Photochemical Michael reaction of silyl enol ethers with 2′-nitro- and 2′,2′-dicyanostyrenes

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Photolysis of silyl enol ethers with 2′-nitro- and 2′,2′-dicyanostyrene acceptors yields the corresponding Michael adducts in moderate yield and diastereoselectivity. The desilylation of the silyl enol ethers to the corresponding ketones and *cis-trans* isomerization of the olefinic acceptors competes with the photochemical Michael addition. Under similar conditions, α,β-unsaturated carbonyl compounds give only *cis-trans* isomerization. A mechanism involving the regiospecific addition of silyl enol ether to the π-π* excited Michael acceptor to form a zwitterionic intermediate is proposed.

Introduction

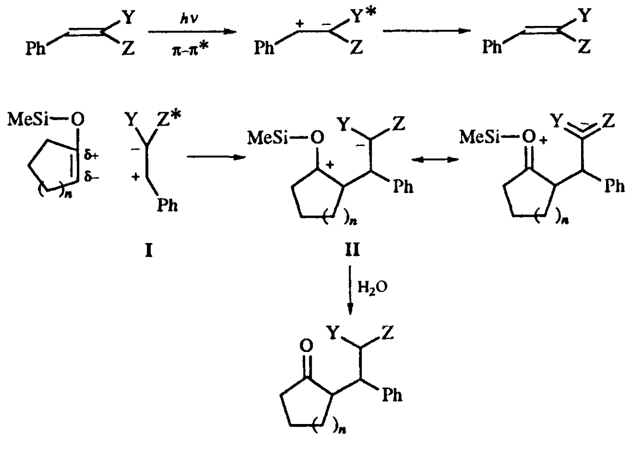
The Michael reaction is a commonly used C–C bond forming reaction of high synthetic utility, involving the addition of a carbon nucleophile (Michael donor, electron-rich species) to an electron-deficient double bond (Michael acceptor).[1] The addition of silyl enol ethers and ketene silyl acetals to Michael acceptors in the presence of a Lewis acid catalyst is known as the Mukaiyama–Michael reaction and offers a convenient route for the synthesis of 1,5-dicarbonyl compounds.[2] The photoactivation of the Michael reaction has only occasionally been described.[3] Our interest in the photochemistry of electron donor–acceptor complexes[4] has initiated a study on the photoactivation of the Michael reaction of silyl enol ethers with 2′-nitro- and 2′,2′-dicyanostyrenes.

Results and discussion

The photolysis of an equimolar mixture of **2** and **3a** in CH_2Cl_2 or CH_3CN using a Pyrex filter yielded the Michael adduct **5a** which was separated by column chromatography and characterized by IR, ^1H and ^{13}C NMR spectroscopy and mass spectral data, reaction (1). The results obtained with various Michael acceptors are given in Table 1. In all cases the crude product consisted of the Michael adduct, unreacted Michael acceptor and the ketone from the hydrolysis of the silyl enol ether. The Michael adducts were obtained as a pair of diastereoisomers and the ratio of the diastereoisomers was obtained from integration of the high resolution ^1H NMR spectra of the purified products. In the case of acceptors **3c**, **3h** and **3i**, the corresponding Michael adducts were not formed even after prolonged irradiation with the silyl enol ethers. Instead, these substrates underwent only *cis-trans* isomerization and the silyl enol ethers remained intact.

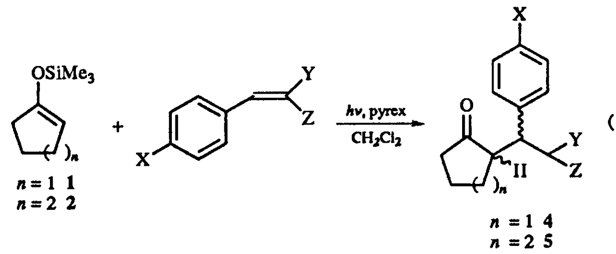
The mechanism of the photochemical Michael reactions

