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NOVEL APPLICATIONS OF THE MODIFIED POLONOVSKI REACTION - V[1]

SILYL ENOLATES AS NUCLEOPHILIC ALKYLATING REAGENTS

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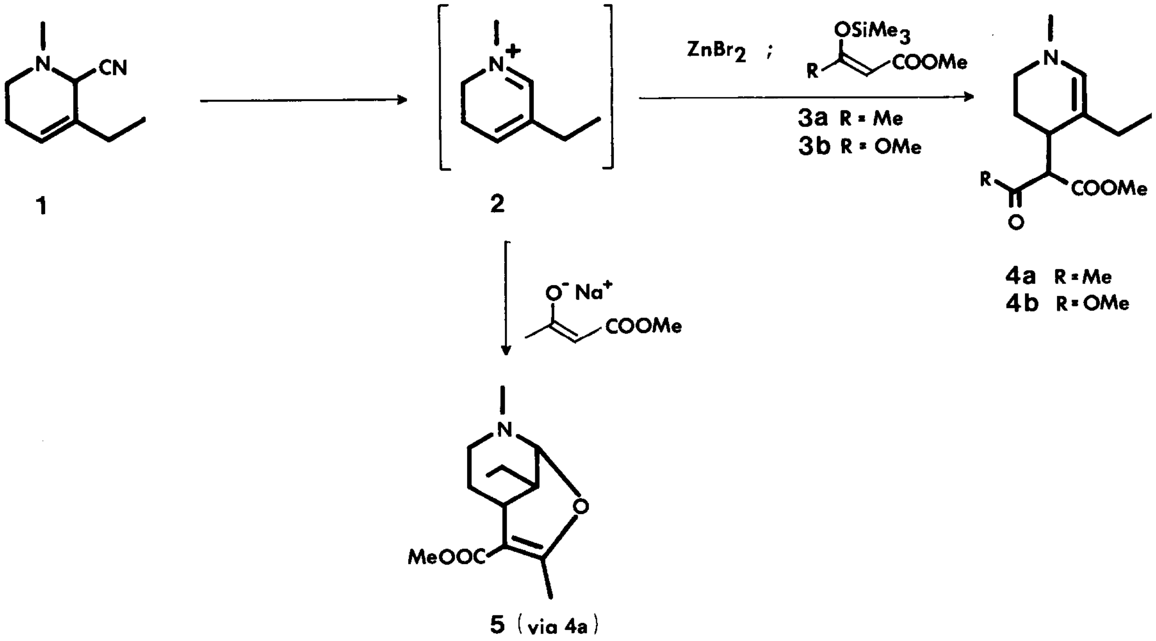
Summary: *A practical high-yield condensation reaction between 2-cyano-1,2,5,6-tetrahydropyridines and silyl enolates under mild Lewis acid catalysed conditions is described.*

2-Cyano-1,2,5,6-tetrahydropyridine derivatives are easily accessible from the corresponding pyridinium salts *via* a route employing the modified Polonovski reaction[2]. The synthetic utility of α-aminonitriles is further increased by the regiocontrol which can be exerted over their formation[3]. Of utmost preparative value to indole alkaloid chemistry is the conjugate addition of organometallic reagents and metal enolates to the 5,6-dihydropyridinium ion equivalent 1. This has been achieved in several cases by the use of silver tetrafluoroborate[2]. The effect of the Lewis acid can be seen as two-fold: the silver ion enhances the leaving potential of the cyano group[4] and the *electrophilicity* of the resulting 5,6-dihydropyridine intermediate is increased[5]. The more general ability of Lewis acids to effect the transformation has recently been rationalized[6,7].
The use of metal enolates, however, diminishes the generality of the reaction and in some cases causes unwanted side-reactions to take place. We now report that these problems can be avoided by using Lewis acid catalysed alkylation of *O*-silylated enolates with vinylogous iminium salts of the general type 2. Our method also provides the first example of silyl chemistry being applied to introduce an alkyl substituent at the 4-position of a piperidine unit, a problem often encountered in alkaloid chemistry[8].

In a typical experiment, the silyl enolate 3a[9] (1.2 mmol) was added *via* syringe to a solution of the aminonitrile 1[2] (1 mmol) in 2 ml anhydrous solvent (CH_2Cl_2 or dimethoxyethane) under argon at room temperature. Then a catalytic amount of powdered anhydrous $ZnBr_2$ (*ca.* 25 mg, 0.1 mmol) was added and the reaction mixture was stirred at ambient temperature for 48 h. Usual work-up gave 180 mg (80 %) 4a[10]. In a similar experiment, reaction of 1 with 3b[11] gave 4b[2] in 75 % yield. It is noteworthy that the use of Na enolate of methyl acetoacetate prevented the isolation of 4a, which is easily rearranged to the cyclised product 5 under the Husson reaction conditions[2].



In summary, we have found that the use of silyl enolates increases the synthetic utility of 2-cyano-1,2,5,6-tetrahydropyridines by allowing the reactions to be performed easily under mild conditions. Moreover, the spectrum of the nucleophiles available for the alkylation can be extended beyond those of only trivial structure. Further studies to explore the utility of the method towards indole alkaloid synthesis is in progress.

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References and Notes:

1. Part IV: T. Langenskiöld and M. Lounasmaa, *Heterocycles*, submitted.
2. D.S. Grierson, M. Harris and H.-P. Husson, *J. Am. Chem. Soc.* 102, 1064 (1980).
3. M. Lounasmaa and A. Koskinen, *Heterocycles* 19, 2115 (1982); A. Koskinen and M. Lounasmaa, *Tetrahedron*, in press.
4. H. Ahlbrecht, W. Raab and C. Sonderheid, *Synthesis* 127 (1979).
5. cf. eg. E. Colvin, Silicon in Organic Synthesis, Butterworths, London, 1981.
6. F. Guibe, D.S. Grierson and H.-P. Husson, *Tetrahedron Lett.* 23, 5055 (1982).
7. Unpublished results from our laboratory.
8. E. Wenkert, *Pure & Appl. Chem.* 53, 1271 (1981).
9. S. Torkelson and C. Ainsworth, *Synthesis* 722 (1976).
10. IR: 1750-1720, 1630 cm^{-1}. ^1H NMR($CDCl_3$, 60 MHz)δ 0.92 (3H, t, 7 Hz), 1.5-2.0 (3H, m), 2.17 (2H, q, 7 Hz), 2.27 (3H, s), 2.40 (3H, s), 2.58 (2H, m), 3.50 (1H, br s), 3.74 (3H, s), 5.41 (1H, br s).
^{13}C NMR($CDCl_3$, 15 MHz)δ 11.0, 22.1, 26.9, 29.9, 37.3, 43.9, 49.7, 50.5, 58.8, 108.3, 132.2, 167.4, 200.3. MS m/z (%): 239 (M^+, 20), 224 (10), 196 (15), 124 (100).
11. C. Ainsworth, F. Chen and Y.-N. Kuo, *J. Organometal. Chem.* 46, 59 (1972).

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