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Photochemical SET Induced 1,4-Conjugate Additions of Silyl Phosphites to Cyclic Enones

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Abstract: Irradiation of cyclic enones 5-8 in the presence of $Me_3SiOP(OMe)_2$ or $Me_3SiOP(OEt)_2$ gives phosphonosilylation products of 1,4conjugate addition which are hydrolyzed to the phosphonoketones 11-14 in 82-92% isolated yields. An SET process in which the triplet enone accepts an electron from the silvl phosphite is proposed to be the key initiation step in these reactions. © 1999 Elsevier Science Ltd. All rights reserved.

Properly substituted phosphonates can serve as key intermediates for the synthesis of biologically active compounds.¹ The additions of silyl phosphites (2) to α,β -unsaturated aldehydes and ketones (1) to give the desirable 1,4-adducts of *phosphonosilylation* (3), and their β -ketophosphono hydrolysis products (4), have been much studied.² Unfortunately, unlike their acyclic counterparts, reactions of *cyclic* enones do not occur



readily. Thus, reaction of $Me_3SiOP(OEt)_2$ with 2-cyclohexenone (6) requires 12 h at 180 °C to give nearquantitative yields of adducts in 1,4/1,2 ratio of 16/1; i.e., predominantly the 1,4-phosphonosilyl precursor to 12.^{2b} (See Table 1 for structures 5-16.) The methyl analog, $Me_3SiOP(OMe)_2$, was essentially unreactive.^{2b,c}

Continuing interest in these reaction systems is shown by the very recent report of the ability of trimethylsilyl triflate to catalyze, at 0 °C, the nearly exclusive formation of the 1,4-adducts on reaction of cyclic enones, including 5 and 6, with trimethylsilyl phosphites (Me₃SiOP(OR)₂; R = Et, and sometimes Me, PhCH₂, Ph).^{2a} On hydrolytic workup (eq 1), the cyclic β -ketophosphonates were obtained in 75-98% isolated yields. However, with enone 10 the *1,2-adduct* was the major product (68% 1,2; 20% 1,4).

Our interest in photoinduced single electron transfer (SET) reactions of three-coordinate phosphorus compounds³ led us to attempt *photochemical* phosphonosilylation by irradiation of cyclic α , β -unsaturated ketones in the presence of Me₃SiOP(OR)₂ (R = Me, Et). The envisaged initiation step is electron transfer to the *triplet excited* state of the enone to generate the radical ion pair **17/18**, as illustrated for **5** by eq 2:

(2) 5
$$\stackrel{\text{hv}}{\longrightarrow}$$
 5 $[T_1]^*$ $\stackrel{\text{2}}{\xrightarrow{\text{SET}}}$ 17 $\stackrel{\text{OSiMe}_3}{\longrightarrow}$ $\stackrel{\text{P(OR)}_2}{\xrightarrow{\text{ISC}}}$ 18

The analogous reduction of triplet excited states of α , β -unsaturated ketones by amines and allylstannanes, to give radical anion intermediates such as 17, has been extensively studied.⁴

We report here the photochemical phosphonosilylation of the cyclic α , β -unsaturated ketones **5-8** to give high isolated yields of **11-14** (Table 1), formed by hydrolytic workup of the cyclic, 1,4-phosphonosilyl adducts analogous to **3**. Conjugate 1,4-addition occurs essentially exclusively, as shown by GC and ³¹P NMR analysis of reaction product solutions before workup. Phosphites Me₃SiOP(OEt)₂ and Me₃SiOP(OMe)₂ work comparably well. The 2-methyl-substituted enone **8** affords ketophosphonate **14** in high yields. However, methyl substitution at C-3 renders phosphite

10 resistent to 1,4-addition. The mechanism proposed for formation of phosphonosilylated products involves hitherto unrecognized reactions of the radical cations of $Me_3SiOP(OR)_2$. Very significantly, a solution of 5 and $Me_3SiOP(OMe)_2$ that was kept in the dark for 48 h gave no evidence of reaction (GC).