The silyl enol ethers do not have absorption above 270 nm. Under the photolysis conditions only the Michael acceptors absorb light. In the case of 2′-nitrostyrene **3a** and its derivatives **3b–c** the lowest energy absorption lies in the region of 300–350 nm. This strong absorption of the 2′-nitrostyrenes corresponds to π-π* excitation and shows a bathochromic shift with increasing solvent polarity. (λ_{max} in cyclohexane and CH_2Cl_2 for **3a**: 300 and 313 nm; **3c**: 335 and 353 nm.) It has been shown previously by experiments and theoretical calculations that the π-π* state is an intramolecular charge-transfer state and is dominated by the charge transfer from the highest filled molecular orbital of the styryl moiety (PhCH=CH) to the lowest unoccupied molecular orbital.[5] The latter orbital is located almost exclusively on the acceptor nitro group. In terms of the valence bond structure, the π-π* excited state of the 2′-nitrostyrenes can be represented in the zwitterionic form **I** (Scheme 1). Thus, the excited state 2′-nitrostyrenes have higher electrophilicity in the α position compared to that in the ground state. The enhanced electrophilicity of the α position of the excited state Michael acceptors can be compared to the Lewis acid co-ordinated Michael acceptors which also show enhanced reactivity in the thermal Mukaiyama–Michael reaction.[6] Formation of the Michael adduct in the photochemical reaction can be explained by the regiospecific orientation of the silyl enol ether and the excited state 2′-nitrostyrene followed by bond formation to give the zwitterionic intermediate **II**, either directly or through the formation of an exciplex intermediate. Though the latter mechanism involving an exciplex intermediate is similar to Corey's proposal for the [2 + 2] cycloaddition of excited cyclic enones to electron-rich olefins,[7] more recent work, largely due to Weedon,[8] seems to imply that it is not necessary to include exciplex formation in the mechanism of [2 + 2] photocycloaddition reactions. In the present mechanism (Scheme 1), formation of 1,4-diradical intermediates may be ruled out because such intermediates generally lead to products of [2 + 2] cycloaddition, namely cyclobutane derivatives which are not observed as intermediates in the photochemical Michael reactions. Analysis of the ^1H NMR spectra of the crude reaction mixtures before chromatographic separation clearly indicated the absence of cyclobutane derivatives. Atmospheric oxygen had no effect on the reaction. Moreover, the zwitterionic intermediate **II** derives resonance stabilization. Formation of the zwitterionic intermediate **II** in the photochemical Michael reaction is akin to the formation of similar intermediates in the thermal [2 + 2] cycloaddition of



Scheme 1

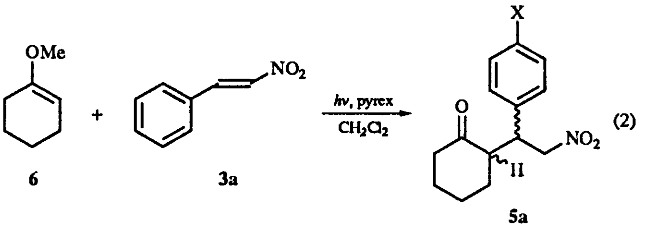
Table 1 Photochemical Michael addition of silyl enol ethers to 2′-nitro- and 2′,2′-dicyanostyrenes



Donor		Acceptor X	Y	Z	Conversion[a] (%)	Yield[b] (%)	Ratio of diastereoisomers[c]
1	**3a**	H	NO_2	H	40	55	1:1.3
2	**3a**				40	35	1:1.7
1	**3b**	Cl	NO_2	H	25	60	1:2.0
2	**3b**				30	35	1:1.5
1	**3c**	OMe	NO_2	H	0	0	
2	**3c**				0	0	
1	**3d**	H	CN	CN	32	62	1:4.0
2	**3d**				40	51	1:3.0
1	**3e**	NO_2	CN	CN	40	58	1:3.4
2	**3e**				50	51	1:3.5
1	**3f**	Cl	CN	CN	40	60	1:3.6
2	**3f**				32	40	1:2.7
1	**3g**	Me	CN	CN	25	34	1:2.7
1	**3h**	H	COMe	H	0	0	
2	**3h**				0	0	
2	**3i**	H	COMe	COMe	0	0	

[a] Conversion based on recovered acceptor. [b] Yield based on unrecovered acceptor. [c] From peak integration of the 400 MHz ^1H NMR spectra of the product.

electron-rich olefins to electron-poor olefins.[9] Further evidence for the zwitterionic mechanism comes from the dealkylation observed when methyl enol ether **6** was used instead of silyl enol ether **2**. Thus, photolysis of a mixture of **6** and **3a** using a Pyrex filter yielded only the Michael adduct **5a**, albeit in lower yield compared to the silyl enol ether case, reaction (2). The observed dealkylation in the case of **6** is best explained by the formation of a zwitterionic intermediate which is an oxocarbenium ion as well.



Hydrolysis of the zwitterionic intermediate (oxocarbenium ion) gives the Michael adduct. Formation of the Michael adduct by the hydrolysis of a cyclobutane derivative[9] [2 + 2 cycloaddition product] in this case is unlikely because the alkoxycyclobutanes are more stable to hydrolysis compared to the corresponding silyloxy derivatives.[3a]

The energy wasting *cis-trans* isomerization of the acceptors could occur from the π-π* excited state, which has been previously reported for 2′-nitrostyrenes.[10] In fact, direct excitation of the 2′-nitrostyrenes in the absence of silyl enol ethers gave only *cis-trans* isomerization.

