and, indeed, in each case in which subsequent equilibration was not possible (entries 3 and 7), a single, cis-fused annulation product (**31** and **37**) was produced in high yield. In other experiments (entries 1, 2, and 4–6) varying degrees of equilibration occurred under the conditions of ring closure. In each of these cases, the cyclized product(s) were equilibrated (MeONa, MeOH, reflux, 18 h) and the equilibrium ratios were determined (Table I). Interestingly, the equilibrium **27** ⇌ **28** favored exlusively the trans isomer **28**, while attempted equilibration of the cis-fused ketone **36** gave no detectable amount of the corresponding trans-fused isomer.[9]

The "best" overall yields of the annulation sequences summarized in Table I varied from 40% (entry 4) to 70% (entry 1). Taking into account the brevity of the process and the fact that the methylenecyclohexane moiety is a fairly common structural feature in the terpenoid family of natural products, it appears that the methodology described herein should find use in organic synthesis. We are actively investigating a number of possible applications.

Acknowledgment. We are very grateful for financial support from the Natural Sciences and Engineering Research Council of Canada and from Merck and Co., Inc., and Merck Frosst Canada, Inc.

Registry No. **7**, 92490-53-4; **11**, 89045-21-6; **12**, 92490-54-5; **13**, 930-68-7; **14**, 1193-18-6; **15**, 1121-18-2; **16**, 78-59-1; **17**, 930-30-3; **18**, 2758-18-1; **19**, 1120-73-6; **20**, 92490-55-6; **21**, 92490-56-7; **22**, 92490-57-8; **23**, 92490-58-9; **24**, 92490-59-0; **25**, 92490-60-3; **26**, 92490-61-4; **27**, 92490-62-5; **28**, 92490-63-6; **29**, 92490-64-7; **30**, 92490-65-8; **31**, 92490-66-9; **32**, 92490-67-0; **33**, 92490-68-1; **34**, 92490-69-2; **35**, 92490-70-5; **36**, 92490-71-6; **37**, 92490-72-7; cyclohexanone, 108-94-1.

Supplementary Material Available: Representative experimental procedures for the preparation of compounds **20**, **27**, and **28** and spectral data for compounds **20** and **27–37**, inclusive (3 pages). Ordering information is given on any current masthead page.

(8) Conia, J. M.; Rouessac, F. *Tetrahedron* **1961**, *16*, 45, Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107.

(9) Treatment of **36** with MeONa–MeOD gave the expected (cis-fused) trideuterio ketone.

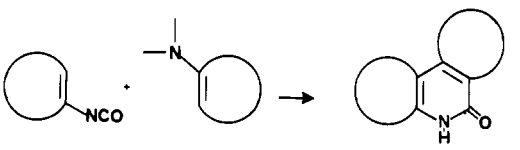
Edward Piers,* Bik Wah Anissa Yeung
Department of Chemistry
University of British Columbia
Vancouver, British Columbia, Canada V6T 1Y6
Received June 21, 1984

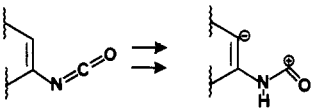
Vinyl Isocyanate Cyclization Reactions in Synthesis. An Expedient Construction of the Octahydrophenanthridinone Ring System

Summary: The octahydrophenanthridinone ring system is assembled in one step via a thermally induced reaction of vinyl isocyanates and enamines.

Sir: Vinyl isocyanates are particularly attractive intermediates for application to synthetic problems by virtue of their high degree of reactivity and relative ease of preparation. However, to date this grouping has received relatively little attention in this context.[1] We were particularly intrigued with the possibility of exploiting this functionality as an equivalent for the useful 1,4-dipolar species A. This type of species could be envisioned to

Scheme I

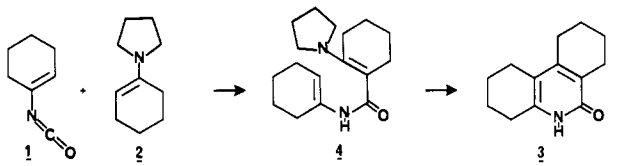




A

participate in a highly convergent ring forming process which would quickly assemble complex heterocyclic systems. To demonstrate this concept, we report herein the facile reaction of substituted vinyl isocyanates with enamines to provide highly substituted 2-pyridones[2] (Scheme I). The 2-pyridone moiety is a prominent structural feature in a number of interesting natural products,[3] and the hydrophenanthridine systems made available by this route are displayed in one form or another by several classes of alkaloids.

