The mixture was evaporated in vacuo and the residue was crystallized from diisopropyl ether/dichloromethane to give an oil which was purified by column chromatography on silica gel, gradient elution with dichloromethane and ethyl acetate, to give perillaketone (30) as an amber oil. The analytical sample was obtained by stirring a solution of perillaketone (30) in diethyl ether for 2 h, the solution was stirred to room temperature and the reaction mixture was evaporated in vacuo to give an oil which was purified by column chromatography on silica gel, gradient elution with dichloromethane and ethyl acetate, to give perillaketone (30) as an amber oil.

References and Notes

(8) E stereochemistry is assigned to the enaminoketones by analogy with 1-dimethylamino-2-benzoylethylene derived from acetophenone, in which \[ \delta_{\text{H}} = 11.5 \text{ Hz} \]. E stereochemistry is assigned on the same basis to the \( \alpha \beta \)-unsaturated ketones. See H. Meerwein, W. Florian, G. Schon, and G. Stopp, Justus Liebig Ann. Chem., 841, 1 (1961), for use of DMP acetals as formylating agents.

Annalogue of Ethyl Propiolate with Ethyl Piperocate

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Received May 1, 1978

In conjunction with studies of the alkaloid slaframine and the cycloaddition of ethyl propiolate to ethyl piperolate, we undertook a search for routes to \( \Delta^2 \) derivatives of 1-oxo-octahydroindolizolines (31). The cycloaddition of ethyl propiolate to ethyl piperolate (1) was formally attractive for this purpose although an earlier attempt by Winterfeldt and Dillingar to effect a similar condensation of dimethyl acetylenedicarboxylate with methyl vinylketone resulted in a lower yield and better yields (31). 11-oxo-octahydroindolizolines were isolated from a mixture of diethyl ether and ethanol to give ethyl piperolate (30) as an amber oil. The analytical sample was obtained by column chromatography over 45 g of silica gel (Woelm Act. 1) using dichloromethane as eluant: NMR (CDCl3, Me2Si) 6 0.6-1.65 (m, 7 H, CH3(CH2)2), 2.33 (q, 2 H, J = 8 Hz, -CH2-), 6.67 (t, 1 H, J = 8 Hz, -CH=), 6.85-7.5 (5 H, aromatic), 9.50 (s, 1 H, CH=O); M+ m/e 188; n\( ^{13} \)C 1524.

Acknowledgments. We thank Professor Leo A. Paquette of Ohio State University for critical evaluation of the work. Professors Jack E. Baldwin of M.I.T. and Edward C. Taylor of Princeton University are thanked for helpful discussions. We thank Mr. Paul L. Unger for providing spectrographic support and Mr. George M. Maciak for combustion analyses.

Registry No.—25, 25564-22-1; 27, 14313-09-8; 28, 67382-49-4; 29, 34348-59-9; 30, 553-84-4; 31, 67382-50-7; 32, 67382-51-8; N,N-dimethylformamide dimethyl acetal, 4637-24-5.

References and Notes

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Notes

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temperature, the NMR spectrum showed, in addition to 2, a substantial amount of a second product having a vinyl proton singlet at 6.75 ppm. Integration indicated the molar ratio of 2 and the new compound in the product mixture to be 62:38. When refluxing hexane (70 °C) was employed as the solvent, the latter compound represented 54% of the product mixture; with refluxing heptane (100 °C) it reached 7%. GLC showed only the two products being formed and these compounds were separated by preparative GLC although substantial losses, particularly of 3, were experienced during the process due to air-oxidation and thermal degradation. The new compound was identified as 3 on the basis of spectral data and elemental analyses. Compounds 2 and 3 are both formed by pathways which are irreversible under the reaction conditions, the relative yields being independent of reaction times. Moreover, 2 when resubmitted to refluxing heptane was not converted into 3, proving that it is not a precursor of 3 in the condensation reaction.

Attack of ethyl propiolate on ethyl piperidolate probably occurs axially to give cis zwitterion 4a having the two substituents on the same face of the piperidine ring, although trans zwitterion 4b arising by equatorial attack would also be capable of cyclization. In ethanol, proton transfer from solvent intercepts 4 before intramolecular acylation can occur but in hydrocarbon solvents, where the zwitterion is the only source of protons, acylation competes effectively with inter- and intramolecular proton transfer.

