Purification as described in part A gave hemiketal **42**, 288 mg (0.95 mmol, 60% yield).

***trans*-6-Hydroxy-7-methoxy-3-methyl-2,3,4,4a,5,6,6a,10c-octahydro-1*H*-[1]benzopyrano[4,3,2-*ef*]isoquinoline (44) and *trans*-6,7-Dihydroxy-3-methyl-2,3,4,4a,5,6,6a,10c-octahydro-1*H*-[1]benzopyrano[4,3,2-*ef*]isoquinoline (45).** Potassium *tert*-butoxide (1.5 g, 12.5 mmol) containing residual *tert*-butyl alcohol was added to degassed DMF (30 mL) under argon, and the suspension was degassed with argon for 1 h. EtSH (1.5 mL, 1.26 g, 20.25 mmol) was then added to provide a ca. 0.68 M solution of EtSK in DMF. Amino ketone **38** (60 mg, 0.2 mmol) was added to the EtSK/DMF solution (2.5 mL, 1.7 mmol) and heated at 100 °C (bT) under argon for 8 h. The solution was allowed to cool and after 12 h was evaporated, the residue was dissolved in 0.6 M aqueous NaOH (20 mL), the solution was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic phases were dried and evaporated to an oil which crystallized from PhH to give **44**: 25 mg (0.087 mmol, 43%); mp 125–140 °C; IR ($CHCl_3$) 3330, 3280 cm^{-1}; ^1H NMR (60 MHz) δ 6.90 (m, 3 H), 6.55 (br s), 4.87 (s, 3 H), 2.49 (s, 3 H), 3.5–1.2 (m); mass spectrum, *m/z* (relative intensity) 289 (19), 218 (13), 45 (100). Anal. Calcd for $C_{17}H_{23}NO_3 \cdot 0.15H_2O$: C, 69.9; H, 8.1; N, 4.8. Found: C, 69.9; H, 8.3; N, 4.7.

The aqueous phase was acidified (pH 1), washed with $CHCl_3$ (2 × 10 mL), basified (pH 8.5), and extracted with 3/1 $CHCl_3$/*i*-PrOH (3 × 15 mL). The combined organic extracts were washed with saturated aqueous NaCl (15 mL), dried, and evaporated to yield **45**: 30 mg (0.11 mmol, 55%); yellow oil; ^1H NMR (60 MHz, Me_2SO-d_6) δ 7.18–6.56 (m, 3 H), 3.89 (m, 1 H), 3.80 (br s, 2 H), 2.27 (s, 3 H), 3.1–0.9 (m); mass spectrum, *m/z* (relative intensity) 275 (59), 274 (21), 165 (21), 109 (24), 57 (100); exact mass calcd for $C_{16}H_{21}NO_3$ *m/z* 275.1510, found 275.1520.

Treatment of amino ketone **38** as described above for amido ketone **35** afforded **44** in 60% yield.

Acknowledgment. This research was supported in part by the National Institute on Drug Abuse.

Registry No. 5, 86-51-1; **6a**, 39059-72-8; **6b**, 81011-95-2; **7a**, 81011-96-3; **7b**, 81011-97-4; **8a**, 81011-98-5; **8b**, 81011-99-6; **9**, 81012-00-2; **10**, 81012-01-3; **11**, 81012-02-4; **12**, 61209-85-6; **13**, 61209-87-8; **14**, 61527-89-7; **15**, 61527-90-0; **16**, 79618-99-8; **17**, 79619-00-4; **18**, 79619-13-9; **19**, 79619-14-0; **20**, 81012-03-5; **21**, 81012-04-6; **22**, 81012-05-7; **23**, 81012-06-8; **24**, 81012-07-9; **25**, 81012-08-0; **26**, 81012-09-1; **27**, 79631-85-9; **29**, 79619-02-6; **30**, 79619-07-1; **31**, 79619-11-7; **32**, 81012-10-4; **33**, 81012-11-5; **34**, 81012-12-6; **35**, 81064-05-3; **36**, 81012-13-7; **37**, 81012-14-8; **38**, 81012-15-9; **39**, 81012-16-0; **40**, 81012-17-1; **41**, 81012-18-2; **42**, 81012-19-3; **44**, 81012-20-6; **45**, 81012-21-7; **46**, 81012-22-8; **47**, 81012-23-9; **48**, 81012-24-0; **49**, 81012-25-1; **50**, 81012-26-2; **51**, 79619-12-8; **52**, 81012-27-3; **53**, 81012-28-4; **54**, 81012-29-5; **55**, 81012-30-8; **56**, 81012-31-9; **57**, 81012-32-0; **58**, 81012-33-1; **59**, 81012-34-2; i, 81012-35-3; ii, 81012-36-4; $EtO_2CCH_2CO_2H$, 1071-46-1; $NCCH_2CO_2H$, 372-09-8.

Supplementary Material Available: Textual and experimental details for the following: (1) selective reduction of amides in the presence of esters; (2) alternative routes to amino ester **11**; (3) alternative methods for allylic oxidation of α-methylene lactams; (4) developmental aspects of the SeO_2 reaction including the effect of solvent, water content, stoichiometry, time, temperature, and aromatic substitution pattern on the yield (15 pages). Ordering information is given on any current masthead page.

Diazoethenes: Their Attempted Synthesis from Aldehydes and Aromatic Ketones by Way of the Horner–Emmons Modification of the Wittig Reaction. A Facile Synthesis of Alkynes[1-3]

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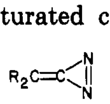
Received December 29, 1981

The base-promoted reaction of dimethyl (diazomethyl)phosphonate (**8**) with aldehydes and aryl ketones at low temperatures has been investigated. Alkynes, in modest to excellent yields, are the predominant products of these reactions, a result consistent with the intervention of diazoethenes (**3**). The latter appear to be unstable toward unimolecular decomposition at −78 °C and yield nitrogen and alkylidenecarbenes (**1**).

General interest exists in the physical and chemical properties of the unsaturated carbenes **1**,[4] and these

$R_2C{=}C:$

1



2

$R_2C{=}CN_2$

3

species, which we shall refer to as alkylidenecarbenes,[5] have therefore been the recent subject of both theoretical[7] and experimental[8] investigations. However, a review of the literature relevent to the chemistry of such species failed

Table I. Theoretical Values of Singlet–Triplet Gap for Vinylidene (**1**, R = R = H)[a]

method	$\Delta H_{f(T_1)} - \Delta H_{f(S_0)}$, kcal/mol	ref
ab initio (HF)	15.7	7g
SCF (MINDO/2)	20.5	7c
ab initio (HF)	27.2	7f
SCF (MINDO/3)	28.2	this work
ab initio (HF)	31.0	7e
ab initio (SCEP)	32.4	7f
SCF (MNDO)	41.7	this work
ab initio (DEC 1-RSPT-4)	45.2	7g
ab initio (GVB)	45.9	7e
ab initio (MBPT-4)	49.7	7g
ab initio (MBPT-8)	51.1	7g
ab initio (MBPT-[3-3])	51.1	7g
ab initio (MBPT-[1-1])	51.3	7g

[a] Arbitrarily listed according to the increasing magnitude of the gap and not according to the relative sophistication of the theoretical method.

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(1) This paper is dedicated to Professor William von E. Doering on the occasion of his 65th birthday.

(2) A preliminary account of portions of this work has been published: Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1979**, *44*, 4997.

(3) Taken in part from the dissertation of U.W. submitted in partial fulfillment of requirements for the Ph.D. degree.

(4) Reviews: (a) Hartzler, H. In "Carbenes"; Jones, M., Jr., Moss, R. A., Eds.; Wiley-Interscience: New York, 1975; Vol II. (b) Stang, P. J. *Acc. Chem. Res.* **1978**, *11*, 107. (c) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383. (d) Schaefer, H. F., III. *Acc. Chem. Res.* **1979**, *12*, 288.

(5) This category of carbene has variously been referred to as methylene carbenes[4a] and vinylidenes,[4d] in addition to the term[4b,c] used herein, which is recommended by *Chemical Abstracts*.[6]

(6) Newman, M. S.; Patrick, T. B. *J. Am. Chem. Soc.* **1970**, *92*, 4312.

