

Secondary Mannich Bases via Trimethylsilyl Trifluoromethanesulphonate Promoted Addition of Silyl Enol Ethers to Schiff Bases

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A convenient route to *N*-aryl- β -aminoketones is reported involving addition of silyl enol ethers to Schiff bases activated with 15 mol % of trimethylsilyl trifluoromethanesulphonate.

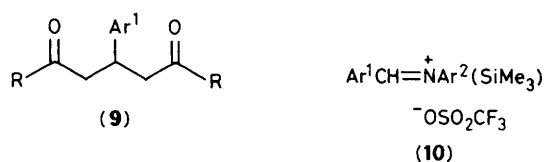
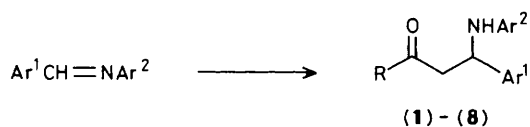
The Mannich reaction is a well known method for the synthesis of β -aminoketones but the harsh conditions generally employed, the lack of regioselectivity with unsymmetrical

ketones, and poor yields of secondary Mannich bases when primary amines are used are some of its limitations.¹ Additions of silyl enol ethers to *N,N*-dimethylinium

Table 1. Preparation of *N*-aryl- β -aminoketones.^a

Product ^b	R	Ar ¹	Ar ²	M.p., t/°C ^c	Yield, % ^d
(1)	Ph	Ph	Ph	163—165	50
(2)	Bu ^t	Ph	Ph	145—147	52
(3)	Ph	<i>p</i> -NO ₂ C ₆ H ₄	Ph	117—118	66
(4)	Bu ^t	<i>p</i> -NO ₂ C ₆ H ₄	Ph	128—129	62
(5)	Ph	Ph	<i>p</i> -BrC ₆ H ₄	175—176	74
(6)	Bu ^t	Ph	<i>p</i> -BrC ₆ H ₄	118—119	75
(7)	Ph	Ph	<i>p</i> -IC ₆ H ₄	166—167	98
(8)	Bu ^t	Ph	<i>p</i> -IC ₆ H ₄	125—127	67

^a Molar ratio imine:silyl enol ether:TMSOTf = 1:2:0.15. ^b Spectral and elemental analytical data are in accordance with the proposed structures. ^c Not corrected. ^d Yields based on chromatographed material.



Reagents: TMSOTf (15 mol %), then $\text{CH}_2=\text{C}(\text{R})\text{OSiMe}_3$.

salts²⁻⁴ have been described as a regioselective entry to the corresponding tertiary Mannich bases and titanium tetrachloride promoted addition of silyl ketene acetals to imines was introduced as an efficient route to *N*-aryl- β -aminoesters and β -lactams.⁵

The report by MacLean *et al.*⁶ on the addition of the lithio derivative of 3-cyano-4-methylpyridine to *N*-trimethylsilyliminium trifluoromethanesulphonates prompts us to disclose our results on the addition of silyl enol ethers to activated Schiff bases. $\text{BF}_3\cdot\text{OEt}_2$, TiCl_4 , SnCl_4 , and trimethylsilyl trifluoromethanesulphonate (TMSOTf) were employed to promote the reaction and good yields of *N*-aryl- β -aminoketones (1)–(8)[†] were obtained when 15 mol % of TMSOTf was employed (Table 1).[‡] $\text{BF}_3\cdot\text{OEt}_2$ led to lower yields of β -aminoketones while TiCl_4 and SnCl_4 afforded the symmetrical 1,5-diketones (9) as the major products, albeit in low

yields (ca. 20%). The assumption that the *N*-silylated iminium cation (10) is an intermediate in the reaction is supported by the isolation of an insoluble product formed after addition of TMSOTf to a solution of benzylideneaniline in chloroform which showed the azomethine proton resonance as a singlet at δ 9.34 (1.0 p.p.m. downfield shift), in $(\text{CD}_3)_2\text{SO}$, and a 50 cm^{-1} increase in the $\text{C}=\text{N}$ i.r. stretching frequency with respect to the imine.⁷

The diastereofacial selectivity of the reaction is under investigation.

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[†] Characteristic methine resonances (^1H : δ 4.80–5.15; ^{13}C : δ 54.0–54.9; CDCl_3) were observed.

[‡] In a typical experiment, TMSOTf (0.15 equiv.) was added to a solution of the imine in dichloromethane, at 0°C and under argon. After 10 min a solution of the silyl enol ether (2.0 equiv.) in dichloromethane was added dropwise and the precipitate initially formed redissolved. After 2–3 h at room temperature the reaction was quenched with aqueous sodium hydrogen carbonate and the β -aminoketone was isolated after washing the crude product with hexanes.