been reported elsewhere,[37] are also vastly different from that of 2-phenyltetralin.

We feel that the evidence presented here indicates that the CID spectrum for 2-phenyltetralin is almost certainly unique, even though we have not investigated all possible $C_{16}H_{16}$ isomers. The similarity in the spectra of the collision complex and 2-phenyltetralin coupled with the evidence gleaned from the deuterium-labeling experiments allows us to conclude that the structure of the collision complex for the ion–molecule reaction between the *o*-quinodimethane radical cation and neutral styrene is that of 2-phenyltetralin. On the basis of this conclusion, we infer that the reaction is an ionic analogue of a [4 + 2] cycloaddition, and that the structure of the $C_8H_8^{+\cdot}$ is that of *o*-quinodimethane. However, we cannot rule out partial ring closing of the *o*-quinodimethane to give benzocyclobutane radical cation although it seems unlikely that the ring-closed form would be reactive with neutral olefins such as styrene. It is noteworthy that the gas-phase reaction involves the reaction of an ionized diene, whereas solution Diels–Alder reactions are preferred if the reactant dienophile is ionized.[2]

We can envision two applications of this experimental approach. First, the identification of isomeric ions (or their neutral precursors) which give nearly identical EI or collision-induced decomposition spectra (such as C_8H_8 isomers) can be accomplished by "derivatizing" the ion or neutral in a high-pressure source followed by analysis using MS/MS.[38] For example, we anticipate that of the isomeric C_8H_8 compounds only neutral styrene will give 2-phenyltetralin by reaction with the *o*-quinodimethane "reagent ion". Second, it may be possible to execute the synthesis of reference compounds and obtain their mass spectra in a matter of minutes by using these methods. The actual synthesis yields the gas-phase radical cation as a product and is conducted on the microsecond time scale. By use of the strategy developed here, reference CID spectra of 2-phenyltetralin and its specifically deuterium-labeled forms could be obtained without resorting to preparative procedures in a synthesis laboratory followed by conventional mass spectrometric analysis.

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Registry No. I, 84985-65-9; II, 100-42-5; III, 2471-91-2; IV, 17373-93-2; V, 89-95-2; VI, 14019-65-9; VII, 612-14-6; 1-phenyltetralin, 3018-20-0; 3-phenyltetralin-2,2-d_2, 85049-24-7; 3-phenyltetralin-2,2-d_2 radical cation, 85049-25-8; 2-phenyltetralin, 29422-13-7.

(38) This method was first proposed by: Dymerski, P. P.; McLafferty, F. W. *J. Am. Chem. Soc.* **1976**, *98*, 6070.

Notes

Inversion of Reactivity (Umpolung) of α,β-Ethylenic Ketones and Aldehydes. Electrochemical Deprotection of γ-Thioacetalated Phosphonium Salts

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Organophosphorus compounds have been exploited for reversible inversion of reactivity (umpolung) of α,β-ethylenic ketones and aldehydes by heteroatom exchange.[1] Except for a special case,[1d] a Wittig or a Wittig–Horner reaction was used to remove the phosphorus group in such a way that the carbonyl compound was the only electrophilic counterpart to be used as the β-acylvinyl anion equivalent.

We are developing a synthetic route (Scheme I) for reversible d^3 inversion of reactivity[2] of α,β-ethylenic ketones and aldehydes 1 in which the ylides 3, obtained[3] from phosphonium salts 2, are synthetic equivalents of β-acylvinyl anions. As a part of this program[4] we have devised and wish to report an efficient electrochemical deprotection of γ-thioacetalated phosphonium salts 4 followed by base elimination of the phosphorus group with subsequent generation of β-branched α,β-ethylenic ketones or aldehydes 6.