The failure of **3c** to undergo the photochemical Michael addition is probably due to the reduced electrophilicity of the α-carbon of the styryl moiety in the excited state due to the electron-releasing nature of the *para* methoxy group. Those α,β-unsaturated carbonyl compounds which are not part of a ring system are known to undergo an effective energy-wasting *cis-trans* isomerization.[11] In the present study, both **3h** and **3i** failed to undergo the photochemical Michael addition reaction due to competing *cis-trans* isomerization.

Experimental

Materials

1-Trimethylsilyloxycyclopentene **1** and 1-trimethylsilyloxycyclohexene **2** were prepared according to the literature procedure[12] and purified by vacuum distillation. 2′-Nitrostyrene **3a** [mp 56 °C (lit.,[13] 56–58 °C)], 4-chloro-2′-nitrostyrene **3b** [mp 112 °C (lit.,[14] 111–112 °C)], 4-methoxy-2′-nitrostyrene **3c** [mp 86 °C (lit.,[15] 87 °C)], 2′,2′-dicyanostyrene **3d** [mp 85 °C (lit.,[16] 85 °C)], 4-chloro-2′,2′-dicyanostyrene **3f** [mp 161 °C (lit.,[17] 162–163 °C)], 4-nitro-2′,2′-dicyanostyrene **3e** [mp 160 °C (lit.,[17] 159–160 °C)], 4-methyl-2′,2′-dicyanostyrene **3g**,[17] *trans*-benzalacetone **3h**,[18] 3-benzylideneacetylacetone **3i**[19] and 1-methoxycyclohexene **6** [bp 137–138 °C (lit.,[20] 137–138 °C)] were prepared according to the literature procedure and were purified either by recrystallization from ethanol or by distillation under vacuum. Michael adducts **4a–b**, **5a–b**, **4d–e** and **5d–e** have been reported previously[21] and in the present study they were characterized by IR, ^1H and ^{13}CNMR spectroscopy and mass spectral data, and also by comparison with authentic samples by TLC. Dichloromethane was distilled over P_2O_5 and stored under a nitrogen atmosphere. The instrumentation used has been described previously.[4a] The photochemical reactions were performed using the output from a 150 W xenon arc lamp source (Oriel Corporation) or a 450 W Hanovia lamp using a Pyrex filter.

Typical procedure for photolysis

The photolysis was carried out in a water-jacketed Pyrex vessel using the output from the above-mentioned lamps. In a typical experiment a mixture of 1-trimethylsilyloxycyclohexene **2** (0.35 g, 2 mmol) and 2′-nitrostyrene **3a** (0.29 g, 2 mmol) in dichloromethane (10 cm^3) was photolysed and the course of the reaction was followed by TLC. After photolysis for 24 h, solvent was removed from the reaction mixture at room temperature using a rotary evaporator and the solid residue was separated by column chromatography over silica gel (60–120 mesh). Elution with a mixture of hexane and ethyl acetate (90:10 v/v) yielded, in the following order, cyclohexanone, 2′-nitrostyrene and the product, namely, 2-(2-nitro-1-phenylethyl) cyclohexanone **5a**. The product **5a** was further purified by recrystallization from hexane–ether (2:1 v/v).

Spectroscopic characterization of Michael adducts

2-[2,2-Dicyano-1-(4-chlorophenyl)ethyl]cyclopentanone 4f. Yield 60%, ratio of diastereoisomers 1:3.6, ν_{max}(KBr)/cm^{-1} 2896, 2256 (CN), 1718 (C=O), 1587, 1491; δ_H($CDCl_3$) isomer **I**: 7.36 (2 H, d, *J* 8.3), 7.12 (2 H, d, *J* 8.3), 5.22 (1 H, d, *J* 10.74), 3.48 (1 H, dd, *J* 10.74 and 4.39), 2.8 (1 H, m), 2.5–1.5 (6 H, m); isomer **II**: 7.41 (2 H, d, *J* 8.3), 7.31 (2 H, d, *J* 8.3), 5.5 (1 H, d, *J* 4.39), 3.2 (1 H, dd, *J* 11.23 and 4.39), 2.7 (1 H, m), 2.5–1.5 (6 H, m); δ_C($CDCl_3$) isomer **I**: 219.5 (s), 135.2 (s), 133.3 (s), 129.8 (d), 129.5 (d), 112.0 (s), 111.9 (s), 49.36 (d), 46.9 (d), 39.5 (t), 27.5 (d), 26.36 (t), 20.4 (t); isomer **II**: 219.1 (s), 135.3 (s), 133.8 (s), 129.9 (d), 129.7 (d), 111.8 (s), 111.7 (s), 48.3 (d), 46.1 (d), 38.5 (t), 29.4 (d), 27.0 (t), 19.8 (t); *m/z* (EI, 70 eV) 272 (M^+, 6), 245 (16), 207 (28), 188 (40), 84 (100); HRMS found: 272.07102 $C_{15}H_{13}N_2OCl$ requires 272.06810.