Although its scope is not fully defined, the photoinduced SET approach to phosphonosilylation has potential advantages synthetically. As with the Me₃SiOTf-catalyzed phosphonosilylations,^{2a} one avoids the high temperatures and long reaction times required in the direct thermal reactions of Me₃SiOP(OEt)₂ with enones (180 °C, 12 h for **5**, **6**, and the cyclohexenone analog of **8**).^{2b} Moreover, the *absence* of added Me₃SiOTf in the photoinduced SET reactions precludes competing silylation of other sites that could lead to unwanted side reactions in multifunctional molecules. Furthermore, SET-induced phosphonosilylation is successful with a seven-membered ring enone (**7**), Table 1, a reaction not reported for the thermal Me₃SiOP(OEt)₃/cyclic enone or triflate-catalyzed phosphonosilylations.

enones		product	isolated yields (%)	
			R = Me	R = Et
5	Å	11 P(OR)2	92	82
6	°	12 0 0 P(OR) ₂ 0 0	89	91
7	\bigcirc		81	78
8	Me		86	87
9	Me Me	15 Me Me Ö	a	c
10	O Me	16 0 Me	b	c

Table 1: Photoinduced SET Reaction of Cyclic Enones with Me 3SiOP(OR)2

a) Isolated 57% yield of three products with MS M+ for 1:1 adduct; major product 90% (^{31}P NMR). b) <5%, GC/MS. c) Reaction not run.

The procedure for reaction of 2-cyclopentenone (5) with Me₃SiOP(OMe)₂ is typical: In a water bath at room temperature, a 50 mL deoxygenated CH₃CN solution, 10.0 mM in 5 and 15 mM in Me₃SiOP(OMe)₂, in a septum-capped Pyrex tube was irradiated (450 W medium pressure Hg lamp) to complete consumption of 5 in 4.6 h (GC). The *single new peak* observed in the GC showed by GC/MS an M⁺ peak (m/z = 264) corresponding to a 1:1 adduct of 5 and (MeO)₂POSiMe₃, 22 (R = Me); ³¹P NMR (C₆D₆) $\delta = 35.9$. Hydrolysate 11 (R = Me, $\delta^{31}P = 33.8$) was absent. Solvent removal under vacuum, dissolution of the residue in stirred ethyl acetate (75 mL), addition of water (5 mL), separation of the organic layer, which was then dried over Na₂SO₄, and removal of solvent left an oil. Silica gel chromatography (2% methanol-ethyl acetate) furnished 0.18 g (92% yield) of product ketophosphonate 11 (R = Me) which was

characterized spectroscopically.5

The structures of 11 (R = Et) and 12-14 (R = Me or Et) also are totally supported by their ³¹P, ¹H, ¹³C NMR and MS/HMRS spectral data. Both diastereomers (cis and trans) of 14 (4/1 ratio, R = Me; 1/1 ratio, R = Et) were observed (¹H, ¹³C, ³¹P NMR chemical shifts; e.g. for R = Me, $\delta^{31}P = 30.9$ and 30.4, CDCl₃).

In a larger scale photoreaction, irradiation of enone 6 (1.25 g, 13.0 mmol) and Me₃SiOP(OMe)₂ (3.12 g, 17.1 mmol) in 230 mL of CH₃CN in the jacket of an immersion well (450 W Hg, Pyrex filter) allowed isolation of the initial phosphonosilylation product itself (21): 2.8 g (76% yield), 92% pure (GC), bp 89-90 °C (0.005 mmHg), containing 8% of its hydrolysis product (12, R = Me).

The proposed SET initiation step (eq 2) is estimated for 2-cyclopentenone (5) by the Rehm-Weller equation⁶ to be favorable if the oxidation potential $(E_{\nu_1}^{ox})$ for Me₃SiOP(OR)₂ is about 0.6 eV less than $E_{\nu_1}^{ox}$ for (MeO)₃P (1.6 eV⁷);⁸ Indeed, α -Me₃Si substitution reduces the $E_{\nu_2}^{ox}$ of alkylamines by 0.2-0.5 eV⁹. For 2-cyclopentenone: $E_{\nu_1}^{red} = -2.16 \text{ eV}^{10}$ $E_{\tau} = 3.21 \text{ eV}^{11}$.

