$H_3)_3$; $R^2 = H$; R^3 = phenyl), 78808-49-8; **6** ($R^1 = CH_3$; $R^2 = H$; R^3 = cyclohexyl), 81435-42-9; **6** ($R^1 = CH_3$; $R^2 = H$; R^3 = phenyl), 78808-42-1; **6** ($R^1 = Si(CH_3)_3$; $R^2 = CH_3$; R^3 = cyclohexyl), 81435-43-0; **6** ($R^1 = Si(CH_3)_3$; $R^2 = CH_3$; R^3 = phenyl), 81435-44-1; **6** ($R^1 = CH_3CH_2$; $R^2 = CH_3$; R^3 = cyclohexyl), 81435-45-2; **6** (R^1 = phenyl; $R^2 = CH_3$; R^3 = cyclohexyl), 81435-46-3; **6** (R^1 = phenyl; $R^2 = CH_3$; R^3 = phenyl), 81435-47-4; **8** ($R^1 = Me_3Si$; R^2 = Me; R^3 = cyclohexyl), 81435-48-5; **8** ($R^1 = Me_3Si$; R^2 = Me; R^3 = phenyl), 81435-49-6; **8** (R^1 = phenyl; R^2 = Me; R^3 = cyclohexyl), 81435-50-9; **8** (R^1 = Et; R^2 = Me; R^3 = cyclohexyl), 81435-51-0; **8** ($R^1 = Me_3Si$; R^2 = OTHP; R^3 = cyclohexyl), 81435-52-1; **8** ($R^1 = Me_3Si$; R^2 = OTHP; $R^3 = C_5H_{11}$), 81435-53-2; **8** (R^1 = Me; R^2 = OTHP; R^3 = cyclohexyl), 81435-54-3; **8** (R^1 = Me; R^2 = OTHP; $R^3 = C_5H_{11}$), 81435-55-4; **8** (R^1 = Me; $R^2 = OCMe_2OMe$; $R^3 = C_5H_{11}$), 81435-56-5; **8** (R^1 = Me; R^2 = OTHF; R^3 = cyclohexyl), 81435-57-6; **8** (R^1 = Me; R^2 = OTHF; $R^3 = C_5H_{11}$), 81435-58-7; **9** ($R^1 = Me_3Si$; R^2 = Me; R^3 = cyclohexyl), 81435-59-8; **9** ($R^1 = Me_3Si$; R^2 = Me; R^3 = phenyl), 81435-60-1; **9** (R^1 = phenyl; R^2 = Me; R^3 = cyclohexyl), 81435-61-2; **9** (R^1 = Et; R^2 = Me; R^3 = cyclohexyl), 81435-62-3; **9** ($R^1 = Me_3Si$; R^2 = OTHP; R^3 = cyclohexyl), 81495-67-2; **9** ($R^1 = Me_3Si$; R^2 = OTHP; $R^3 = C_5H_{11}$), 81495-68-3; **9** (R^1 = Me; R^2 = OTHP; R^3 = cyclohexyl), 81495-69-4; **9** (R^1 = Me; R^2 = OTHP; $R^3 = C_5H_{11}$), 81495-70-7; **9** (R^1 = Me; $R^2 = OCMe_2$; $R^3 = C_5H_{11}$), 81435-63-4; R^3CHO (R^3 = cyclohexyl), 2043-61-0; R^3CHO (R^3 = phenyl), 100-52-7; R^3CHO ($R^3 = C_5H_{11}$), 66-25-1; $R^1C{\equiv}CCH_2R^2$ ($R^1 = Si(CH_3)_3$; $R^2 = H$), 6224-91-5; $R^1C{\equiv}CCH_2R^2$ ($R^1 = CH_3$; $R^2 = H$), 503-17-3; $R^1C{\equiv}CCH_2R^2$ ($R^1 = Si(CH_3)_3$; $R^2 = CH_3$), 62108-37-6; $R^1C{\equiv}CCH_2R^2$ ($R^1 = CH_3CH_2$; $R^2 = CH_3$), 928-49-4; $R^1C{\equiv}CCH_2R^2$ (R^1 = phenyl; $R^2 = CH_3$), 622-76-4; $R^1C{\equiv}CCH_2R^2$ ($R^1 = Me_3Si$; R^2 = OTHP), 36551-06-1; $R^1C{\equiv}CCH_2R^2$ (R^1 = Me; R^2 = OTHP), 39637-48-4; $R^1C{\equiv}CCH_2R^2$ (R^1 = Me; $R^2 = OCMe_2OMe$), 81435-64-5; $R^1C{\equiv}CCH_2R^2$ (R^1 = Me; R^2 = OTHF), 81435-65-6; titanium tetraisopropoxide, 546-68-9.