2-[2,2-Dicyano-1-(4-methylphenyl)ethyl]cyclopentanone 4g. Yield 34%, ratio of diastereoisomers 1:2.7, ν_{max}(KBr)/cm^{-1} 2926, 2220 (CN), 1728 (C=O), 1599, 1520, 1344; δ_H($CDCl_3$) isomer **I**: 7.22 (4 H, m), 5.22 (1 H, d, *J* 12.1), 3.44 (1 H, dd, *J* 12.0 and 4.7), 2.76 (1 H, m), 2.35 (3 H, s), 2.4–1.28 (6 H, m); isomer **II**: 7.16 (2 H, d, *J* 8.0), 7.04 (2 H, d, *J* 8.0), 5.44 (1 H, d, *J* 4.8), 3.14 (1 H, dd, *J* 4.82 and 11.76), 2.76 (1 H, m), 2.38 (3 H, s), 2.4–1.25 (6 H, m); δ_C($CDCl_3$) isomer **I**: 218.17 (s), 138.9 (s), 131.7 (s), 130.1 (d), 128.3 (d), 112.0 (s), 111.9 (s), 49.2 (d), 47.3 (d), 39.6 (t), 27.5 (d), 26.3 (t), 20.4 (q), 19.8 (t); isomer **II**: 219.1 (s), 138.9 (s), 132.3 (s), 129.8 (d), 128.2 (d), 111.9 (s), 111.8 (s), 48.5 (d), 46.3 (d), 38.5 (t), 29.5 (d), 27.2 (t), 21.1 (q), 19.8 (t); *m/z* (EI, 70 eV) 252 (M^+, 13), 225 (20), 187 (30), 168 (42), 148 (10), 121 (30), 119 (80), 117 (100), 84 (20); HRMS found: 252.12444, $C_{16}H_{16}N_2O$ requires 252.12628.

2-[2,2-Dicyano-1-(4-cholorophenyl)ethyl]cyclohexanone 5f. Yield 40%, ratio of diastereoisomers 1:2.7, ν_{max}(KBr)/cm^{-1} 2928, 2832, 2224 (CN), 1705 (C=O), 1484, 1398; δ_H($CDCl_3$) isomer **I**: 7.36 (2 H, d, *J* 8.79), 7.27 (2 H, d, *J* 8.79), 4.85 (1 H, d, *J* 9.28), 3.30 (1 H, two overlapping dd), 3.03 (1 H, dt, *J* 11.97 and 6.60), 2.5–1.5 (8 H, m); isomer **II**: 7.30 (2 H, d, *J* 8.79), 7.24 (2 H, d, *J* 8.79), 5.0 (1 H, d, *J* 4.39), 3.30 (1 H, two overlapping dd), 2.93 (1 H, dt, *J* 11.23 and 4.80), 2.5–1.5 (8 H, m); δ_C($CDCl_3$) isomer **I**: 210.5 (s), 134.8 (s), 134.1 (s), 130.0 (d), 129.3 (d), 112.0 (s), 111.9 (s), 51.2 (d), 47.2 (d), 42.3 (t), 32.1 (d), 29.6 (t), 26.9 (t), 24.8 (t); isomer **II**: 212.1 (s), 135.1 (s), 133.5 (s), 129.7 (d), 129.5 (d), 111.8 (s), 111.6 (s), 50.9 (d), 45.1 (d), 42.7 (t), 33.6 (d), 28.5 (l), 27.3 (t), 25.1 (t); *m/z* (EI, 70 eV) 286 (M^+, 10), 259 (10), 221 (21), 188 (44), 98 (100); HRMS found: 286.08730, $C_{16}H_{15}N_2OCl$ requires 286.08499.

Conclusions

Silyl enol ethers **1** and **2** underwent photochemical Michael addition to 2′-nitro- and 2′,2′-dicyanostyrenes to yield the corresponding adducts in moderate yields and diastereoselectivity. A mechanism involving the regiospecific addition of the silyl enol ether to the π-π^* excited state of the Michael acceptor has been proposed. The *cis-trans* isomerization of the excited state Michael acceptors competed with the photochemical Michael reaction. α,β-Unsaturated carbonyl compounds failed to undergo photochemical Michael addition with silyl enol ethers because the *cis-trans* isomerization was the predominant process.

Acknowledgements

Financial support from CSIR and DST, New Delhi is gratefully acknowledged. One of the authors (D. R.) thanks CSIR, New Delhi for a Senior Research Fellowship. We thank the Regional Sophisticated Instrumentation Centre, IIT, Madras, for the high resolution NMR and mass spectral data.

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Paper 5/05903H
Received 6th *September* 1995
Accepted 6th *December* 1995