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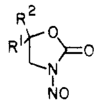
to reveal any instances in which the triplet carbene was implicated as an intermediate. This presumably is because the methods that have been purported to generate alkylidenecarbenes are anticipated to yield the singlet electronic state initially. Subsequent relaxation to the triplet state, by way of collisional deactivation, for example, as in the case of saturated carbenes,[9] is unavailable to 1 if the theoretical predictions currently available are to be believed; all are in agreement that vinylidene (1, R = R = H) is more stable in the singlet rather than the triplet electronic state, although there is considerable spread in the calculated endothermicity of this transformation (Table I). The calculated magnitudes of the singlet–triplet gap, in fact, would obviously preclude establishment of a measurable equilibrium between the two electronic states. In any event, the triplet manifold of alkylidenecarbenes (1) remains completely unexplored experimentally.[10]

It appeared that a viable, although hardly novel, approach to triplet alkylidenecarbenes might be by way of photosensitized decomposition of an appropriate precursor, a technique that has found much success for generation of various saturated triplet carbenes.[12] Because of the anticipated difficulties in generating alkylidenediazirines (2), attention was first directed toward producing diazoalkenes (3), and aspects of this work are described herein.

Diazoalkenes have been proposed as possible, albeit undemonstrated, intermediates in several processes, including the nitrosation of primary vinylamines 4,[13] the base-promoted decomposition of both *N*-nitrosooxazolidones 5,[14] and *N*-nitrosoacetylamino alcohols 6[15] and the thermal decomposition of *N*-tosylazoalkenes 7.[16] However, none of these methods appeared particularly attractive as a means of producing diazoalkenes 3 for two important reasons. First of all, there is considerable uncertainty about whether any of these approaches involves the diazo compound, even as a transient intermediate. Second, there exist significant limitations on the temperatures at which these reactions can be performed; we wished to generate the diazoalkenes at the lowest possible temperature to maximize the possibility of their isolation, and none of the methods used previously is effective below −20 °C.

$R_2C{=}CHNH_2$

4



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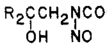


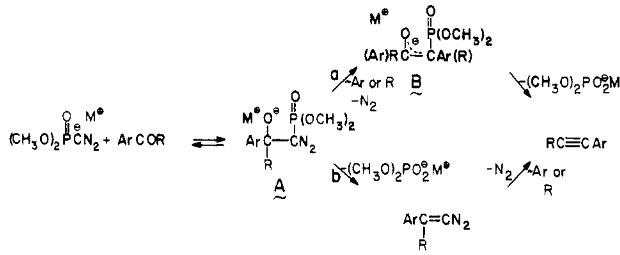
$\underset{\text{OH}}{R_2CCH_2}\underset{\text{NO}}{N}COCH_3$

6

$R_2C{=}CHN{=}NSO_2C_6H_4CH_3$

7

Scheme I. General Mechanistic Pathways for Alkyne Production



A potentially appealing way to produce diazoalkenes rested on intriguing observations reported by Colvin and Hamill.[17] These workers noted that reaction of the anion of dimethyl (diazomethyl)phosphonate (8) with diaryl ketones or electrophilic aryl aldehydes afforded alkynes in good yields (eq 1). That this transformation did *not*

$$\underset{\mathbf{8}}{(CH_3O)_2P(O)CHN_2} \xrightarrow[\text{2. ArCOR}]{\text{1. }n\text{-BuLi or KO-}t\text{-Bu}} ArC{\equiv}CR \quad (1)$$

involve a semipinacol-type of rearrangement (path a, Scheme I) was inferred from their observation that the diazo aldol 9 could be converted to 1-ethynyl-4-nitrobenzene (10) when treated with base whereas 11 could not (eq 2). The argument was that deprotonation of 9 and

$$\underset{11}{(CH_3)_2P(O)CH_2C(O)Ar} \overset{\text{KO-}t\text{-Bu}}{\not\longrightarrow} \underset{10}{HC{\equiv}CAr} \xleftarrow{\text{KO-}t\text{-Bu}} \underset{9}{(CH_3O)_2P(O)C(N_2)CH(OH)Ar} \quad (2)$$

Ar = 4-nitrophenyl

11 should yield betaines having structures corresponding to A and B, respectively (Scheme I), and that the latter betaine must fail to eliminate. Consequently, path b (Scheme I), which involves production of a diazoalkene, was proposed to explain the data.

These results encouraged us to attempt generation of diazoalkenes by way of the overall transformation shown in eq 3. There appeared to be some severe limitations on

$$8 + R_2CO \xrightarrow{\text{base}} \underset{\mathbf{3}}{R_2C{=}CN_2} \quad (3)$$

the potential of the method as a general approach to these diazo compounds, however. Thus, it was reported that the use of enolizable substrates (acetophenone and phenylethanal) or of insufficiently electrophilic aldehydes afforded low yields of alkynes at best;[17] this implies correspondingly low yields of the precursor diazoalkenes 3. Moreover, it was unclear what thermal requirements were associated with the transformation of carbonyl substrate either to the alkyne (eq 1) or to the presumed diazoalkene

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[7] (a) Gleiter, R.; Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 5457. (b) Hopkinson, A. C.; Yates, K.; Csizmadia, I. G. *J. Chem. Phys.* **1971**, *55*, 3835. (c) Bodor, N.; Dewar, M. J. S.; Wasson, J. S. *Ibid.* **1972**, *94*, 9095. (d) Strausz, O. P.; Norstrom, R. J.; Hopkinson, A. C.; Schoenborn, M.; Csezmadia, I. G. *Theor. Chim. Acta* **1973**, *29*, 183. (e) Davis, J. H.; Goddard, W. A., III; Harding, L. B. *J. Am. Chem. Soc.* **1977**, *99*, 2919. (f) Dykstra, C. E.; Schaefer, H. F., III. *Ibid.* **1978**, *100*, 1378. (g) Kenney, J. W.; Simons, J.; Purvis, G. D.; Bartlett; R. J. *Ibid.* **1978**, *100*, 6930. (h) Conrad, M. P.; Schaefer, H. F., III. *Ibid.* **1978**, *100*, 7820. (i) Apeloig, Y.; Schrieber, R. *Tetrahedron Lett.* **1978** 4555. (j) Stang, P. J.; Apeloig, Y.; Schrieber, R. *Ibid.* **1980**, 411.

[8] (a) Wentrup, C.; Winter, H. W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 609. (b) Stang, P. J.; Fox, D. P.; Collins, C. J.; Watson, C. R., Jr. *J. Org. Chem.* **1978**, *43*, 364. (c) Wentrup, C.; Byrne, E. W.; Müller, P. *Tetrahedron Lett.* **1979**, 4249. (d) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1979**, *62*, 852. (e) Armstrong, R. J.; Brown, R. F. C.; Eastwood, F. W.; Romyn, M. E. *Aust. J. Chem.* **1979**, *32*, 1767.

[9] See, for example: Gaspar, P. P.; Hammond, G. S. In "Carbenes"; Moss, R. A., Jones, M., Jr., Eds.; Wiley: New York, 1975; Vol. II, p 300 ff.

[10] It is conceivable that reactions of triplet C_2, generated from the carbon arc, could involve triplet 1, but the experimental observations certainly do not require its intervention.[11]

[11] Skell, P. S.; Havel, J. J.; McGlinchy, M. J. *Acc. Chem. Res.* **1973**, *6*, 97 and references cited therein.

[12] E.g.: (a) Jones, M., Jr.; Ando, W.; Hendrick, M. E., Kulczycki, A., Jr.; Howley, P. M.; Hummel, K. M.; Malement, D. S. *J. Am. Chem. Soc.* **1972**, *94*, 7469. (b) Chang, K.-T.; Schechter, H. *Ibid.* **1979**, *101*, 5082.

[13] Curtin, D. Y.; Kampmeier, J. A.; O'Connor, B. O. *J. Am. Chem. Soc.* **1965**, *87*, 863.

[14] (a) Newman, M. S.; Okorodudu, A. O. M. *J. Am. Chem. Soc.* **1968**, *90*, 4189. (b) *J. Org. Chem.* **1969**, *34*, 1220.

[15] (a) Pfeil, E.; Weissel, O. *Chem. Ber.* **1958**, *91*, 1170. (b) Newman, M. S.; Din, Z. *J. Org. Chem.* **1973**, *38*, 547. (c) Newman, M. S.; Van der Zwan, M. C. *Ibid.* **1974**, *39*, 761.

[16] (a) Rosini, G.; Cacchi, S. *J. Org. Chem.* **1972**, *37*, 1856. (b) Stang, P. J.; Fox, D. P. *Ibid.* **1977**, *42*, 1667.

[17] (a) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Chem. Commun.* **1973**, 151. (b) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869.