The structure of the zwitterionic intermediate appears to be crucial to this annelation reaction. Only Michael adduct 5 was obtained from the condensation of ethyl propiolate with the ethyl ester of proline, probably because eclipsing interactions hinder cis attack of ethyl propiolate on the proline ester. Trans zwitterion 6, which forms instead, is structurally incapable of cyclization and consequently undergoes a proton transfer to give 5. Cyclization is unlikely with zwitterionic intermediates which are conformationally mobile. Although the condensation of methyl acetylenedicarboxylate with dimethyl fumarate was carried out by Winterfeldt and Dillingar in tert-butyl alcohol which precluded cyclization, we have obtained a similar result from the condensation of methyl acetylenedicarboxylate with ethyl propiolate in refluxing heptane. The latter reaction gave predominantly Michael adduct 7; a trace of a second component, possibly pyrrole 8 or 9, was obtained but the compound was unstable and was not fully characterized.

**Experimental Section**

NMR spectra were obtained with a JEOL MH-100 100 MHz spectrometer operating in the external lock mode. Spectra were obtained in dilute solution in CDCl3 or CCl4. Mass spectra (70 eV) were obtained with an LKB-9000 spectrometer using the direct inlet. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

**Condensations of Ethyl Propiolate with Esters of Amino Acids.**

**Ethyl Pipecaolate.** A solution of ethyl propiolate (0.4 g, 4.1 mmol) in 5 mL of heptane was added dropwise to 0.64 g (4.1 mmol) of ethyl piperidolate in refluxing heptane (10 mL) under N2. After 15 min, a sample was removed and added to CDCl3; the NMR spectrum showed the reaction was essentially complete and had given a 24:76 mixture of 2 and 3. Heptane was removed under a stream of N2 and the residue was partitioned by GLC on a column of 3% OV-17 (Chromosorb W) at 240 °C. Compound 3, ethyl 1-oxo-1,5,6,7,8,8a-hexahydroindolizine-2-carboxylate, eluted first: NMR δ 1.3 (t) and 4.3 (q, CH3), 6.75 (s, not exchangeable with D2O, 3-CH), the remaining protons appeared in unresolved multiplets at 5.3-8.7 ppm. Integration indicated the molar ratio of 3,4, and 5 to be 4:1:5. The new compound in the product mixture to be 3,4, and 5 was obtained but the compound was unstable and was not fully characterized.

**Proline Ethyl Ester.** Similar treatment of the ethyl ester of proline gave exclusively Michael adduct 5: NMR δ 1.25 (2 t X CH2), 4.15 (2 t X CH2), 5.2 (2 H, 2 × CH2), 7.65 (d, J = 13 Hz, CH-CH=CO-), 8.12 (d, ring CH's, J = 13 Hz, -CH=CH-), 209 (parent). The compound was sensitive to oxygen and was stored under N2 at -10 °C.

Anal. Calcd for C10H17N04: C, 63.6; H, 7.18; N, 6.70. Found: C, 62.95; H, 7.11; N, 6.68.

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**Acetylenedicarboxylate.** A solution of ethyl propiolate (5 mL) under N2. After 15 min, a sample was removed and added to CDCl3; the NMR spectrum showed the reaction was essentially complete and had given a 24:76 mixture of 2 and 3. Heptane was removed under a stream of N2 and the residue was partitioned by GLC on a column of 3% OV-17 (Chromosorb W) at 240 °C. Compound 3, ethyl 1-oxo-1,5,6,7,8,8a-hexahydroindolizine-2-carboxylate, eluted first: NMR δ 1.3 (t) and 4.3 (q, CH3), 6.75 (s, not exchangeable with D2O, 3-CH), the remaining protons appeared in unresolved multiplets at 5.3-8.7 ppm. Integration indicated the molar ratio of 3,4, and 5 to be 4:1:5. The new compound in the product mixture to be 3,4, and 5 was obtained but the compound was unstable and was not fully characterized.

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Vinyl Phenyl Selenide: A \( ^{1}CH=CH^- \) Synthon

**Summary:** Vinyl phenyl selenide (1) may be utilized as a \( ^{1}CH=CH^- \) synthon by reaction with alkyllithiums, trapping of the resulting \( \alpha \)-lithioalkyl phenyl selenides 2 with electrophiles to give 3, and oxidative elimination of phenylselenenic acid to produce the disubstituted alkenes 4.