Several chemical methods have been developed for the hydrolysis of the thioacetal group;[5] their usefulness depends essentially on their selectivity toward other functional group in the molecule. Although it has never been optimized for preparative scale, the electrochemical method has been shown to be effective for the hydrolysis of simple dithianes, and the fixed-potential electrolysis can produce the desired selectivity.[6] Moreover, the phos-

(1) (a) Stowell, J. C.; Keith, D. R. *Synthesis* **1979**, 132. (b) Bell, A.; Davidson, A. H.; Earnshaw, C.; Norrish, H. K.; Torr, R. S.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1978**, 988. (c) Blatcher, P.; Grayson, J. I.; Warren, S. *Ibid.* **1978**, 657. (d) Corbel, B.; Paugam, J. P.; Dreux, M.; Savignac, P. *Tetrahedron Lett.* **1976**, 835. (e) Martin, S. F.; Garrison, P. J. *Ibid.* **1977**, 3875. (f) Shevchuk, M. I.; Megera, I. V.; Burachenko, N. A.; Dombrovskii, A. V. *Zh. Org. Khim.* **1974**, *10*, 167.

(2) A general nomenclature for the inversion of reactivity (umpolung) has been proposed by Seebach (Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239). In this work d^3 means a donor site at three carbon atoms from the O-heteroatom.

(3) Cristau, H. J.; Vors, J. P.; Christol, H. *Synthesis* **1979**, 538.

(4) For the general strategy of the method and a second route that begins with a Wittig reaction on the ylide 3, see: Cristau, H. J.; Vors, J. P.; Beziat, Y.; Niangoran, C.; Christol, H. "Phosphorus Chemistry, Proceedings of the 1981 International Conference"; Quin, L. D., Verkade, J. G., Eds.; American Chemical Society: Washington, D.C., 1981; 59.

(5) Gröbel, B. T.; Seebach, D. *Synthesis* **1977**, 357.

(6) (a) Gourcy, J.; Martigny, P.; Simonet, J.; Jeminet, G. *Tetrahedron* **1981**, *37*, 1495. (b) Porter, Q. N.; Utley, J. H. P. *J. Chem. Soc., Chem. Commun.* **1978**, 255.

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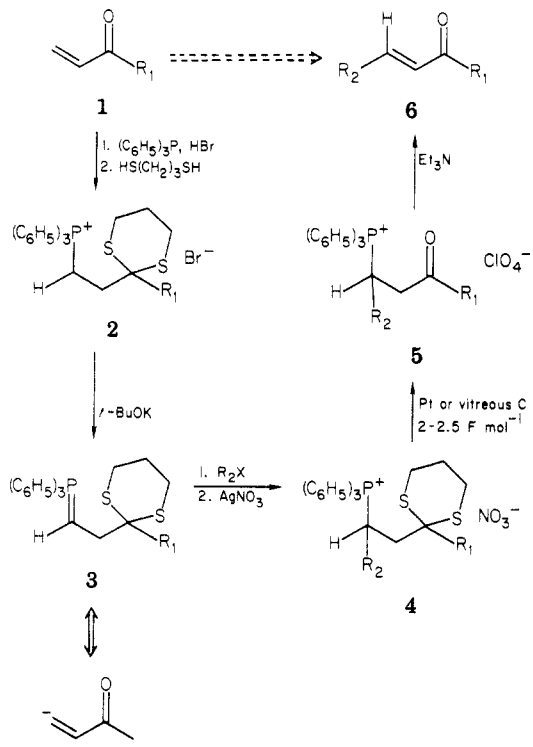
Scheme I



	R_1	R_2	yield, % 5	6
a	CH_3	H	96	65
b	CH_3	CH_3	95	80
c	CH_3	n-C_4H_9	100	82
d	CH_3	C_6H_5	100	93
e		$-(CH_2)_3-$	90	50
f	H	CH_3	75	85
g	H	C_6H_5	80	74

phonium group is inert toward oxidation and the electrochemical method does not introduce reduction products that can complex with the phosphonium salt.