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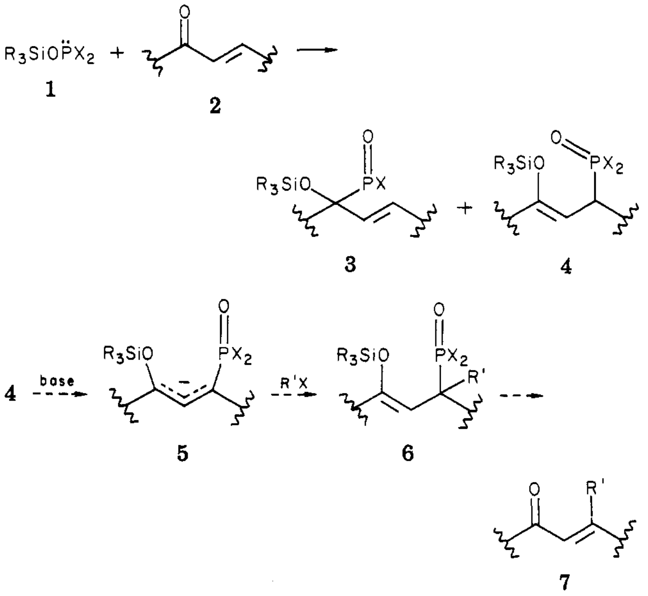
Phosphonosilylations of Cyclic Enones

Summary: Diethyl trimethylsilyl phosphite reacts smoothly with a variety of cyclic enones to produce β-phosphonotrimethylsilyl enol ethers.

Sir: The synthetic utility of dipole reversal (umpolung) reactions is now well-established.[1] Recently, we have become interested in a specific type of dipole reversal process, namely, the conversion of enones into adducts which serve as enone β-anion equivalents. Examination of the literature indicates that a number of different protocols have been developed toward this end.[2] One of these involves reaction of various mixed phosphorous-silicon reagents with unsaturated aldehydes and ketones to produce 1,2- and/or 1,4-adducts of this original substrate.[3] In principle, these adducts could then be deprotonated, alkylated, and unmasked to yield the alkylated analogue of the original substrate (vide infra). However, one of the severest limitations of this methodology involves the inability of cyclic enones to form adducts, such as **4**, with these mixed phosphorous-silicon reagents. For example, Evans has previously reported that cyclohexenone (**8**) fails to undergo any detectable 1,4-addition with reagents of general structure **1** (e.g., **1a**, R = Me, X = OMe or **1b**, R = Me, X = NMe_2).[3a] In this communication we report that under the proper experimental conditions, diethyl trimethylsilyl phosphite (**1c**, R = Me, X = OEt)[4] reacts smoothly with a variety of cyclic enones to, in most cases, regioselectively produce 1,4-adducts of type **4**. Specific results are listed in Table I.



We have developed two slightly different sets of reaction conditions which are particularly effective for inducing adduct formation. These involve heating the substrate in question in acetonitrile in the presence of 1.8 equiv of diethyl trimethylsilyl phosphite (**1c**) for varying lengths of time at either 80 °C (simple reflux) or 180 °C (sealed tube). That the regioselectivity of these additions is in some cases significantly affected by temperature at which the reaction is performed suggests that the product ratios are the result of thermodynamic rather than kinetic control. This is easily verified by exposing a given adduct mixture, formed at 80 °C, to the 180 °C reaction conditions and then determining the changes, if any, in the adduct ratio. In all cases the newly determined isomer ratios conformed to within ±10% to those performed at 180 °C.

Simple cyclic enones such as **8** or **10** react with **1c** to form 1,4-adducts with good regioselectivity. As long as the β-carbon and the carbonyl carbon atoms are at least comparably hindered, 1,4-adduct formation clearly represents the dominant reaction pathway. However, as the degree of hindrance around the β-carbon atom increases, the relative amount of 1,4-adducts formed correspondingly decreases. This is seen most graphically in the reaction

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(1) (a) Seebach, D.; Kolb, M. *Chem. Ind.* **1974**, 687. (b) Lever, O. W. *Tetrahedron* **1976**, *32*, 1943.

