hydrazono or α-azo esters.

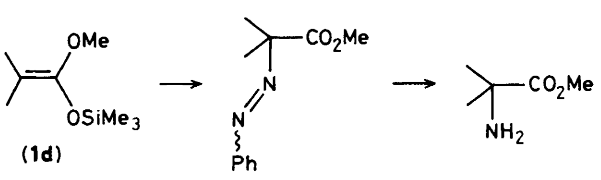
The ketene silyl acetal (**1a**) (1 mmol), prepared by deprotonation of methyl phenylacetate with lithium diisopropylamide followed by quenching with chlorotrimethylsilane, was dissolved in pyridine (3 ml) and treated with solid benzenediazonium tetrafluoroborate (1.3 equiv.) at 0 °C for 2 h. The resulting mixture was diluted with ether, washed successively with 1.5 M hydrochloric acid, water, and brine, dried over anhydrous magnesium sulphate, and concentrated *in vacuo*. The residual oil was chromatographed on silica gel to give 188 mg (73%) and 25 mg (10%) of (*E*)- and (*Z*)-hydrazono ester (**3a**), respectively. Other ketene silyl acetals reacted in a similar manner (see Scheme 1, Table 1). However, the disubstituted ketene silyl acetal (**1d**) afforded the α-azo ester (**2d**), owing to the lack of an α-hydrogen atom (see Scheme 2). The structures of (**3a—c**) and (**2d**) were confirmed by spectral and analytical data.

The α-hydrazono (**3a—c**) and α-azo (**2d**) esters formed were readily reduced into α-amino acid esters in nearly quantitative yields when treated with hydrogen in the presence of palladium on carbon.[8]



a; R = Ph
b; R = $PhCH_2$
c; R = Me

Scheme 1. i, PhN_2BF_4, 0 °C, 2 h, pyridine; ii, H_2 (5 atm), Pd–C, room temp., 2.5 h, MeOH.



(1d) (2d)

Scheme 2

Table 1. Reaction of ketene silyl acetals and benzenediazonium salts.

Ketene acetal[a]	Hydrazono or azo ester Yield (%)[b]	$(E):(Z)$
(**1a**)	(**3a**) 83	7:1
(**1b**)	(**3b**) 76	(E) only
(**1c**)	(**3c**) 59	(E) only
(**1d**)	(**2d**) 90	—

[a] Mixtures of (E)- and (Z)-forms. [b] Isolated yields by t.l.c.

Active methylene compounds like acetoacetates and malonates react with arenediazonium salts in highly basic media to give hydrazono esters (Japp–Klingemann reaction).[9] However, simple esters do not work. In addition, the Japp–Klingemann reaction is not applicable to α-disubstituted acetoacetates nor malonates, which are possible starting materials for α-substituted α-amino acids, because its occurrence requires an acidic α-hydrogen. On the other hand, ketene diethylacetals have been known to react with diazonium salts, but the non-selective formation of 1-aryl-4-ethoxypyridazin-6-ones, ethyl diarylformazanylformates, and other products results.[10] Thus the sequence exemplified herein constitutes an entirely new methodology for introducing an amino group onto the α-carbon of simple esters using arenediazonium salts as amino cation equivalents.

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References

1 E. W. Colvin, 'Silicon in Organic Synthesis,' Butterworths, London, 1981.
2 W. P. Weber, 'Silicon Reagents in Organic Synthesis,' Springer–Verlag, Berlin, 1983.
3 P. Brownbridge, *Synthesis*, 1983, 1 and 85.
4 M. Tanaka, T. Kobayashi, and T. Sakakura, *Angew. Chem.*, 1984, **96**, 519, and references cited therein.
5 For the double carbonylation of organic halides giving α-keto acids, see M. Tanaka, T. Kobayashi, and T. Sakakura, *J. Chem. Soc., Chem. Commun.*, 1985, 837.
6 We have observed another double carbonylation of organic halides which affords α-keto esters; M. Tanaka, T. Kobayashi, T. Sakakura, H. Itatani, S. Danno, and K. Zushi, *J. Mol. Catal.*, 1985, **32**, 115.
7 M. Tanaka and T. Sakakura, *J. Chem. Soc., Chem. Commun.*, 1985, in the press.
8 For the hydrogenation of α-hydrazono acids, see N. H. Khan and A. R. Kidwai, *J. Org. Chem.*, 1973, **38**, 822.
9 R. R. Phillips, *Org. React.*, 1959, **10**, 143.
10 S. M. McElvain and A. Jelinek, *J. Am. Chem. Soc.*, 1943, **65**, 2236.