Nitrates[7] of the γ-thioacetalated phosphonium salts **4a–e** (e.g., thioprotected ketonic phosphonium salts) give a sharp irreversible peak on cyclic voltammetry at platinum or vitreous-carbon electrodes (CH_3CN/H_2O (90:10), $LiClO_4$ 0.1 M), which indicates a rapid chemical reaction that follows up the initial electron transfer.[6] A fixed-potential electrolysis at the potential of this peak requires the passage of 2 F mol^{-1} and affords in good yield the perchlorate form[8] of the keto phosphonium salts **5a–e** together with an insoluble material that has been previously identified as a polymeric sulfur compound.[6b,9]

Thioprotected aldehydic phosphonium salts **4f** and **4g** display the same irreversible oxidation peak. However, the deformation of the voltammogram denotes a passivation of the electrode, and when preparative electrolyses are run, the current decreases sharply from the starting value of the electrolysis. We could prevent the deactivation of the electrode which had been already described[6b] by adding 10% dimethyl sulfoxide to the system CH_3CN/H_2O.[10] Controlled-potential electrolysis at the potential of the peak in the solvent mixture $CH_3CN/H_2O/Me_2SO$, when run until 2.5 F per mole are passed,[11] results in the isolation of the aldehydic phosphonium perchlorate in satisfactory yield.[12]

The base elimination of triphenylphosphine from the seven different phosphonium salts is easily accomplished by adding, at room temperature, 2 equiv of triethylamine[13] to a solution of the salt in $CHCl_3/CH_3OH$ and affords the E-β-branched α,β-ethylenic ketone or aldehyde.[14]

In summary, this two-step procedure, which involves the electrochemical hydrolysis of the γ-thioacetalated phosphonium salts, allows for the facile preparation of β-branched α,β-ethylenic ketones and aldehydes in a five-step process that includes the reversible d^3 inversion of reactivity of the parent α,β-ethylenic ketone or aldehyde through a phosphonium ylide. Investigations on the selectivity of the method toward other functional groups are in progress in the laboratory.

Experimental Section

Measurements. Melting points are uncorrected and were measured on an automatic Mettler FP 51 melting-point apparatus (heating rate 2 °C/min) or a microscope with heating-stage Leitz when decomposition of the compound occurred. Infrared spectra were recorded on a Perkin-Elmer Model 221 spectrophotometer by using samples as KBr disks. ^1H NMR spectra were measured with a Varian EM-360L spectrometer with Me_4Si as internal standard. ^{31}P NMR spectra were recorded on a Brucker WP 80 DS by using H_3PO_4 (86% in water) as the external standard. Satisfactory analytical data were obtained for all new compounds.

Electrochemistry. Electrochemical measurements were performed on a Princeton Applied Research Model 173 potentiostat connected to a PAR Model 175 universal programmer and a Sefram TGM-101 X–Y recorder for cyclic voltammetries (CV) or a PAR Model 179 digital coulometer for preparative electrolyses. The microanode used for CV was a polished disk of platinum (A = 0.8 mm^2). The anodes assigned to macroelectrolyses were sheets of platinum or vitreous-carbon V-25 (Carbone-Lorraine, France) of 8 and 26 cm^2 in surface. The electrolysis cell used in the preparative work was a divided cell. The anode compartment (100 mL) was separated from the cathode compartment by a Nafion-415 membrane (du Pont de Nemours). Potential measurements were made vs. a saturated calomel electrode connected to the cell through a 0.1 M KCl bridge.

Synthesis of the Nitrate Form of the γ-Thioacetalated Phosphonium Salts (4). Silver nitrate (11 mmol) dissolved in 10 mL of water was added to 10 mmol of the phosphonium bromide dissolved in 150 mL of chloroform. The mixture was vigorously stirred in the dark, at room temperature, for 15 min. Most of the silver bromide precipitate was then removed by filtration, and the organic phase was dried (Na_2SO_4) and passed twice through a short column of Celite (40 g) to eliminate the residual silver bromide. The organic phase was concentrated to about 30 mL and added dropwise to 300 mL of ether. The

(7) The nitrate form of the phosphonium must be used since bromide anions are oxidized into bromine on platinum or on vitreous-carbon electrodes prior to the thioacetal group.