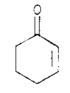
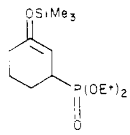
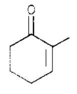
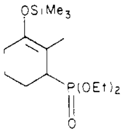
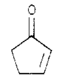
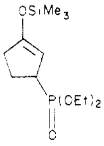
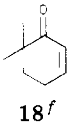
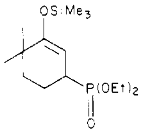
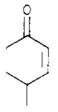
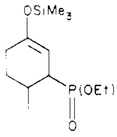
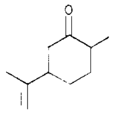
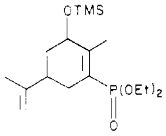
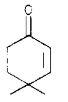
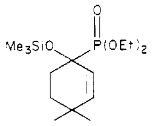
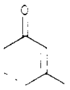
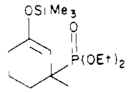
(2) (a) Kondo, K.; Tsunemoto, D. *Tetrahedron Lett.* **1975**, 1007. (b) Corey, E. J.; Erickson, B. W.; Noyori, R. *J. Am. Chem. Soc.* **1971**, *93*, 1724. (c) Nakai, T.; Shiono, H.; Okawara, M. *Tetrahedron Lett.* **1974**, 3625. (d) Cohen, T.; Bennett, D. A.; Mura, A. J. *J. Org. Chem.* **1976**, *41*, 2506. (e) Lansbury, P. T.; Britt, R. W. *J. Am. Chem. Soc.* **1976**, *98*, 4578. (f) Wade, M.; Nakamura, H.; Taguchi, T.; Takei, H. *Chem. Lett.* **1977**, 345. (g) Corey, E. J.; Kim, C. U.; Chen, R. H. K.; Takeda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4395. (h) Debal, A.; Civigny, T.; Larchavigne, M. *Tetrahedron Lett.* **1977**, 3187. (i) Cooper, G. K.; Dolby, L. J. *Ibid.* **1976**, 4675. (j) Bakuzis, P.; Bakuzis, M. L. V.; Weingartner, T. F. *Ibid.* **1978**, 2371. (k) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 7360. (l) Evans, D. A.; Andrews, G. C., *Acc. Chem. Res.* **1974**, *7*, 147.

(3) (a) Evans, D. A.; Hurst, K. N.; Truesdale, L. K.; Takacs, J. M. *Tetrahedron Lett.* **1977**, 2495. (b) Hata, T.; Hashizume, A.; Nakajima, M.; Sekine, M. *Tetrahedron Lett.* **1978**, 363. (c) Evans, D. A.; Hurst, K. M.; Takacs, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 3467. (d) Evans, D. A.; Takacs, J. M.; Hurst, K. M. *Ibid.* **1979**, *101*, 371.

(4) Diethyl trimethylsilyl phosphite (**1c**) is easily prepared by reactions of the sodium salt of diethyl phosphite with trimethylsilyl chloride in ether at room temperature (yield, >95%). This reagent, although easily hydrolyzed, exhibits a greater shelf stability than its dimethyl analogue **1a**.

0022-3263/82/1947-2227$01.25/0

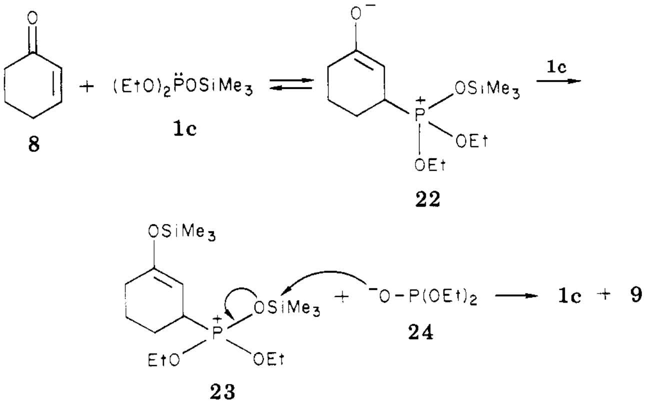
Table I

substrate	major product[a]	temp, °C	time, h	adduct ratio (1:4/1:2)[b]	% yield	substrate	major product[a]	temp, °C	time, h	adduct ratio (1:4/1:2)[b]	% yield
 **8**	 **9**	80 180	75 12	8:1 16:1	98 99	 **16**[e]	 **17**	80 180	16 12	4:1 99:1	100 94
 **10**	 **11**	80 180	12 12	100:0 100:0	97 100	 **18**[f]	 **19**	180	12	100:0	90
 **12**[c]	 **13**	80 180	12 16	 9:5	NR 94	 **20**	 **21**	80 180	12 72	 100:0	NR 82
 **14**[d]	 **15**	80 180	200 18	2:3 1:19	100 87			80 180	20 120	 >19:1	NR 100