Table II. Alkynes from Aldehydes and Ketones[a]

entry	substrate	solvent	product	yield,[b,c] %
1	1-phenylethanal	THF	3-phenyl-1-propyne	80 (30)
2	1-phenylethanal	MeOH	3-phenyl-1-propyne	69
3	2-ethylhexanal	THF	3-ethyl-1-heptyne	79
4	2-furaldehyde	THF	2-ethynylfuran	50
5	4-methoxybenzaldehyde	THF	1-ethynyl-4-methoxybenzene	88
6	4-chlorobenzaldehyde	THF	1-ethynyl-4-chlorobenzene	60
7	4-nitrobenzaldehyde	THF/*t*-BuOH[d]	1-ethynyl-4-nitrobenzene	[84]
8	4-nitrobenzaldehyde	toluene[e]	1-ethynyl-4-nitrobenzene	63
9	(*E*)-3-phenyl-2-propenal	THF	*f*	
10	(*E*)-2-methyl-3-phenylpropenal	THF	(*E*)-3-methyl-4-phenyl-3-buten-1-yne	40
11	(*E*)- and (*Z*)-3,7-dimethyl-2,6-octadienal	THF	(*E*)- and (*Z*)-4,8-dimethyl-3,7-nonadien-1-yne	27
12	acetophenone	THF	1-phenyl-1-propyne	67 (22)
13	acetophenone	MeOH	1-phenyl-1-propyne	*g*
14	4-nitroacetophenone	MeOH[d]	1-(4-nitrophenyl)-1-propyne	55
			(*E*)- and (*Z*)-2-(4-nitrophenyl)-1-methoxypropene	32
15	benzophenone	THF/Et_2NH	1,2-diphenylethyne	[92] (94)

[a] Reactions performed by using KO-*t*-Bu as the base and at −78 °C unless otherwise noted. Reaction conditions have not been optimized. [b] Determined by integration of the ^1H NMR spectrum of samples containing an internal standard (see Experimental Section). [c] Yields in brackets are isolated yields; those in parentheses are those reported in ref 17b. [d] Reaction performed at room temperature. [e] Potassium hydride (23% dispersion in mineral oil) used as the base. [f] Analysis of the ^1H NMR spectrum suggests 1,4-addition or 1,3-dipolar cycloaddition may have occurred. [g] Not determined; however, only resonances attributable to unchanged acetophenone and to 1-phenyl-1-propyne, in a ratio of 1:4, could be detected by ^1H NMR spectroscopy.

Table III

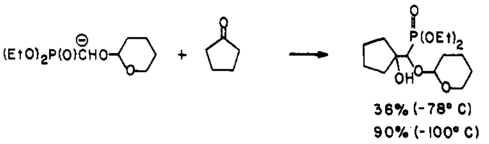
time, min[a]	$C_6H_5COCH_3$/$C_6H_5C{\equiv}CCH_3$ ratio[b]	time, min[a]	$C_6H_5COCH_3$/$C_6H_5C{\equiv}CCH_3$ ratio[b]
8	1.0:1.0	360	1.0:2.2
38	1.0:1.5	540	1.0:2.3
113	1.0:2.0	1200	1.0:4.0

[a] Amount of time reaction mixture was held at −78 °C prior to withdrawal of aliquot, warming to ambient temperature, and quenching. [b] Determined by ^1H NMR analysis of reaction mixture.

(eq 3). The reaction conditions developed by Colvin and Hamill generally involved irreversible deprotonation at −78 °C of the (diazomethyl)phosphonate **8** with *n*-butyllithium, addition of the carbonyl substrate at this same temperature, and subsequently allowing the reaction mixture immediately to warm to room temperature;[17,18] as a result, the actual formation of diazo compounds **3** and of alkynes could have occurred at any of a relatively wide range of temperatures.

Results and Discussion

The thermal and structural parameters for the conversion of carbonyl substrates to alkynes were initially studied as a means of qualitatively assessing the potential of the proposed method (eq 3). To accomplish this, two modifications of the experimental procedure of the previous workers were introduced. One was the selection of potassium *tert*-butoxide instead of *n*-butyllithium as the base in order to make the counterion of A (Scheme I) potassium rather than lithium; such a change is known to enhance the rate of decomposition of betaines.[19] The second was maintainance of the reaction mixture at −78 °C for a more extended period of time, primarily to minimize potential problems (e.g., aldol condensations) associated with enolization of the carbonyl compounds and with thermal decomposition of the anion of **8**.[17b] The latter would be a problem assuming that consumption of the anion by reaction with carbonyl compounds to give **3** was not rapid at −78 °C so that some of the anion remained as the reaction mixture warmed to room temperature. The conjecture that deleterious side reactions associated with enolization of carbonyl substrates by anions of phosphonates would be suppressed by maintaining low temperatures was prompted by Kluge's report of precisely this effect, albeit at −100 °C rather than −78 °C, in the reaction of (alkoxymethyl)phosphonates with cyclopentanone (eq 4).[20]



(4)

These modifications were extremely successful in broadening the scope and efficiency of the conversion of aldehydes and aryl ketones to alkynes (eq 1), as shown by the results collected in Table II. Not only can enolizable aldehydes and ketones (entries 1–3, 12–14) and aryl aldehydes of relatively low electrophilicity (entry 5) be transformed successfully, but so can α,β-unsaturated aldehydes (entries 10, 11), although only modest yields of enynes have been obtained.[21]

The relative rate of the reaction (eq 1), as assessed by spectroscopic examination (^1H NMR) of crude reaction mixtures, depends upon the electrophilicity and/or steric encumbrance of the carbonyl carbon atom, as might be expected. Thus, 80% conversion of carbonyl substrate to alkyne required about 12, 12, and 20 h at −78 °C for phenylethanal, benzophenone, and acetophenone, respectively. Monitoring the conversion of the latter ketone to 1-phenyl-1-propyne as a function of time provided data (Table III) showing that base-promoted reaction between

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(18) The same general sequence of events appears to have occurred in the one instance wherein potassium *tert*-butoxide rather than *n*-butyllithium was used as the base.[17b]

(19) Schlosser, M.; Tuong, H. B.; Tarchini, C. *Chimia* **1977**, *31*, 219.

(20) (a) Kluge, A. F. *Tetrahedron Lett.* **1978**, 3629. (b) Kluge, A. F.; Cloudsdale, I. S. *J. Org. Chem.* **1979**, *44*, 4847.

(21) We have attempted this reaction with acyclic α,β-unsaturated ketones. However, in related studies, it has been found that **8** does not react with 4,4-dimethyl- and 4-methyl-4-phenyl-2-cyclohexen-1-one, and 3,3,5-trimethyl-2-cyclohexen-1-one, suggesting that such ketones are insufficiently electrophilic (Weerasooriya, U., unpublished results).

8 and carbonyl compounds can be a relatively slow process at −78 °C; this obviously must be considered in attempting to optimize yields of alkynes produced by this method.

Highly reactive substrates can undergo transformation to alkynes rapidly and efficiently at room temperature. For example, 4-nitrobenzaldehyde reacted with 8 instantaneously under ambient conditions to give 1-ethynyl-4-nitrobenzene (10, eq 2) in 84% yield (entry 7, Table II), and a similar reaction (entry 14, Table II of 4-nitroacetophenone and 8, except that methanol rather than a mixture of tetrahydrofuran and *tert*-butyl alcohol was used as the solvent, afforded the expected alkyne 12 and a mixture of *E* and *Z* enol ethers 13 (eq 5) in 55% and 32% yields,

$$4\text{-}O_2NC_6H_4C(O)CH_3 + \mathbf{8} \xrightarrow[\text{CH}_3\text{OH, room temp}]{\text{KO-}t\text{-Bu}} \underset{\mathbf{12}}{4\text{-}O_2NC_6H_4C{\equiv}CCH_3} + \underset{\mathbf{13}}{4\text{-}O_2NC_6H_4C(CH_3){=}CHOCH_3} \qquad (5)$$

respectively; consequently, 87% of the ketone has reacted with 8 in a process that is complete in less than 5 min, judging from the cessation of gas evolution.

