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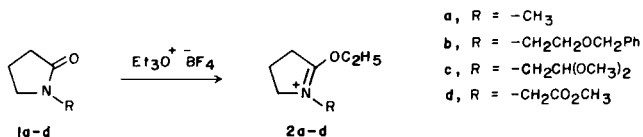
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O-Ethyl-*N*-substituted pyrrolidonium fluoroborate salts were condensed under basic conditions with active methylene compounds to give vinylogous carbamates and cyanamides.

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Since the condensation of orthoamides [2] onto active methylene compounds was first reported by Meerwein [3], formamide orthoamides and vinylogous orthoamides have found many uses in organic synthesis [4]. Orthoamides larger than formamide, however have not been as widely used. Meerwein [3] reported the orthoamide of *N*-methylpyrrolidinone and its condensation with several compounds. Smith and Shroff [5] recently reported the preparation of the *O*-ethyl fluoroborate salt of *N*-vinyl pyrrolidinone but all attempts to convert this salt to an orthoamide gave abnormal products with no orthoamide being observed. Even less used in condensations are the *O*-alkyl amide salt precursors of the orthoamides. Another uncommon parameter for the Meerwein reaction process is the condensation of carbanions on the *O*-amide salt. For example Severin, Brück, and Kullmer [6] have used sodium ethoxide to condense nitromethane onto an *O*-methyl salt of DMF. This latter technique was seen as offering some advantages as a synthetic procedure in that (i) one could prepare the salt *in situ* prior to carbanion addition, (ii) the orthoamide need not be isolated and purified in a separate step and (iii) those products that would require the condensation of thermally unstable orthoamide and/or nucleophiles could still be formed under ionic conditions. With these possibilities in mind we have been exploring the Meerwein condensation with pyrrolidinone derivatives. The *O*-ethyl pyrrolidonium salts, which were easily prepared and highly stable, were found to condense smoothly with various active methylene compounds under moderate to strongly basic conditions.



- a, R = -CH₃
 b, R = -CH₂CH₂OCH₂Ph
 c, R = -CH₂CH(OCH₃)₂
 d, R = -CH₂CO₂CH₃

Salt Formation: The *N*-Substituted pyrrolidinones [7] **1a-d**, were added to triethyloxonium fluoroborate to give the *O*-ethyl salts, **2a-d**, (Table 1), in excellent yield. Such salts are sometimes made in methylene chloride or chloroform since the reactants and products are all soluble in these solvents [5,8]. It was found to be more convenient,

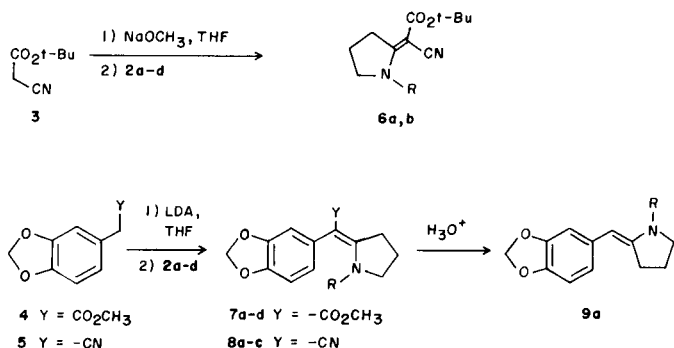
Table I
O-Ethyl Pyrrolidonium Salts

| Salt | Yield % | N=C cm ⁻¹ | IR NMR (H, ppm) |
|-----------|---------|----------------------|---|
| 2b | 95.4 | 1660 | 1.4 (t, 3H, -CH ₂ CH ₃), 2.1-2.5 (m, 2H, -CH ₂ -CH ₂ -CH ₂), 3.15 (t, 2H, *N=C-CH ₂), 3.7 (s, 4H, *N-CH ₂ CH ₂ O), 3.9 (t, 2H, *N-CH ₂ -CH ₂ -CH ₂), 4.45 (s, 2H, Ph-CH ₂ -O), 4.5 (q, 2H, O-CH ₂ -CH ₃), 7.3 (s, 5H, phenyl H's) |
| 2c | 95.7 | 1655 | 1.5 (t, 3H, -CH ₂ CH ₃), 2.1-2.5 (m, 2H, -CH ₂ -CH ₂ -CH ₂), 3.2 (t, 2H, N=C-CH ₂), 3.4 (s, 6H, -CH(OCH ₃) ₂), 3.6 (d, 2H, *N-CH ₂ -CH(OCH ₃) ₂), 3.9 (t, 2H, *N-CH ₂ -CH ₂), 4.6 (t, 1H, -CH(OCH ₃) ₂), 4.7 (q, 2H, OCH ₂ O) |
| 2d | 97.2 | 1665 | 1.4 (t, 3H, -CH ₂ CH ₃), 2.0-2.5 (m, 2H, -CH ₂ CH ₂ -CH ₂), 3.2 (t, 2H, N=C-CH ₂), 3.7 (s, 3H, -CO ₂ CH ₃), 3.9 (t, 2H, N-CH ₂ CH ₂), 4.3 (s, 2H, N-CH ₂ -CO ₂ CH ₃), 4.7 (q, 2H, OCH ₂ CH ₃) |

however, to effect this *O*-alkylation in anhydrous ether with an excess of the amide. The Meerwein salt which is not soluble in ether is slowly transformed to an oily pyrrolidinone salt and the ether is decanted. Several times anhydrous ether is added, stirred, and decanted to remove the slight excess of pyrrolidinone starting material, and the remaining ether is removed *in vacuo*.