[a] Products were characterized on the basis of their NMR, IR, and mass spectra. [b] Isomer ratios were determined spectroscopically. [c] Wilds, A. L.; Nelson, N. A. *J. Am. Chem. Soc.*, **1953**, *75*, 5360. [d] Dauben, W. G.; Schaffer, G. W.; Vietmeyer, N. D. *J. Org. Chem.* **1968**, *33*, 4060. [e] Warnhoff, E. W.; Marten, D. G.; Johnson, W. S. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, p 162. [f] Holysz, R. P. *J. Am. Chem. Soc.*, **1953**, *75*, 4432. Freppel, C.; Poirier, M.; Recher, J.; Maroni, Y.; Manuel, G. *Can. J. Chem.* **1974**, *52*, 4133.

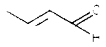
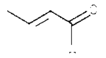
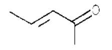
of **14** with **1c** which produced **15** as the major product even under the milder reaction conditions (80 °C).

A plausible mechanism for the formation of 1,4-adducts is illustrated below for the conversion of **8** to **9**. It involves the reversible formation of intermediate **22**, which then undergoes an *intermolecular* silylation/desilylation to produce **9**. The driving force for the production of **9** is probably due in large measure to the high thermodynamic stability associated with a phosphorus–oxygen double bond. The regioselectivity of the process is most readily rationalized by the principles of hard–soft acid–base theory, i.e., the soft phosphorous nucleophile preferentially attacks the softer β-carbon atom rather than the harder carbonyl carbon.



The major question to be answered is why reactions of **1c** with cyclic enones result in adduct formation, while reactions involving similar reagents, such as **1a** or **1b**, apparently fail. In our opinion a number of factors contribute. First, the ability of **1c** to form adducts with cyclic enones is clearly solvent dependent. For example, reactions performed under similar sets of conditions but which utilize chloroform as a solvent instead of acetonitrile proceed at a markedly slower rate. Presumably, this is simply a function of the charged intermediates being better stabilized by solvents of higher polarity. Since in cyclic enones geometric constraints prevent the silicon transfer step from being intramolecular (vide supra), charge factors are likely to be more important in reactions involving cyclic enones.[5] Moreover, since previous attempts to utilize **1a** and **1b** were carried out either neat or in anhydrous THF, it is conceivable that solvent polarity could be in part responsible for apparent differences in reactivity. Examination of the data given in Table II lends credence to this supposition.

Table II

substrate	reagent	solvent, temp (°C), time (h)	adduct ratio (1:4/1:2)	% yield	ref
	1a	neat, 55, 18	1:3	90	3a
	1c	benzene, 25, 21	0:100	73	this work
	1c	CH_3CN, 25, 8	0:100	93	this work

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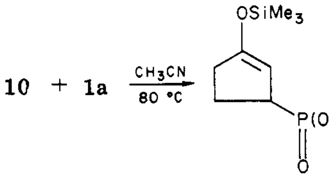
(5) In ref 3c, Evans presents strong evidence for the fact that the silicon transfer step is intramolecular with acyclic enones.

(6) Fellow of the Alfred P. Sloan Foundation, 1980–1984. Recipient of a Camille and Henry Dreyfus Teacher-Scholar Fellowship, 1981–1986.

Second, as can be noted by comparison of Tables I and II, the reaction times and temperatures required for efficient adduct formation with cyclic enones far exceed those required for the corresponding acyclic systems. In fact, when **1a** is allowed to react with **10** at 80 °C for 12 h, **25** is formed as the only observable product. Therefore the reported inability of cyclic enones to form adducts with **1a** or **1b** is simply the result of the experimental conditions chosen rather than the intrinsic inability of cyclic enones to undergo this type of reactions. This sluggish reactivity is most probably due to the fact that the silicon transfer step must be intermolecular with α,β-unsaturated ketones locked in a transoid geometry.[5]



25

Further applications of this methodology will be the subject of future reports.

Acknowledgment. Financial support for this work was provided by the National Institutes of Health.