It was possible to prove by low-temperature NMR analyses that the alkynes were being formed at −78 °C. Thus, 1 h after 2-ethylhexanal had been added to a solution of 8 and potassium *tert*-butoxide in THF at −78 °C (eq 6), the ^{13}C NMR spectrum, taken at −85 °C, exhibited

$$CH_3(CH_2)_3CH(C_2H_5)CHO + \mathbf{8} \xrightarrow[-78\ ^\circ\text{C/THF}]{\text{KO-}t\text{-Bu}} \underset{\mathbf{14}}{CH_3(CH_2)_3CH(C_2H_5)C{\equiv}CH} + (CH_3O)_2PO_2K \qquad (6)$$

resonances at δ 87.6 and 72.1 due to the sp-hybridized carbon atoms of 3-ethyl-1-heptyne (14). Moreover, the ^{31}P NMR spectrum, also obtained at −85 °C, revealed that the resonance of 8 at 21.9 ppm had been replaced by one at 2.0 ppm,[22] the chemical shift expected for potassium dimethyl phosphate.[23,26] The evidence, therefore, is entirely

Scheme II. Detailed Mechanistic Pathways for Alkyne Production

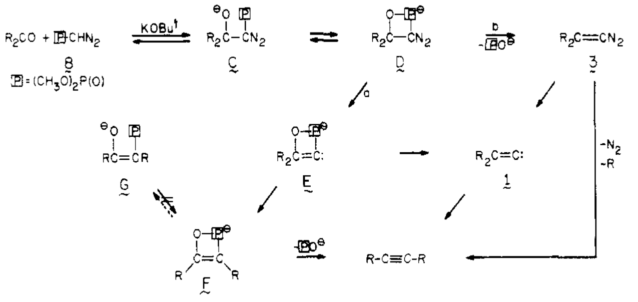
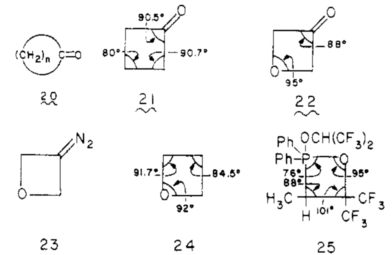


Chart I



in accord with the contention that the transformation of eq 1 is occurring at −78 °C.[30]

Two alternate general mechanisms for the reaction of dimethyl (diazomethyl)phosphonate (8) with aldehydes and ketones are outlined in Scheme II.[31] Both involve the sequential[32] formation of intermediates C and D but di-

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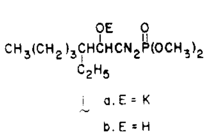
(22) Chemical shifts downfield of 85% H_3PO_4 have been assigned positive values.

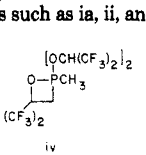
(23) Potassium *diethyl* phosphate has a shift of 0.62 ppm in aqueous solution (pH 7.0).[24] *Literature data*[25] *indicate that the dimethyl analogue* should have its resonance downfield of this value by some 2 ppm.

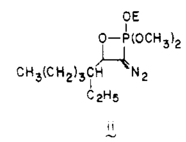
(24) Costello, A. J. R.; Glonek, T.; Van Wazer, J. R. *Inorg. Chem.* **1976**, *15*, 973.

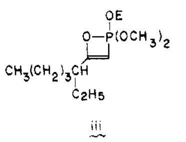
(25) Crutchfield, M. M.; Dungan, C. H.; Letcher, J. H.; Mark, V.; Van Wazer, J. R. *Top. Phosphorus Chem.* **1967**, *5*, 1.

(26) Other phosphorus-containing substances such as ia, ii, and iii were





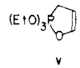




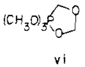
considered as possible sources of this signal but cannot account for it. The first possibility can be eliminated because ib, the conjugate acid of ia, has a chemical shift of 23.8 ppm, and it is known that charge has little effect on chemical shifts of phosphorus.[24] In contrast, both ii and iii could resonate in the proper region, on the basis of the reported shift of iv at 10 ppm.[27,28] They were eliminated in the following way. It was first determined that base-promoted reaction of 2-ethylhexanal and 8 at room temperature for 10 min yielded 14 (eq 6), showing that these conditions are sufficient for the conversion of aldehyde to alkyne. Then, it was found *that if the* NMR *sample previously described* was warmed to room temperature[29] and then recooled to −85 °C, the ^{31}P spectrum obtained was unchanged from the original. Consequently, this evidence invalidates *any* phosphorus-containing precursor to 14 as the source of the signal, unless the precursor and potassium dimethyl phosphate have coincidental chemical shifts.

(27) Gibson, J. A.; Roschenthaler, G.-V.; Wray, V. *J. Chem. Soc., Dalton Trans.* **1977**, 1492.

(28) Relative to ii and iii, iv is at a lower oxidation state, of course. However, replacement of the P–C bond of iv with a P–O bond should further *shield* the phosphorus, leading to a *larger* negative value for δ. This conclusion is based on the chemical shifts of $(CH_3)_2P(O)OEt$ and $CH_3P(O)(OEt)_2$, which are 50.3 and 30 ppm, respectively.[25] The presence of unsaturation in iii should not effect the chemical shift dramatically relative to the model compound iv if the ^{31}P shifts of the five-membered ring analogues v and vi[25] are taken as indicative of this type of effect.



δ(^{31}P) − 30.1



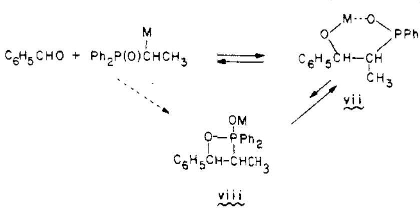
δ(^{31}P) − 32.8 or − 34.2

(29) No gas evolution can be discerned during this operation, providing further evidence against ii as the source of the ^{31}P signal.

(30) Efforts are currently being made to observe transient phosphorus-containing intermediates involved in the formation of the alkynes.

(31) Review of mechanism of reaction of phosphonates with carbonyl compounds: Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87.

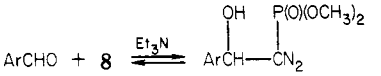
(32) (a) It is conceivable that C is bypassed and that F is formed directly by a $[_\pi 2_s + {}_\pi 2_a]$ process, which has recently[33] been postulated for the Wittig reaction itself. We have no data that bear on this possibility and shall therefore adhere to the generally accepted mechanism that would include C as a first intermediate. (b) It is interesting to note that to our knowledge there has been reported only a single ^{31}P NMR study of the nature of intermediates in a modified Wittig reaction (eq i).[34] This



(i)

study demonstrated the salt vii as a detectable species which was more stable, in fact, than the oxyphosphetane analogue viii. However, this work involved lithium salts that may well stabilize the open-chain form, as is the case with betaines,[33b] thereby distorting the equilibrium between vii and viii. In other words, it is possible that with potassium as the counterion viii is generated directly and proceeds to products or reverts to reactants without intervention of vii.

verge at the latter point. The generation of the tetrahedral species C would be expected to be reversible, on the basis of studies involving other types of phosphonate anions[34] as well as on the existence of equilibria of the type shown in eq 7.[35] The results of two experiments show that this



$$\mathrm{ArCHO} + \mathbf{8} \xrightleftharpoons{\mathrm{Et_3N}} \mathrm{Ar}\underset{}{\overset{\mathrm{OH}}{\mathrm{CH}}}-\overset{\mathrm{P(O)(OCH_3)_2}}{\mathrm{CN_2}} \tag{7}$$

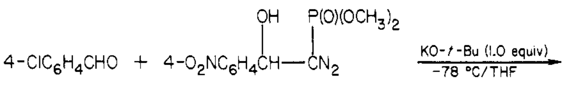
15

remains true when the counterion of the conjugate base of the diazo aldol **15** (eq 7) is potassium. First, the reaction of **8** with an *equimolar* mixture of 4-chloro- and 4-nitrobenzaldehyde (**16** and **17**, respectively) gave the corresponding alkynes in a ratio of 1:5.3, the remaining aldehydes now being present in a ratio of 7.5:1 (eq 8). In the

$$\underset{\mathbf{16}\ (1.0\ \text{equiv})}{4\text{-}\mathrm{ClC_6H_4CHO}} + \underset{\mathbf{17}\ (1.0\ \text{equiv})}{4\text{-}\mathrm{O_2NC_6H_4CHO}} \xrightarrow[\substack{\mathrm{KH}\ (1.0\ \text{equiv})\\ -78\ ^\circ\mathrm{C/THF}}]{\mathbf{8}\ (1.0\ \text{equiv})}$$

$$\mathbf{16} + \mathbf{17} + \underset{\mathbf{18}}{4\text{-}\mathrm{ClC_6H_4C{\equiv}CH}} + \underset{\mathbf{19}}{4\text{-}\mathrm{O_2NC_6H_4C{\equiv}CH}} \tag{8}$$

second experiment, treatment of the diazo aldol **9**[35] with potassium *tert*-butoxide in the presence of 6 equiv of **16** afforded **18** and **19** in a ratio of 1:1.5 (eq 9). It is concluded



$$\underset{\substack{\mathbf{16}\\(6.0\ \text{equiv})}}{4\text{-}\mathrm{ClC_6H_4CHO}} + \underset{\substack{\mathbf{9}\\(1.0\ \text{equiv})}}{4\text{-}\mathrm{O_2NC_6H_4}\overset{\mathrm{OH}}{\mathrm{CH}}-\overset{\mathrm{P(O)(OCH_3)_2}}{\mathrm{CN_2}}} \xrightarrow[-78\ ^\circ\mathrm{C/THF}]{\mathrm{KO}\text{-}t\text{-}\mathrm{Bu}\ (1.0\ \text{equiv})} \mathbf{18} + \mathbf{19} \tag{9}$$

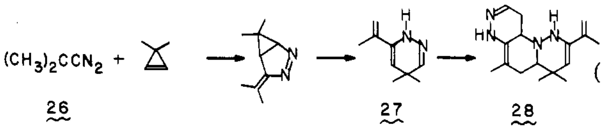
not only that attack of the anion of **8** on the carbonyl-containing substrate is reversible[36] but also that the establishment of the equilibrium to give C is essentially complete prior to the occurrence of any irreversible steps that ensue from this intermediate.