(8) Although no explosions occured during the course of the investigation, isolation and recrystallization of large batches of these phosphonium perchlorates is not recommended (see related ref 14).

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(10) We presume that the electrode was passivated by the formation of a polymeric insulating film containing sulfur since when the electrode was washed with chloroform, dried, and then burnished in a flame, it evolved a characteristic smell of sulfur.

(11) Higher potentials are necessary to oxidize the thioacetal group of salts **4f,g** than those of salts **4a–e**. At these potentials a part of the electrolysis current is due to a partial oxidation of the solvent, giving the observed lower faradaic yields for the desired deprotection.

(12) Preliminary results (see: Cristau, H. J.; Vors, J. P.; Christol, H. *Tetrahedron Lett.* **1979**, 2377) suggested that the deprotection could be easily done in every case by reacting the phosphonium bromide with Ce^{IV} (e.g., cerium ammonium nitrate). However the method could not be generalized since sensitive structures reacted with bromine generated by Ce^{IV} oxidation of bromide ions. If now the nitrate form of the phosphonium salt is reacted with Ce^{IV}, it affords as single product the monosulfoxide of the γ-thioacetalated phosphonium salt.

(13) A twofold excess of triethylamine was found to give the best yield and reaction time.

(14) The solvent mixture $CHCl_3/CH_3OH$ was choosen to avoid isolation of phosphonium perchlorates during large-scale preparations (see Experimental Section).

precipitate obtained was dried and recrystallized (chloroform/ethyl acetate). (3,3-Trimethylenedithiobutyl)triphenylphosphonium nitrate (**4a**) showed the following: mp 219 °C; ^{1}H NMR δ 4.13–3.26 (m, 2 H, $^+PCH_2$), 3.00–1.72 (m, 8 H), 1.62 (s, 3 H, CH_3); ^{31}P NMR δ 25.52.

Electrochemical Deprotection of γ-Thioacetalated Phosphonium Nitrates (4). In method A (compounds **4a–e**), the electrolysis cell was charged with 2 mmol of the phosphonium nitrate and 90 mL of a 90:10 mixture of CH_3CN/H_2O containing 0.1 M $LiClO_4$. The mixture was oxidized at the potential of the peak recorded on CV until the current had decayed to 10% of its initial value. The amount of current passed was 2 ± 0.2 F mol^{-1}. The mixture was filtered, concentrated in vacuo to about 30 mL, and then diluted with chloroform to 200 mL. The organic phase was washed with water (30 mL, three times), dried (Na_2SO_4), concentrated in vacuo to about 50 mL, and added dropwise to 500 mL of ether. The precipitate was dried (P_2O_5, room temperature, 24 h), and a part of it (about 500 mg) was recrystallized from acetone/ethyl acetate for analytical purposes.

The procedure followed **in method B** (compounds **4f,g**) was identical with that of A with the exception that the electrolysis solvent was a mixture of $CH_3CN/H_2O/Me_2SO$ (80:10:10) and electrolyses were terminated after 2.5 F mol^{-1} had passed. (3-oxobutyl)triphenylphosphonium perchlorate (**5a**) showed the following: mp 212 °C dec; IR 1716 cm^{-1}; ^{1}H NMR δ 3.80–2.57 (m, 4 H, $^+PCH_2CH_2$), 2.12 (s, 3 H, CH_3); ^{31}P NMR δ 24.70.

Synthesis of β-Branched α,β-Ethylenic Ketones and Aldehydes (6). The dried chloroformic phase resulting from the electrochemical hydrolysis of 5 mmol of compounds 4 was concentrated in vacuo to 100 mL and diluted with 100 mL of methanol. Triethylamine (10 mmol) was added and the reaction allowed to stirr at room temperature until the complete disappearance of the phosphonium salt (monitored by TLC on silica). The reaction mixture was then concentrated in vacuo to about 50 mL and diluted with chloroform to about 200 mL. The organic phase was washed (30 mL, three times), dried (Na_2SO_4), concentrated in vacuo to about 50 mL, passed through a short plug of silica (elimination of perchlorates), and concentrated in vacuo to an oily crude mixture. Purification by column chromatography (silica gel, hexane/dichloromethane (10:90)) afforded the pure β-branched α,β-ethylenic ketone or aldehyde **6**. The compounds were identified by coinjection on GC and by comparison of their IR and NMR spectra with those of authentic samples.