Registry No. 1a, 36198-87-5; **1c**, 13716-45-5; **8**, 930-68-7; **9**, 81435-27-0; **10**, 930-30-3; **11**, 81435-28-1; **12**, 5515-76-4; **13**, 81435-29-2; **14**, 1073-13-8; **15**, 81435-30-5; **16**, 1121-18-2; **17**, 81435-31-6; **18**, 6553-64-6; **19**, 81435-32-7; **20**, 99-49-0; **21**, 81435-33-8; **25**, 81435-34-9; 2-butenal, 4170-30-3; diethyl [1-[(trimethylsilyl)oxy]-2-butenyl]-phosphonate, 66731-79-1; 3-methyl-2-cyclohexen-1-one, 1193-18-6; diethyl [1-methyl-3-[(trimethylsilyl)oxy]-2-cyclohexenyl]-phosphonate, 81435-35-0.

Supplementary Material Available: Experimental details for the conversion of **10** to **11** (1 page). Ordering information is given on any current masthead page.

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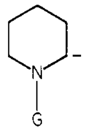
Received December 8, 1981

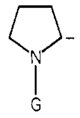
A Novel Entry into Indole Alkaloids

Summary: By use of α-amino carbanions generated from β-carbolines and the successful blocking of indole nitrogen, the elaboration of these systems to indole alkaloids is described.

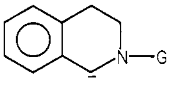
Sir: The indole class of alkaloids has been the subject of extensive synthetic efforts over the years.[1] However, modern methodology has added a new dimension to the synthesis of these substances. Among the more conceptual advances in alkaloid syntheses has been the work of Shono[2] using electrochemical techniques and the generation of carbanions adjacent to a modified amino function (A–D) which upon alkylation produces the elaborated heterocycles.[3]



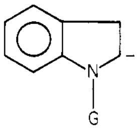
A



B



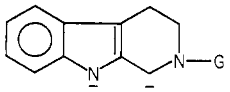
C



D

G = NO,[3a] C(=O)CR$_3$,[3b] PO(NMe$_2$)$_2$,[3c] CH=N-*t*-Bu[3d]

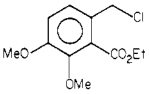
We now report that the amino carbanion derived from tetrahydro-β-carboline has been successfully employed as a viable precursor to indole alkaloids, affording three representative systems **7**, **10**, and **13** (Scheme I). To our knowledge there is no precedent for generating the carbanion from the tetrahydrocarbolines and this may have been the result of the inability to generate the dianion E



E

or the difficulty in finding a suitable protecting group for the indole nitrogen.[4] The indole alkaloid approach begins with the conversion of tetrahydro-β-carboline to its formamidine derivative **1** by heating with 3.0 equiv of *N*,*N*-dimethyl-*N′*-*tert*-butylformamidine[5] in toluene overnight (80%, mp 168–170 °C after chromatography on silica, 10% Et$_3$N, 20% acetone, 70% hexane). Efforts to generate the dianion E with various bases (LDA, *sec*-BuLi, *t*-BuLi) failed and only the use of 2.0 equiv of *n*-butylpotassium[6]

Table I. Synthetic Yields Leading to 7, 10, and 13 from 4

electrophile	% yield[a]	% hydrazinolysis[a]	% hydrolysis	mp, °C
MeI	5 (84)	6a (68)	7a (77)[f]	177–180[i]
i-BuI	5 (87)	6b (91)[c]	7b (78)[g]	258–260[j]
PhCHO	5 (89)			
Cl(CH$_2$)$_4$Br	8[b]	9 (68)[d]	10 (77)[g]	150–152[k]
	11 (89)	12 (83)[e]	13 (75)[h]	253–255[h]

[a] Following chromatography. [b] Not purified, carried on to 9. [c] Mp 72–73 °C (pentane). [d] Overall yield from 4. [e] Mp 165–166 °C, M$^+$ 392. [f] Stirred for 15 min with 3 N HCl, neutralized to pH 10 with NaOH, stirred for 1 h at 25 °C. [g] Heated at 60–65 °C for 1 h in 3 N HCl–THF (1:1), neutralized to pH >11, two layers stirred overnight. [h] Same conditions as in *g* except heating was continued for 5.5 h. [i] Mp 178–180 °C: Badger, G. M; Beecham, A. F. *Nature* (*London*) 1951, *168*, 517. [j] Hydrochloride salt, mp 257–259 °C: Slywka, G. W. A.; Locock, R. A. *Tetrahedron Lett.* 1969, 4635. [k] Mp 147–149 °C: Johansen, J. E.; Christie, B. D.; Rapoport, H. *J. Org. Chem.* 1981, *46*, 4914. [h] Recrystallized from ethyl acetate–hexane, analytical data satisfactory.

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