Condensation: The pyrrolidonium salts, **2a-d**, were condensed with either the sodium or lithium enolates of **3**, **4**, and **5** to give the vinylogous carbamate and cyanamide systems, **6a-b**, **7a-d**, **8a-c** [9] in yields from 35-95% as mixtures of the *E* and *Z* isomers (Table 2). The vinylogous carbamates, **7a-d**, were characterized in the ir spectra by a carbonyl absorption of 1670-1680 cm⁻¹ and an enamine band at 1555-1565 cm⁻¹. The vinylogous cyanamides, **8a-c**, were characterized by a strong 2170-2180 cm⁻¹ nitrile band and a 1580-1585 cm⁻¹ enamine absorption in the ir spectra. In the ¹H nmr spectra of **6a,b** and **7a-d**, the pyrrolidine ring was characterized by absorptions at δ 1.65-2.15 (m, -CH₂-CH₂-CH₂), 2.9-3.2 (t, J = 7 Hz, -CH₂-C=C), and 3.35-3.55 ppm (t, J = 7 Hz, N-CH₂-). The *E* and *Z* isomers were clearly recognizable in the ¹H nmr spectra

of **8a-c**. The *E* isomers at **8a-c** were characterized by absorptions at 2.95-2.97 (t, $-\text{CH}_2-\text{C}=\text{C}$) and 3.53-3.55 (t, $\text{N}-\text{CH}_2-$), while in the *Z* [10] isomers these absorptions appeared at δ 2.55-2.6 and 3.5-3.65 ppm respectively.



Acid hydrolysis and decarboxylation converted compound **7a** to the enamine **9a** [11] which is a candidate for alkylation and acylation to provide a route to more complex adducts.

The reported procedure is an experimentally convenient alternative to the orthoamide condensation. The amide salts used in this condensation are easily prepared in high purity and can be stored with no apparent decomposition unlike the corresponding orthoamides.

General Procedure for the Condensation of active Methylene Compounds onto *O*-Ethylpyrrolidonium Salts.

To a stirred solution of the base (1 and 1.1 equivalents) in dry THF (-78° for LDA, 0° for sodium methoxide) was added the substrate, **3-5**, (1 equivalent). After 15 minutes the *O*-ethyl pyrrolidonium salt (1 to 1.25 equivalents) in THF was added quickly with vigorous stirring and the solution was allowed to warm to room temperature. After 1

Table III

| | | | Calcd. | Found % |
|-----------|--|---|--------|---------|
| 2b | $\text{C}_{15}\text{H}_{22}\text{NO}_2\cdot\text{BF}_4$ | C | 53.76 | 53.69 |
| | | H | 6.62 | 6.63 |
| | | N | 4.18 | 4.16 |
| 2c | $\text{C}_{10}\text{H}_{20}\text{NO}_3\cdot\text{BF}_4/1.1\text{Et}_2\text{O}$ | C | 42.13 | 42.39 |
| | | H | 7.14 | 7.25 |
| | | N | 4.72 | 4.61 |
| 2d | $\text{C}_9\text{H}_{16}\text{NO}_3\cdot\text{BF}_4/0.03\text{CDCl}_3$ | C | 39.21 | 39.00 |
| | | H | 5.85 | 5.94 |
| | | N | 5.06 | 5.41 |
| 6a | $\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_2$ | C | 64.84 | 64.61 |
| | | H | 8.16 | 8.30 |
| | | N | 12.60 | 12.84 |
| 6b | $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_3/0.4\text{H}_2\text{O}$ | C | 68.70 | 68.92 |
| | | H | 7.73 | 7.69 |
| | | N | 8.01 | 8.03 |
| 7a | $\text{C}_{15}\text{H}_{17}\text{NO}_4/1\text{CDCl}_3$ | C | 63.12 | 62.85 |
| | | H | 6.03 | 5.96 |
| | | N | 4.88 | 4.63 |
| 7b | $\text{C}_{23}\text{H}_{25}\text{NO}_5$ | C | 69.86 | 69.98 |
| | | H | 6.37 | 6.23 |
| | | N | 3.54 | 3.21 |
| 7c | $\text{C}_{18}\text{H}_{23}\text{NO}_6$ | C | 61.88 | 61.51 |
| | | H | 6.64 | 6.35 |
| | | N | 4.01 | 3.82 |
| 7d | $\text{C}_{17}\text{H}_{29}\text{NO}_6$ | C | 61.26 | 61.34 |
| | | H | 5.45 | 5.73 |
| | | N | 4.20 | 4.24 |
| 8a | $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2/1\text{H}_2\text{O}$ | C | 64.03 | 64.20 |
| | | H | 5.45 | 5.56 |
| | | N | 10.52 | 10.37 |
| 8b | $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_3/1\text{H}_2\text{O}$ | C | 72.55 | 72.31 |
| | | H | 6.14 | 6.23 |
| | | N | 7.69 | 7.82 |
| 8c | $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_4/2.5\text{EtOAc}$ | C | 63.89 | 63.97 |
| | | H | 6.55 | 6.78 |
| | | N | 8.28 | 8.03 |
| 9a | $\text{C}_{13}\text{H}_{15}\text{NO}_2$ | C | 71.87 | 71.56 |
| | | H | 6.96 | 6.78 |
| | | N | 6.45 | 6.53 |