The fate of the oxaphosphetane D, a key intermediate claimed for both the Wittig[37] and the modified Wittig[31] reactions, is given by pathways a and b. The former route posits generation of the novel carbene E, whereas the latter involves the sought-after diazoethene **3**. Loss of nitrogen from **3** could give the alkylidenecarbene **1**, which would be expected[4] to rearrange to the alkyne (vide infra). Similarly, E could eliminate potassium dimethyl phosphate to give **1**, and thereby yield alkyne, but a more probable fate would be its rearrangement to F followed by decomposition to alkyne. Reversion of F to G, of course, would have to be slow relative to its conversion to alkyne, since G is the type of anion that has been found by Colvin and Hamill *not* to eliminate to alkyne (eq 2).[17]

The viability of path a is difficult to assess definitively, but arguments can be marshalled against it. First of all, it is not clear why D should lose nitrogen at −78 °C when **8**, for example, is stable at this temperature. It might be argued that incorporation of the diazomethyl moiety into a small ring, as in D, lowers the activation barrier for unimolecular loss of nitrogen, and one such compound, diazocyclopropane (**20**, $n = 2$, Chart I) is indeed believed to decompose to cyclopropylidene at −20 °C.[38] However, diazocyclobutane (**20**, $n = 3$) appears to be stable at −40 °C, and its decomposition to give the azine is slow at 0 °C.[39] Because it has been postulated[38] that the lesser stability of diazocyclopropane may arise from the tendency for the diazo group to be out of the plane of the ring in order to decrease angle strain, it becomes relevant to consider the possible existence of a similar destabilizing factor in D. Analysis of its probable molecular geometry permits this, as follows.

Diazocyclobutane (20, $n = 3$) presumably has an overall geometry modeled adequately by cyclobutanone (**21**), which is believed to be planar and has the angles shown.[40] Replacement of the C-3 methylene by oxygen, as in oxetanone (**22**), leaves the geometry of the molecule essentially unchanged in that planarity is retained and the intra-ring angles are only slightly modified.[41] Therefore, one would predict that the hypothetical 3-diazooxetane (**23**) would also be planar and have a C_2–C_3–C_4 angle of about 90°. The question now arises as to whether introduction in **23** of phosphorus in lieu of C_2, in order to model oxaphosphetane D, would dramatically change the preferred structure, and the answer appears to be that it would not. Thus, oxetane (**24**) is also essentially planar[42a] and has the indicated bond angles.[41b] Replacement in it of C_α by phosphorus to give the oxaphosphetane **25**[43a] again results in a ring that is nearly planar, the dihedral angle about the axis joining C_2 and O being only 11°.[43b] Note that the P–C_2–C_3 and the C_3–O–P angles are the same as those is **22**, the model for the geometry of **23**, so that it can be argued that replacement of the CH_3CH group of **25** with the N_2C moiety required to generate D should not require unusual distortions in the molecular structure. In summary, we would argue that D should have the diazo moiety coplanar with the ring and a thermal stability, with respect to the loss of nitrogen, analogous to that of diazocyclobutane (**20**, $n = 3$). This clearly could not be the case if pathway a were operable.

A second line of evidence against pathway a is derived from the recent observation that base-promoted reaction of dimethyl (diazomethyl)phosphonate (**8**) with acetone in the presence of 3,3-dimethylcyclopropene affords the tricyclic molecule **28**, which is believed to result from dimerization of the unisolated dehydropyridazine **27** (eq 10).[44] Formation of the latter is most easily rationalized



(10)

26 27 28

as arising from reaction between 2-methyl-1-diazopropene (**26**) and the cyclopropene. Isolation of **28** is therefore considered presumptive evidence for the formation of the diazopropene **26** and supports operation of pathway b in preference to a. Consequently, the remainder of this

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(33) (a) Vedejs, E.; Snoble, K. A. *J. Am. Chem. Soc.* **1973**, *95*, 5778. (b) Vedejs, E.; Meier, G. P.; Snoble, K. A. *Ibid.* **1981**, *103*, 2823.

(34) Schlosser, M.; Piskala, A.; Tarchini, C.; Tuong, H. B. *Chimia* **1975**, *29*, 341.

(35) Disteldorf, W.; Regitz, M. *Chem. Ber.* **1976**, *109*, 546.

(36) Unambiguous exclusion of mechanisms for formation of **18** from reaction of **16** with species derived from **9**, but still having the C_1–C_2 bond intact, is not possible, but such mechanisms are considered unlikely (a concern of this type has been expressed in ref 32b).

(37) Reviews: (a) Johnson, A. W. "Ylid Chemistry"; Academic Press: New York, 1966. (b) Wittig: Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1. (c) Wittig: Schlosser, M. In Karte, F.; Zimmer, H.; Niedenzer, K. "Methodicum *Chimicum*"; Georg Thieme Verlag: Stuttgart, 1976; Vol. 7, p 529.

(38) Jones, W. M.; Grasley, M. H.; Brey, W. S., Jr. *J. Am. Chem. Soc.* **1963**, *85*, 2754.

(39) Applequist, D. E.; Greer, D. E. *J. Am. Chem. Soc.* **1960**, *82*, 1965.

(40) Bauder, A.; Tank, F.; Günthard, H. H. *Helv. Chim. Acta* **1963**, *46*, 1453.

(41) Gibson, J. S.; Harris, D. O. *J. Chem. Phys.* **1972**, *57*, 2318.

(42) (a) Chan, S. I.; Zinn, J.; Fernandez, J.; Gwinn, W. D. *J. Chem. Phys.* **1960**, *33*, 1643. (b) Chan, S. I.; Zinn, J.; Gwinn, W. D. *Ibid.* **1961**, *34*, 1319.

(43) (a) Ramirez, F.; Smith, C. P.; Pilot, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 6726. (b) Haque, M. U.; Caughlan, C. N.; Ramirez, F.; Pilot, J. F.; Smith, C. P. *Ibid.* **1971**, *93*, 5229.

(44) Lahti, P.; Berson, J. *J. Am. Chem. Soc.* **1981**, *103*, 7011.

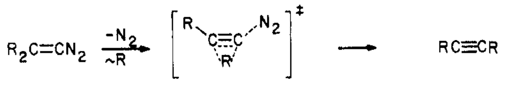
Table IV. Enthalpies of Formation and Activation at 298 K

parameter	compd			
	$CH_2{=}CN_2$	$CH_2{=}C$:	CH_2N_2	CH_2:
$\Delta H_f°$, kcal/mol[d]	102.8	121.5	67.1	106.0
$\Delta\Delta H_f \cong \Delta H_{min}^{\ddagger}$, kcal/mol	18.7		38.9	
$\Delta H^{\ddagger}$, kcal/mol[b]			31.6,[52a] 33.4,[52b] 31.4[52c]	

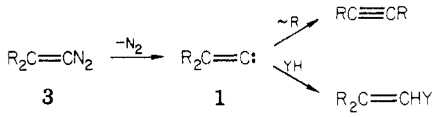
[a] Calculated by MNDO. [b] Experimental values.

discussion will be based on the proposition that pathway b applies.

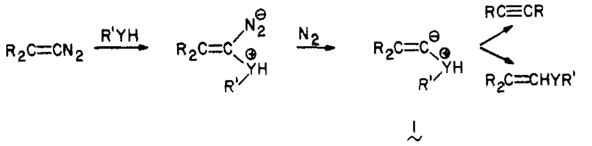
Given diazo compounds **3** as intermediates in the formation of alkynes from reaction of **8** with carbonyl compounds (eq 1), transformation to products may reasonably involve either unimolecular phenomena (eq 11 and 12)[3] or a bimolecular process requiring solvent participation (eq 13). We favor the second of the unimolecular processes (eq 12) for the reasons discussed below.