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Registry No. **4a**, 85066-89-3; **4b**, 85066-91-7; **4c**, 85066-93-9; **4d**, 85066-95-1; **4e**, 85082-15-1; **4f**, 85066-97-3; **4g**, 85066-99-5; **5a**, 43101-01-5; **5b**, 85067-01-2; **5c**, 85067-03-4; **5d**, 43100-94-3; **5e**, 85067-05-6; **5f**, 85067-07-8; **5g**, 85067-09-0; **6a**, 78-94-4; (*E*)-**6b**, 3102-33-8; (*E*)-**6c**, 18402-82-9; (*E*)-**6d**, 1896-62-4; **6e**, 930-68-7; (*E*)-**6f**, 123-73-9; (*E*)-**6g**, 14371-10-9.

Supplementary Material Available: Physical properties of phosphonium salts 4 and 5 (3 pages). Ordering information is given on any current masthead page.

Optically Active Nicotine Analogues. Synthesis of (*S*)-(−)-2,5-Dihydro-1-methyl-2-(3-pyridyl)pyrrole ((*S*)-(−)-3′,4′-Dehydronicotine)

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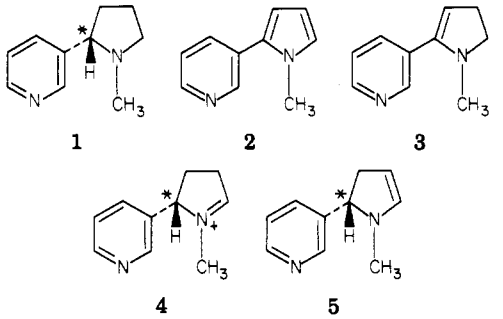
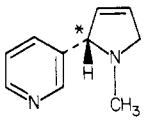
For some time, we have been engaged in the preparation of analogues of nicotine (**1**) for chemical and pharmacological studies.[2] One area of interest concerns the family



1 **2** **3** **4** **5**

of compounds possessing unsaturation in the pyrrolidine ring. The tobacco alkaloid nicotyrine **2**[3] is the most well-known example. *N*-Methylmyosmine (**3**) has been implicated as an intermediate in the degradation of nicotine in tobacco.[4] Recently, **3**, which is highly unstable, was synthesized and fully characterized.[4] There is strong evidence for the formation and intermediacy of the nicotine $\Delta^{1'(5')}$-iminium ion (**4**) in the mammalian metabolic transformation of nicotine to cotinine.[5] The diperchlorate salt of **4** has also recently been prepared.[6] In addition, 4′,5′-dehydronicotine (**5**) has also been proposed as a possible metabolic intermediate.[5,6] Enamine **5**, which would be expected to be rather unstable, has not, as yet, been synthesized.

Of the various dihydropyrrole derivatives, (*S*)-(−)-2,5-dihydro-1-methyl-2-(3-pyridyl)pyrrole (**6**; (*S*)-(−)-3′,4′-dehydronicotine) may most closely mimic **1** in its pharmacological characteristics. Compound **6** has been pre-



6

pared previously, but strictly as a racemic mixture.[7] Racemic **6** has been shown to be significantly more potent than **1** in several insecticidal studies.[8] Due to the significant potency of racemic **6** and the enhanced biological activity of (*S*)-nicotine over (*R,S*)-nicotine, we required a means of obtaining optically active **6**, i.e., the *S* enantiomer. A reported attempt to resolve racemic **6** by fractional crystallization was unsuccessful.[9] We now report an op-

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