A probable mechanism for the formation of phosphonosilylation product 21 from *triplet* radical ion pair $17/18^{12}$ involves the predictably rapid, *but previously unexploited*, fragmentation of 18 to the trimethylsilyl cation and phosphinoyl radical 19 (eq 3). Scission step 3 is favored thermodynamically by the formation of the phosphoryl bond (P=O) and by the excellent capabilities in acetonitrile of Me₃Si⁺ as an electrofuge. Additionally, scission may be assisted *kinetically* by the attack on 18 by the enolate oxygen of 17 (eq 4) to yield directly the pair of neutral radicals 19/20 that rapidly couples to afford product 22 (eq 4):



Analogous silvlations enolate radical anions such as 17 by cation radicals are proposed in the allyl-stannylations of ketones.¹³ α , β -diketones¹⁴, and α , β -unsaturated enones.⁴



The above process (eq 4) is in sharp contrast to the well-studied SET, photo-additions in CH₃CN of $Et_2NCH_2SiMe_3$ to enones (e.g. 6 and 9¹⁵) in which *silylation of the cyclohexenone radical anion to form the equivalent of 17 does not occur*. Instead, rapid proton transfer to the enolate radical ion from the silyl amine radical cation ensues, followed by coupling of the resultant radical pair. Such a proton transfer step is not available to 17/18.

A much less likely mechanistic possibility (eq 5) utilizes the silyl cation from 18 (eq 3) catalytically to generate 23 which reacts with 2 to give intermediate 24 through which 22 is formed and 23 is regenerated.



Presumably, this is the pathway by which Me₃SiOTf catalyzes the phosphonosilylation by Me₃SiOP(OEt)₂ of 5, 6

and related enones at 0 °C^{2a} and gives *in only 1 h* largely 1,2-phosphono-silylation product (68%) from enone **10**, along with a lesser amount (20%) of the 1,4-product.^{2a} However, attempted SET-induced reaction of enone **10** affords (GC/MS) <5% of any product with M⁺ corresponding to a 1:1 phosphonosilylation product *in 14 h* (Table 1), a fact *inconsistent* with a mechanism (eq 5) in which radical ion **18** functions as a Me₃SiOTf equivalent.

In the unsuccessful attempted reactions of enones 9 and 10, Me₃SiOP(OMe)₂ is only partially consumed in 14-18 h of irradiation, suggesting that SET may be inefficient. In fact, a large amount of a dimer of 10 is generated. On extended irradiation, enone 9 and Me₃SiOP(OMe)₂ gave a 57% yield of mixture of three products (one very predominant). The GC/MS of each product showed an M⁺ peak corresponding to a 1:1 adduct. The possibly marginal energetics of SET (eq 2)⁸ also may account for the unreactivity we encountered with acyclic enones whose more highly twisted, geometrically relaxed triplets should have energies that are lower than those of their cyclic counterparts.¹⁶ Steric problems associated with methyl substitution at carbons 3 and 4 in 9 and 10 also may play a role. Acknowledgments. We thank the National Science Foundation (CHE9707038) and Public Health Service (GM53309) for grants in support of this research.

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- 5. ${}^{31}P$ NMR (C₆H₆, 121 MHz) & 33.8. ${}^{1}H$ NMR (C₆H₆, 300 MHz) & 3.35 (d, 3 H, J = 10.5 Hz), 3.34 (d, 3 H, J = 10.7 Hz); 1.58-2.34 (m, 7 H). ${}^{13}C$ NMR (C₆H₆, 75 mHz) & 214.5 (d, J = 16 Hz), 52.5 (d, J = 6.5 Hz), 38.9 (d, J = 3.1 Hz), 37.6 (d, J = 7.2 Hz), 32.8 (d, J = 152.2 Hz), 23.9 (d, J = 3.4 Hz). MS (EI) m/z (rel. intensity): 192 (M⁺, 11) 164 (20), 151 (21), 137 (100), 111 (54), 110 (59), 109 (15), 83 (26), 82 (19). HRMS (EI), M⁺: calcd 192.0551, obsd 192.0553.
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