(11)



(12)



(13)

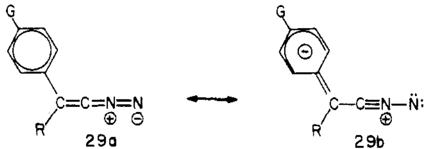
If the sole pathway for decomposition of **3** were the concerted process of equation 11, then diversion of **3** to products other than alkynes should not be possible. This, in fact, is the case for derivatives of **3** in which R is either hydrogen or an aryl group not bearing a strongly electron-withdrawing substituent. As shown in Table II (entries 2, 7, 13), the presence of alcohols or amines, reagents known to lead to aldehydic enol ethers and enamines when **8** is allowed to react with aliphatic ketones (eq 14),[45] fails

$$R_2CO + \mathbf{8} + YH \xrightarrow{KO\text{-}t\text{-}Bu} R_2C{=}CHY \qquad (14)$$

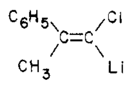
$$Y = RO \text{ or } R_2N$$

to cause diversion of the reaction from production of alkynes to formation of the aldehyde derivatives.[46] However, when the migratory aptitude of an aryl group is modified by incorporation of an electron-withdrawing substituent on the ring, as in 4-nitroacetophenone (entry 14, Table II), such diversion does in fact occur. At the very least, this result requires that the *sole* mode of decomposition of the diazoethene **3** cannot be loss of nitrogen with concomitant migration of R (eq 11).

The bimolecular mechanism involving the solvent-assisted decomposition of a diazoethene **3** (eq 13) can satisfactorily rationalize the observations of Table II and therefore could be an adjunct to or a substitute for the concerted process operating in those derivatives of **3** in which at least one of the two substituents, R, is facile in its ability to migrate to electron-deficient centers. In cases wherein the migratory aptitude of R is decreased, e.g., 4-nitrophenyl, and the electrophilicity of the diazocarbon atom is increased owing to delocalization of electrons into the aromatic ring, as shown by **29b**, nucleophilic attack of solvent can initiate the phenomena of eq 13. Note that the key intermediate I, that partitions between alkyne and trapping products, is written as an ylide, which is conceptually an extreme form of a carbenoid. Carbenoids generated by metalation of vinyl halides are known to rearrange to alkynes (Fritsch–Buttenberg–Wiechell rearrangement)[47] without apparent intervention of the carbene, supporting the proposal of I as a potential common immediate precursor of products (eq 13). Nevertheless, we believe that this mechanism is invalidated by the observation that alkyne formation occurs readily and in high yield even when the reaction is performed in the absence of nucleophilic solvents (entry 8, Table II).



29a **29b**



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The unimolecular decomposition of the diazoethene **3** to an alkylidenecarbene (eq 12) nicely explains the data. For this mechanism to be viable, of course, it is necessary to rationalize the apparently facile unimolecular loss of nitrogen from the diazo compound **3** at −78 °C. The explanation may lie solely in a substituent effect. As noted earlier, small-ring diazo compounds exhibit less thermal stability than acyclic analogues, and a diazoethene could be viewed as having the smallest possible ring size and therefore low thermal stability. Another type of effect can be gleaned from the series CH_2N_2, $HalCHN_2$, and Hal_2CN_2, wherein one proceeds from a diazo compound that is stable toward unimolecular decomposition at room temperature to ones that apparently decompose to carbenes at −40 and −100 °C, respectively.[49] If one assesses this destabilization as arising from the presence of an electronegative nondelocalizing substituent on the diazocarbon atom, this same effect can be recognized in the sp^2 carbon atom bound to C-1 of a diazoethene.

Previously reported[50] theoretical calculations appear also to lend support to the proposition that diazoethenes **3** may be relatively unstable thermally. As the data in Table IV show, the *minimum* enthalpy of activation for decomposition of diazoethene to vinylidene and nitrogen at 195 K is calculated (MNDO)[51] to be 18.9 kcal/mol, some 20 kcal/mol less than the theoretically derived quantity for the same type of reaction of diazomethane. Taken by itself, the magnitude of the value for diazoethene is too great for a unimolecular process that is supposed to be

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(45) (a) Gilbert, J. C.; Weerasooriya, U. *Tetrahedron Lett.* **1980**, 2041. (b) Gilbert, J. C.; Weerasooriya, U.; Wiechman, B.; Ho, L. *Ibid.* **1980**, 5003.

(46) Wolinsky et al. have made a similar observation in a system involving α elimination of a bromostyrene: Wolinsky, J.; Clark, G. W.; Thorstenson, P. C. *J. Org. Chem.* **1976**, *41*, 745.

(47) Köbrich, G.; Buck, P. "Chemistry of Acetylenes"; Viehe, G. Ed.; Marcel Dekker: New York, 1969.

(48) Köbrich, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 41.

(49) Closs, G. L.; Coyle, J. J. *J. Am. Chem. Soc.* **1965**, *87*, 4270.

(50) Gilbert, J. C.; Weerasooriya, U.; Giamalva, D. *Tetrahedron Lett.* **1979**, 4619.

(51) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907.

Table V. Estimated Half-Lives for Diazoethene (3, R = R = H) at 195 K

parameters[a]	$\tau_{1/2}$, min	
	%[b]	abs[c]
52a	3.8×10^4	1.3
52b	2.1×10^4	2.8×10^1
52c	4.7×10^4	2.2×10^{-1}

[a] Literature source of data for kinetics of decomposition of diazomethane. [b] Calculation based on assumption that the percentage error in the theoretical calculation of $\Delta H_{\min}^{\ddagger}$ for diazoethene is the same as that for diazomethane. [c] Calculation based on assumption that the magnitude of error in the theoretical calculation of $\Delta H_{\min}^{\ddagger}$ for diazoethene is the same as that for diazomethane.

facile at the stated temperature unless the entropy of activation for the reaction is unusually large and positive.[52] This is unlikely if the corresponding decomposition of diazomethane is considered an appropriate analogy, since the experimentally derived values for the entropy of activation are small and negative, ranging from −4.4 to −9.8 eu.[52]

It is clear, however, that the theoretical method significantly overestimates the minimum enthalpy of activation for the decomposition of diazomethane, as shown in Table IV, wherein it can be seen that the experimentally observed values are some 5.5–7.5 kcal/mol lower. If the theoretical method is also overestimating the minimum enthalpy of activation for diazoethene, a range of half-lives can be calculated, the lower end of which gives estimates entirely consistent with the requirement that diazoethenes **3** undergo unimolecular decomposition at −78 °C. Thus, Table V contains half-lives of diazoethene at 195 K based on the basis of the assumptions that the preexponential factor for its decomposition is the same as those reported for diazomethane[53] and that the magnitude of error in the theoretical calculation of enthalpy of activation for diazoethene is of either the same percentage or the same absolute value as that for diazomethane. The latter assumption, of course, yields the shorter half-lives that are consistent with our experimental observations. Since it is not unreasonable to suppose that whatever systematic errors in the theoretical method are leading to the overly high estimate for $\Delta H_{\min}$ of diazomethane would result in errors of the same magnitude in the calculation of $\Delta H_{\min}$ for diazoethene, we believe the actual half-lives for diazoethenes **3** will lie toward the lower end of the ranges given in Table V, making proposal of unimolecular decomposition of this class of diazo compounds at −78 °C acceptable.

It is expected that carbene **1**, once formed, would rearrange to alkyne at −78 °C. For example, the carbenoid **30** produces alkyne at −85 °C,[54] a process that should be less facile than with the free species. Theoretical calculations also support the contention that 1,2-migration in the singlet unsaturated carbenes should be facile; specifically, the predicted barrier for the conversion of vinylidene (1, R = R = H) to ethyne is a mere 8 kcal/mol,[55] and it has been suggested that the true barrier "is not less than 5 kcal/mol".[56] Moreover, the transition state for the migration is remarkably late, given the high (240 kcal/mol) estimated heat of the reaction,[55] and therefore it is characterized by considerable bonding between the group R and its migration terminus. Consequently, it comes as no surprise that migration of phenyl is preferred to methyl for the base-promoted decomposition of the vinyl triflate **31** to 1-phenylpropyne by way of the unsaturated carbene (eq 15).[8b]

$$\underset{\textbf{31}\ (* = {}^{14}\mathrm{C})}{\mathrm{C_6H_5C^*(CH_3){=}CHOSO_2CF_3}} \xrightarrow{\text{KO-}t\text{-Bu}} \mathrm{CH_3C^*{\equiv}CC_6H_5} \qquad (15)$$

The existence of a nontrivial activation barrier for the 1,2-shift of alkylidenecarbenes as well as the observation of migratory aptitudes is fully consistent with the data of Table II and the requirement that these carbenes be susceptible to partitioning between rearrangement and trapping (eq 12). Thus, if **1** has R = H or C_6H_5, the barrier to rearrangement is so low as to preclude bimolecular trapping processes. However, if the aromatic ring is made electron deficient (entry 15, Table II), diversion of the carbene from a fate of rearrangement by virtue of an alternate reaction with nucleophiles becomes competitive.