Sir: The use of a variety of synthons for the formation of new carbon to carbon bonds is a well-established strategy in synthetic organic chemistry. In this communication we wish to report the use of vinyl phenyl selenide (1) as a \( ^{1}CH=CH^- \) synthon (Scheme I).

\[
\text{Scheme I}
\]

The addition of alkyllithiums to a number of vinyl derivatives of second-row elements in their lower oxidation states has been reported. We felt that such additions to vinyl phenyl selenides would be particularly useful for the following reasons: (1) The ability of a phenylseleno group to stabilize an adjacent carbanion and the reaction of these carbanions with a variety of electrophiles has been demonstrated; (2) Subsequent to performing its function, the phenylseleno group may be easily removed via oxidative elimination of phenylselenenic acid for instances in which the regiospecificity is unambiguous (e.g., \( E \rightarrow C=O \) or \( 3\alpha \) COH) leads to the formation of the \( E \)-disubstituted alkenes in good overall yield (Table I).

Since the reaction of alkyllithiums with 1 can also lead to \( \alpha \)-deprotonation or carbon–selenium bond cleavage, the proper choice of reaction conditions is essential for the success of the desired addition reaction (Scheme II). In particular,

![Diagram](image_url)

**Table 1. Alkylithium Addition-Electrophile Trapping with Vinyl Phenyl Selenide**

<table>
<thead>
<tr>
<th>Entry</th>
<th>RLi</th>
<th>Electrophile</th>
<th>E</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>n-BuLi</td>
<td>D$_2$O</td>
<td>D-</td>
<td>97</td>
</tr>
<tr>
<td>b</td>
<td>n-BuLi</td>
<td>CH$_3$I$^b$</td>
<td>CH$_3$-</td>
<td>95</td>
</tr>
<tr>
<td>c</td>
<td>n-BuLi</td>
<td>n-C$_6$H$_5$Br$^b$</td>
<td>n-C$_6$H$_5$H$_2$-</td>
<td>80</td>
</tr>
<tr>
<td>d</td>
<td>n-BuLi</td>
<td>PhSeBr</td>
<td>PhSe-</td>
<td>84</td>
</tr>
<tr>
<td>e</td>
<td>n-BuLi</td>
<td>(CH$_3$)$_2$SiCl</td>
<td>(CH$_3$)$_2$Si-</td>
<td>90</td>
</tr>
<tr>
<td>f</td>
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<td>Ph(CH$_2$OH)$^-_1$</td>
<td>71</td>
</tr>
<tr>
<td>g</td>
<td>n-BuLi</td>
<td>CH$_3$COCH$_3$</td>
<td>Ph(CH$_2$COH)$^-_1$</td>
<td>60</td>
</tr>
<tr>
<td>h</td>
<td>n-BuLi</td>
<td>PhCOCH$_3$</td>
<td>Ph(CH$_2$COH)$^-_1$</td>
<td>60</td>
</tr>
<tr>
<td>i</td>
<td>n-BuLi</td>
<td>PhCN</td>
<td>PhCO-</td>
<td>50f,h</td>
</tr>
<tr>
<td>j</td>
<td>t-PrLi</td>
<td>D$_2$O</td>
<td>D-</td>
<td>92</td>
</tr>
<tr>
<td>k</td>
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<td>CH$_3$COCH$_3$</td>
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</tr>
<tr>
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<td>(CH$_3$)$_2$SiCl</td>
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<tr>
<td>m</td>
<td>t-BuLi</td>
<td>D$_2$O</td>
<td>D-</td>
<td>85</td>
</tr>
</tbody>
</table>

$^a$ Yields refer to isolated, purified products. See ref 8. All reactions utilize 1.2 equiv of alkyllithium and 1.2-1.5 equiv of electrophile (except D$_2$O quenches). Reactions with n-BuLi were run in dimethoxymethane; reactions with t-PrLi and t-BuLi were run in diethyl ether. $^b$ 1 equiv of HMPA was added with the electrophile. $^c$ Bis(phenylseleno) acetals may be hydrolyzed to the corresponding aldehydes; thus, 1 is also a CH$_3$CHO synthyn. $^d$ Oxidation of \( \alpha \)-trimethylsilylalkyl phenyl selenides affords the corresponding aldehydes; K. Sachdev and H. S. Sachdev, Tetrahedron Lett., 4223 (1976). $^e$ Intermediate not isolated. $^f$ Overall yield from 1. $^g$ Hydrolyzed with 5% HCl (75 °C, 15 min) prior to oxidation-elimination. $^h$ Only the E isomer was produced.