α-Arylation of Ketones *via* the Reaction of Silyl Enol Ethers with Arenediazonium Salts

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The reaction of the silyl enol ethers of aryl ketones with arenediazonium salts gives α-arylated ketones in good yields under mild conditions.

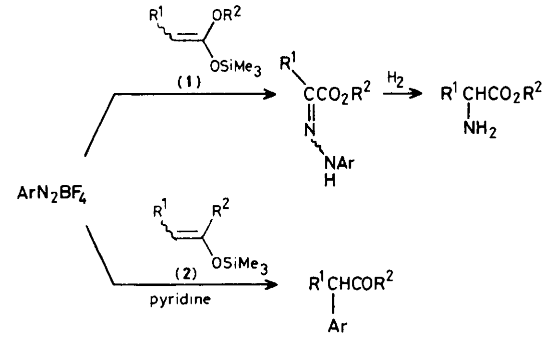
Owing to the lack of a direct substitution reaction of aryl halides with ketone enolates, a variety of tactics for the activation of aryl groups have been devised in order to realize indirect α-arylation of ketones.[1—6] Although metal complex-assisted arylation seems to be promising, it is still unsatisfactory in terms of yield, availability of the starting materials, generality of the reaction, and/or the cost of the catalysts, so that alternative methods, which circumvent these drawbacks, are required.

In previous studies, we have achieved α-amino acid synthesis *via* the reaction of ketene silyl acetals (**1**) with arenediazonium salts followed by reduction [equation (1)].[7]

Table 1. α-Arylation of ketones *via* the reaction of silyl enol ethers with arenediazonium salts.[a]

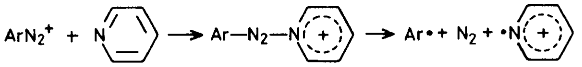
Entry	Silyl enol ether	Diazonium salt	Reaction time/h	Arylated ketone yield/%[d]
1	$CH_2{=}C(OSiMe_3)Ph$	PhN_2BF_4	2.0	72
2	$CH_2{=}C(OSiMe_3)Ph$	$p\text{-}ClC_6H_4N_2BF_4$	3.5	73
3	$CH_2{=}C(OSiMe_3)Ph$	$p\text{-}MeOC_6H_4N_2BF_4$	6.0	65
4	$CH_2{=}C(OSiMe_3)C_4H_3S$[c]	PhN_2BF_4	2.0	58
5[b]	$MeCH{=}C(OSiMe_3)Ph$	PhN_2BF_4	7.0	(71)
6[b]	$CH_2{=}C(OSiMe_3)C_7H_{15}$	PhN_2BF_4	5.0	(31)

[a] The mixture of silyl enol ether (2.0 mmol) and diazonium salt (2.6 mmol) in pyridine (6 ml) was stirred at 0 °C. [b] The amount of diazonium salt was doubled (5.2 mmol) and added in five portions. [c] 1,1-(2-Thienyl)trimethylsiloxyethene. [d] Isolated yields. The figures in parentheses are determined by g.l.c.



(1)

(2)



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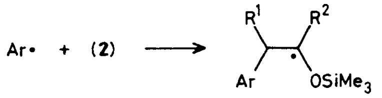

(3)

(4)

This sequence exemplifies the use of arenediazonium salts as amino cation equivalents. However, an interesting dichotomy of reactivity of diazonium salts has now been observed: in contrast to the case of ketene silyl acetals, the reaction of silyl enol ethers with arenediazonium salts has been found to afford α-arylated ketones with loss of nitrogen [equation (2)].

In a typical reaction, 1-(trimethylsiloxy)styrene (2 mmol) dissolved in pyridine (6 ml) was treated with solid benzene diazonium tetrafluoroborate (1.3 equiv.) at 0 °C for 2 h. The resulting mixture was diluted with diethyl 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 (Et_2O–hexane 1 : 10) and was further purified by bulb to bulb distillation to give 282 mg (72%) of 1,2-diphenylethanone.

The reaction could be applied to various combinations of silyl enol ethers and diazonium salts as summarized in Table 1; arenediazonium salts having either electron-withdrawing or electron-donating substituents gave good results. The new procedure could be used for α-arylation of propiophenone silyl enol ether (**2**; R^1 = Me, R^2 = Ph) as well (entry 5), which could not be successfully arylated by the Pd-assisted reaction of bromobenzene with *in situ* formed tin enolate.[5] Thus, the new procedure seems to be general for aryl or heteroaryl ketone enolates. However, 2-(trimethylsiloxy)non-1-ene, a fully aliphatic silicon enolate, exhibited rather low reactivity toward α-arylation, and a substantial amount of nonan-2-one and phenylpyridine was obtained in addition to the desired phenylated ketone.†

As to the reaction mechanism, the following observations are pertinent. The reaction was best carried out in pyridine, followed by hexamethylphosphoramide (11% yield), acetonitrile (2%), and dimethylformamide (<1%) under otherwise identical conditions. In other solvents such as tetrahydrofuran, dichloromethane, and toluene, the arylated ketone was not obtained at all. Since pyridine is able to generate aryl radicals from arenediazonium salts *via* the decomposition of azo-type adducts [equation (3)],[8] the large solvent effect may come from the difference in the rate of formation of the phenyl radical which is captured by the silicon enolate.‡ On the assumption that the reaction proceeds through the radical mechanism, the α-aryl silicon enolate (**2**; R^2 = Ph) might be expected to be more reactive because of the higher stability of the resulting benzylic radical intermediate (**3**; R^2 = Ph) [equation (4)]. In the aliphatic case, the phenyl radical generated will not be so readily captured, and is eventually trapped by the solvent with the formation of a substantial amount of phenylpyridines. The isomer ratio ($o:m:p$ = 5 : 3 : 2), when compared to the reported value, supports the radical mechanism.[9] In the reaction of ketene silyl acetals, which are highly nucleophilic, diazonium ions attack the ketene acetals directly in an ionic fashion. This is the probable origin of the difference in reactivity depending on the substrate.

The reactions of arenediazonium salts with various carbon nucleophiles such as Grignard reagents,[10] enamines,[11] enol ethers,[12] lithium enolates of ketones or esters,[13] and ketene silyl acetals,[7] are all known to result in the formation of azo or hydrazono compounds, and arylation has not been observed previously. Thus, the present method offers a unique method for using arenediazonium salts as aryl cation equivalents in order to introduce aryl groups onto carbon nucleophiles.

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† Nonan-2-one is a genuine product which was formed in the reaction mixture before the acid hydrolysis. Since its formation is accompanied by phenylpyridine, the main proton source required for nonan-2-one formation from the starting material would be pyridine.

‡ The silyl enol ether also seems to intervene subtly in radical formation, because in its absence, phenylpyridine formation was much slower.