Although the original goal of our investigations, namely, entry into the triplet manifold of alkylidenecarbenes **1** by photosensitized decomposition of diazoethenes **3**, has thus far been thwarted, these studies have yielded considerable profit in terms of a useful synthesis of alkynes. In addition, our results strongly suggest that reaction of dimethyl (diazomethyl)phosphonate (**8**) with carbonyl compounds affords the desired diazo compounds (eq 3) but that these are thermally unstable at −78 °C. Additional attempts at isolating and characterizing these novel diazo compounds by use of low-temperature techniques are currently in progress.

Experimental Section

Proton magnetic resonance (^{1}H NMR) spectra were obtained by using either a Varian A-60 or a Varian HA-100 spectrometer. Chemical shifts are reported in parts per million downfield from Me_4Si as an internal reference at 0.00 ppm. Coupling constants (J) are reported in hertz. Ratios of areas of absorptions were obtained by averaging at least two successive integrations. Unless otherwise noted, ^{1}H NMR data are for solution in $CDCl_3$ and are reported in the following manner: parts per million downfield from Me_4Si, multiplicity, coupling constant if applicable, number of protons, and the carbon atom(s) to which the hydrogen atom(s) are attached (if known).

Low-temperature ^{31}P and ^{13}C NMR spectra were obtained with a Bruker WH-90 spectrometer. Such spectra at ambient temperatures were measured with a Varian FT 80-A instrument.

All infrared (IR) spectra were recorded on a Beckman IR-5A spectrophotometer. All absorptions are reported in units of reciprocal centimeters and are calibrated to the absorption at 1601 cm^{-1} in polystyrene; their intensities are designated as s (strong), m (medium), and w (weak). IR analyses of liquids were performed on neat samples held as films between salt plates and those of solids as KBr pellets or as solutions.

Determination of accurate mass was made on a Du Pont (CEC) 21-210 high-resolution mass spectrometer, operating at 70 eV.

Melting points were taken on samples contained in unsealed capillary tubes by using a Mel-Temp apparatus. Both melting and boiling points are uncorrected.

General Procedure for Preparation of Alkynes. A magnetically stirred slurry of potassium *tert*-butoxide (0.8 mmol) in 1.5 mL of dry THF was cooled to −78 °C under an atmosphere of dry nitrogen. A solution of 0.8 mmol of dimethyl (diazomethyl)phosphonate (**8**)[57] in 2 mL of THF was added dropwise

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(52) For example, if the half-life of the diazoethene at 195 K were 1 h, the entropy of activation would be on the order of +79 eu.

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during 1 min, and this mixture was stirred for 5 min. During this time, the color of the reaction mixture changed from pale yellow to brown, indicating formation of the anion of **8**. Subsequently, a solution of the carbonyl substrate (0.7 mmol) in 2 mL of THF was added over a 1-min period. Evolution of nitrogen was usually evident. The resulting solution was stirred at −78 °C for 12–24 h and then allowed to warm to ambient temperature. Stirring was continued for an additional 2–4 h, and then the reaction mixture was quenched with 25 mL of water. Extraction with three 25-mL portions of dichloromethane, washing of the combined extracts with 25 mL of brine, drying (Na_2SO_4), and removal of solvents by rotary evaporation afforded the crude product. A measured quantity of an internal standard (2-propanol, benzene, or dichloromethane) was added, and the entire mixture was transferred to a ^1H NMR tube for spectroscopic analysis.

This same procedure was followed for experiments in which trapping by solvent (alcohols, amines) was studied. The quantity of solvent used was the same as in the above procedure.

3-Phenyl-1-propyne. Reaction (12 h) in anhydrous THF gave an 80% yield of product, which was characterized spectroscopically.[2,58] Reaction in anhydrous methanol afforded the alkyne in 69% yield. No ^1H NMR resonances attributable to the enol ether could be detected.

2-Ethynylfuran. Reaction (8 h) in anhydrous THF provided the alkyne in 53% yield. This labile substance was characterized by its spectra.[2,59]

1-Ethynyl-4-nitrobenzene (10). Reaction between 4-nitrobenzaldehyde and **8** in THF gave the alkyne in 84% yield as a yellow solid [mp 150–152 °C (lit.[60a] mp 152 °C)], the IR (CCl_4) of which was identical with to that published.[60b] This reaction was characterized by development of an intense red color upon combination of the reagents; the color changed to brown with time.

The reaction of this aldehyde and dimethyl (diazomethyl)phosphonate (**8**) was repeated with toluene (5 mL) as solvent and potassium hydride as base. Evolution of gases occurred both upon addition of **8** to the slurry of toluene (anion formation) and upon addition of the aldehyde; the gases are interpreted to be H_2 and N_2, respectively. The color of this mixture was again red and changed to brown as before. The reaction was terminated after 8 h and gave the alkyne in 63% yield.

Spectral data: ^1H NMR δ 3.35 (1 H, s, H_1), 7.65 (2 H, d, J = 8.5 Hz, aromatic H_2), 8.2 (2 H, d, J = 8.5 Hz, aromatic H_3).

3-Ethyl-1-heptyne (14). Reaction (16 h) in anhydrous THF yielded 79% of the alkyne: ^1H NMR δ 1.0 (6 H, 2 t, J = 4.0 Hz, CH_3), 1.13–1.80 (8 H, m, CH_2), 1.86 (1 H, d, J = 2.0 Hz, H_1), 1.92–2.40 (1 H, m, H_3); IR (neat) 3325 cm^{-1} ($C{\equiv}CH$); molecular ion, *m/e* 124.1247 (calcd for C_9H_{16}, 124.1252).

(4-Methoxyphenyl)ethyne. Reaction (24 h) in anhydrous THF provided the alkyne in 88% yield. The IR and ^1H NMR were identical with those reported.[61]

1,2-Diphenylethyne. Reaction (16 h) in a 2:1 mixture of anhydrous THF and diethylamine gave a 92% yield of the alkyne as an off-white solid, a mixture of which with an authentic specimen caused no depression in melting point. Spectroscopic analysis (^1H NMR) of the crude reaction mixture failed to reveal the presence of resonances attributable to the incorporation of the amine.

(*E*)- and (*Z*)-4,8-Dimethylnona-3,7-dien-1-yne. Reaction in anhydrous THF afforded a 27% yield of crude alkyne. Vacuum distillation [room temperature (0.5 mmHg)] gave pure product as a colorless liquid: ^1H NMR δ 1.65 (6 H, d, J = 4 Hz, C-8 vinylic CH_3), 1.85 (3 H, d, J = 5 Hz, C-4 vinylic CH_3), 1.90–2.35 (4 H, m, CH_2), 2.83 (1 H, m, H-1), 4.85–5.30 (2 H, m, H-3, H-7); IR (neat) 3300 (${\equiv}CH$, s), 2100 ($C{\equiv}C$, w), 1650 cm^{-1} (C=C, w); molecular ion, *m/e* 148.1247 (calcd for $C_{11}H_{16}$, 148.1252).

(*E*)-3-Methyl-4-phenyl-3-buten-1-yne. Reaction (16 h) in anhydrous THF with a 2:1 molar ratio of **8** to (*E*)-2-methyl-3-phenyl-2-propenal produced the enyne in 40% crude yield. Distillation [40 °C (0.1 mmHg)] resulted in isolation of the enyne as a colorless oil: ^1H NMR δ 1.98 (3 H, d, J = 1.5 Hz, CH_3), 2.73 (1 H, s, H-1), 6.80 (1 H, m, H-4), 7.15 (5 H, m, aromatic); IR (neat) 3300 ($C{\equiv}CH$), 2100 cm^{-1} ($C{\equiv}C$, w); molecular ion, *m/e* 142.0779 (calcd for $C_{11}H_{10}$ 142.0783).

1-Phenyl-1-propyne. Reaction (16 h) of acetophenone and **8** gave the alkyne in 67% yield. Its IR and ^1H NMR spectra were identical with those published.[62]

Study of the reaction as a function of time gave the results summarized in Table III.

When the reaction was repeated with methanol as the solvent, only alkyne (20% conversion) and acetophenone could be detected by ^1H NMR spectroscopy. No methoxyl resonances appeared.