Table II

Condensation of *O*-Ethyl Pyrrolidonium Salts With Enolates

| Substrate | Salt | Product | Base | Yield % | tlc | IR cm^{-1} [a] | | | | m/e |
|-----------|-----------|-----------|-------|---------|----------|-------------------------|------------|-------|--------------------|------------------|
| | | | | | | CN | C=O | N-C=C | OCH ₂ O | |
| 3 | 2a | 6a | NaOMe | 95 | 0.55 [d] | 2200 | 1690 | 1580 | — | 222 (11.65%) [b] |
| 3 | 2b | 6b | NaOMe | 78 | 0.46 [d] | 2200 | 1690 | 1565 | — | 342 (40.75%) [b] |
| 4 | 2a | 7a | LDA | 91 | 0.52 [e] | — | 1670 | 1555 | 1495 | 275 (100%) [c] |
| 4 | 2b | 7b | LDA | 35 | 0.51 [e] | — | 1680 | 1565 | 1500/1485 | 395 (60.4%) [b] |
| 4 | 2c | 7c | LDA | 75 | 0.55 [d] | — | 1675 | 1560 | 1500/1480 | 349 (29.08%) [c] |
| 4 | 2d | 7d | LDA | 90 | 0.32 [f] | — | 1745, 1685 | 1575 | 1500/1485 | 333 (100%) [c] |
| 5 | 2a | 8a | LDA | 92 | 0.30 [e] | 2170 | — | 1585 | 1490/1475 | 243 (100%) [b] |
| 5 | 2b | 8b | LDA | 52 | 0.42 [e] | 2175 | — | 1580 | 1495/1480 | 362 (0.89%) [c] |
| 5 | 2c | 8c | LDA | 78 | 0.49 [d] | 2180 | — | 1585 | 1500/1485 | 316 (100%) [b] |

[a] Film. [b] 15 eV. [c] 70 eV. [d] 2:3 Ethyl acetate/hexane on silica. [e] 1:4 Ethyl acetate/hexane on silica. [f] 3:7 Ethyl acetate/hexane on silica.

hour, (room temperature), the usual work up yielded the crude product which was chromatographed on silica gel using ethyl acetate/hexane as the eluent.

REFERENCES AND NOTES

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- [2] This research was supported by NSF Grant CHE 8024280 and PHS Grant AM 28802.
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- [7] Compound **1b** was prepared by benzylation of *N*-2-(2-hydroxyethyl)pyrrolidinone with sodium hydride and benzyl bromide. Compound **1c** was prepared by cyclization of aminoacetaldehyde-dimethyl acetal with 4-chlorobutryl chloride.
- [8] W. Reid and E. Schmidt, *Ann. Chem.*, **695**, 217 (1966); W. Reid, D. Piechaczak and E. B. Vollberg, *Ann. Chem.*, **734**, 13 (1970); R. F. Borsch, *Tetrahedron Letters*, 61 (1968); R. R. Fraser and R. B. Swingle, *Can. J. Chem.*, **48**, 2065 (1970).
- [9] Compounds **6a**, **7a** and **8a** have been previously prepared in this (C. A. Wilson, Ph.D. Dissertation, University of South Carolina, 1975) and other research groups (eg. K. Eistetter, H. Schafer and H. Menger, *Chem. Abstr.*, **88**, 169959x (1978)) via the standard Meerwein orthoamide technique. This technique is less reliable as the substitution on the orthoamide nitrogen increases in complexity. See Table II for C, H and N analysis data.
- [10] *E/Z* Geometry was assigned based on analogies to compounds assigned through lanthanide shift ¹H nmr studies of C. A. Wilson (ref [8]).
- [11] Yield: 69%; tlc (silica-ethyl acetate hexanes 1:4): *R_f* = 0.47; ir (film): cm⁻¹ 1630 (N=C=C); ¹H nmr: ppm 1.7-2.0 (m, 3H, -CH₂CH₂CH₂), 2.65 (s, 3H, NCH₃), 2.70 (t, 2H, C=C-CH₂), 3.05 (t, 2H, N-CH₂), 4.85 (s, 1H, Ar-CH=C), 5.75 (s, 2H, -O-CH₂-O), 6.45-6.7 (m, 3H, aromatic H-s); ms: m/e (70 eV): 217 (M, 100%).