1-(4-Nitrophenyl)-1-propyne (12) and (*E*)- and (*Z*)-2-(4-Nitrophenyl)-1-methoxypropene (13). Reaction (1 h) of 4-nitroacetophenone and **8** at 25 °C in MeOH afforded a 1.7:1 mixture of alkyne/enol ethers in an overall yield of 87%. The two types of products were separated by thick-layer chromatography (silica gel) using a 3:7 (v/v) ratio of ethyl acetate and Skelly B.

Data for **1-(4-nitrophenyl)-1-propyne**: ^1H NMR δ 2.07 (3 H, s, H-3), 7.20–8.30 (4 H, m, aromatic H); the IR spectrum was identical with to that reported;[63a] molecular ion, *m/e* 161.0480 (calcd for $C_9H_7NO_2$, 161.0477). The medium-resolution mass spectrum also agreed with that reported.[63b]

Data for **(*E*)- and (*Z*)-2-(4-nitrophenyl)-1-methoxypropene**: ^1H NMR δ 1.92, 1.97 (3 H, 2 d, J = 1.3 Hz, H-3), 3.77, 3.80 (3 H, 2 s, OCH_3), 6.30, 6.67 (1 H, 2 m, H-1), 7.20–8.25 (4 H, m, aromatic H); IR (CCl_4) 1655 cm^{-1} (C=C); molecular ion, *m/e* 193.0741 (calcd for $C_{10}H_{11}NO_3$, 193.0739).

The enol ethers were formed in a ratio of 1:1 under these reaction conditions. ^1H NMR studies using $Eu(fod)_3$ allow tentative assignment of the *E* isomer as the source of the lower field resonances for the pairs of methyl absorptions described above.

(4-Chlorophenyl)ethyne (18). Reaction (2 h) in anhydrous THF gave the alkyne in 61% yield. The IR and ^1H NMR spectra of the product were identical with those reported.[61]

Low-Temperature ^{31}P NMR Study. A dispersion of potassium *tert*-butoxide (132 mg, 1.20 mmol) in THF (1 mL) was placed in an ^{31}P NMR tube equipped with a nitrogen inlet. A slow stream of nitrogen was maintained, and the NMR tube was immersed in a dry ice–isopropyl alcohol bath at −78 °C. A solution of **8** (165 mg, 1.10 mmol) in THF (1 mL) was introduced, followed, after 5 min, by a solution of 2-ethylhexanal (128 mg, 1.00 mmol) in THF (1 mL); gas evolution occurred. The reaction mixture was maintained at −78 °C for 1 h, and methanol-d_4 was added at −78 °C in order to make the reaction mixture homogeneous and also to provide a source of deuterium for the subsequent ^{31}P spectral analysis. The resulting solution was maintained at −78 °C for 1 h and was subjected to ^{31}P NMR analysis at −85 °C. The decoupled ^{31}P spectra of the reaction mixture showed a strong resonance at δ 2.03. The NMR tube was withdrawn from the probe and warmed to ambient temperature. No gas evolution occurred. After 10 min, the sample was recooled to −85 °C and subjected to ^{31}P NMR analysis. A spectrum identical with that originally observed was obtained.

Competition Experiment. The general procedure was followed except that a mixture of 1 equiv each of 4-chlorobenzaldehyde (**16**) and 4-nitrobenzaldehyde (**17**) was used. Only 1 equiv of **8** was added, and 1 equiv of potassium hydride was employed as the base. The reaction was allowed to proceed for 6 h at −78 °C before workup. ^1H NMR analysis of the reaction mixture revealed the ratio of **16**/**17**/**18**/**19** to be 7.5:1.0:1.5:8.

Test of Reversibility. A solution of diazo aldol **9**[35] (151 mg, 0.50 mmol) and **16** (420 mg, 3.0 mmol) in 5 mL of anhydrous THF was cooled to −78 °C under an atmosphere of dry nitrogen. A dispersion of potassium *tert*-butoxide (70 mg, 0.62 mmol) in 2 mL of THF was slowly introduced, and the resulting mixture was held at −78 °C for 4 h. Workup in the usual way afforded **18** and

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19 in a ratio of 1:1.5 (^1H NMR analysis).

Acknowledgment. The partial support of this research by the Robert A. Welch Foundation and the University Research Institute (University of Texas at Austin) is gratefully acknowledged.

Registry No. 8, 27491-70-9; **10**, 937-31-5; **12**, 28289-83-0; (*E*)-**13**, 80907-77-3; (*Z*)-**13**, 80907-78-4; **14**, 55944-43-9; **16**, 104-88-1; **17**, 555-16-8; **18**, 873-73-4; 3-phenyl-1-propyne, 10147-11-2; 2-ethynylfuran, 2-ethynylfuran; 4-methoxyphenylethyne, 123-11-5; 1,2-diphenylethyne, 501-65-5; (*E*)-4,8-dimethylnona-3,7-dien-1-yne, 71869-03-9; (*Z*)-4,8-dimethylnona-3,7-dien-1-yne, 80907-79-5; (*E*)-3-methyl-4-phenyl-3-buten-1-yne, 80907-80-8; (*E*)-2-methyl-3-phenyl-2-propenal, 15174-47-7; 1-phenyl-1-propyne, 673-32-5; acetophenone, 98-86-2; 4-nitroacetophenone, 100-19-6; 2-ethylhexanal, 123-05-7; 2-phenylethanal, 122-78-1; 2-furaldehyde, 98-01-1; 4-onethoxybenzaldehyde, 123-11-5; (*E*)-3-phenyl-2-propenal, 104-55-2; (*E*)-3,7-dimethyl-2,6-octadienal, 141-27-5; (*Z*)-3,7-dimethyl-2,6-octadienal, 106-26-3.

Total Synthesis of (±)-Modhephene and Its Epimer, (±)-Epimodhephene

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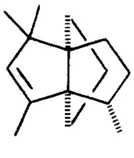
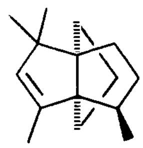
Received December 29, 1981

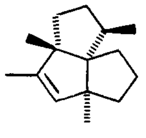
This report presents three synthetic approaches to (±)-modhephene (1α) and (±)-epimodhephene (1β) from enones **10**, **11**, and **14**, the overall yield of modhephene being 10%, 7%, and 1.7%, respectively. The approaches converge upon formation of [3.3.3]propellenone (**9**), the latter derived from acid-catalyzed rearrangement of tricyclic octenones **8** and **12**. β,γ-Unsaturated ketones **8** and **12**, in turn, were prepared from enones **10** and **11** by [2 + 2] photoaddition of 1,2-dichloroethylene and subsequent dehalogenation. Enone **14**, on the other hand, was transformed into the tricyclic octenone **12** via a similar photoaddition–dehalogenation sequence followed by conversion of the ester moiety to a methyl group. Elaboration of propellenone (**9**) to modhephene (1α) and its epimer (1β) was then accomplished via (a) an alkylative 1,3-carbonyl transposition (methyllithium, Jones oxidation), (b) conjugate addition with lithium dimethylcuprate, (c) high-temperature Wittig olefination (methyltriphenylphosphonium bromide, potassium *tert*-amylate in toluene at 92 °C), and (d) isomerization of the exocyclic olefin (*p*-TsOH in dichloromethane) to afforded (±)-modhephene (1α) and its C(6) epimer (1β). Finally, a discussion of the Wiesner model as it pertains to the stereoselectivity in the [2 + 2] photoaddition of acetylene and dichloroethylene to enones **10**, **11**, and **14** is also presented.



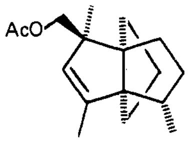
Modhephene
(1α)



Epimodhephene
(1β)



Isocomene
(2)



(3)

In 1978 Zalkow and colleagues[2] isolated a new cyclopentanoid sesquiterpene (1α) from hexane extracts of rayless goldenrod (*Isocoma wrightii*), a plant indigenous to the southwestern United States, known for its toxicity to cattle and sheep,[3] and from which Zalkow, a year earlier, had isolated the closely related sesquiterpene isocomene (2).[4] Given the trivial name modhephene, the structure including absolute configuration was established rigorously via a single-crystal X-ray analysis of a diol prepared via cis hydroxylation.[2] Central to the derived structure was a fused network of cyclopentane rings, the characteristic feature of the triquinane family of compounds, other members of which now include such natural products as pentalenolactone,[5] hirsutene,[6] hirsutic acid,[7] and coriolin.[8] Modhephene, however, was unique in that it was the first

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