Simply heating an equal molar mixture of 1-isocyanato-1-cyclohexene (**1**) and 1-pyrrolidino-1-cyclohexene (**2**)[4] in refluxing toluene provided the octahydrophenanthridinone **3**[5] as the principle isolable product in 81% yield. A variety of other isocyanate and enamine partners also yield pyridone products in a similar fashion (Table I), and in most cases, the polycyclic pyridone compounds produced in this apparently general reaction can be isolated by filtration and recrystallization. The simplicity and mildness of this technology for the construction of relatively elaborate hydrophenanthridinone systems can be contrasted with many of the "classical" preparations of 2-pyridones which are often not amenable to generating such substitution patterns.[6]



In a typical procedure, 1-cyclohexenecarboxylic acid (10 mmol) is stirred with 10 mmol of triethylamine in 10 mL of toluene. DPPA (diphenylphosphoryl azide)[7] (10 mmol) is added via syringe; and after 1 h of stirring at room

(1) (a) Dondoni, A.; Kniezo, L.; Medici A. *J. Org. Chem.* **1982**, *47*, 3994. (b) Takaki, K.; Okamura, A.; Ohshiro, Y.; Agawa, T. *Ibid.* **1978**, *43*, 402. (c) Fuks, R. *Tetrahedron* **1970**, *26*, 2161.

(2) For other pyridone syntheses, see: (a) Earl, R. A.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1983**, *105*, 6991. (b) Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *Ibid.* **1983**, *105*, 5390. (c) Sainte, F.; Poncin, B. S.; Frisque, A. H.; Ghosez, L. *Ibid.* **1982**, *104*, 1428. (d) Overman, L. E.; Tsuboi, S.; Roos, J. P.; Taylor, G. F. *Ibid.* **1980**, *102*, 747.

(3) (a) Lednicer, D.; Mitscher, L. A. "The Organic Chemistry of Drug Synthesis"; Wiley: New York, 1977; Vol. 1; 1980, Vol. 2. (b) Grundon, M. F. "The Alkaloids"; The Chemical Society: London, 1977; Vol. 7.

(4) Enamine additions to the carbonyl carbon of aryl isocyanates have been observed previously: (a) Ried, W.; Kappeler, W. *Liebigs Ann. Chem.* **1964**, *673*, 132. (b) Ried, W.; Kappeler, W. *Ibid.* **1965**, *688*, 177.

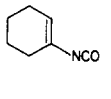
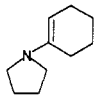
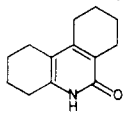
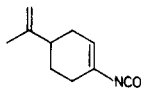
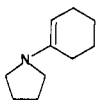
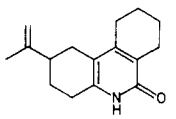
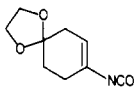
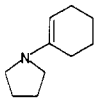
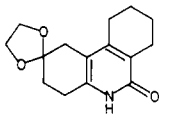
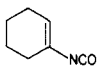
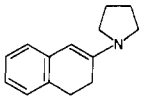
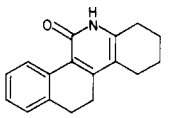
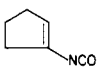
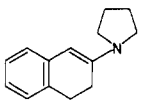
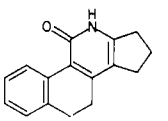
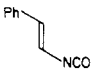
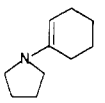
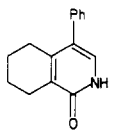
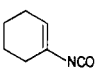
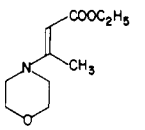
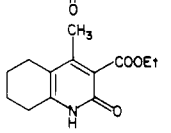
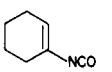
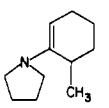
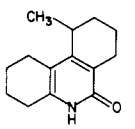
(5) This compound exhibited spectral (^{1}H NMR, ^{13}C NMR, IR, UV, mass spectrum) and analytical data in complete accord with the assigned structure.

(6) Tieckelmann, H. In "Pyridine and its Derivatives", Supplement, Part 3; Abramovitch, R. A., Ed.; Wiley: New York, 1975; Chapter 12, pp 599–728.

(7) Shioiri, T.; Ninomiya, K.; Yamada, S. *J. Am. Chem. Soc.* **1972**, *94*, 6203.

0022-3263/84/1949-4569$01.50/0

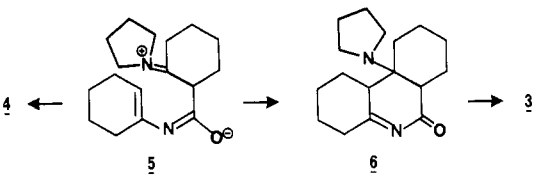
Table I. Production of 2-Pyridones from Vinyl Isocyanates

entry	isocyanate	enamine	pyridone[a]	yield,[b] %	mp, °C
1				73 (81)[e]	295–97[c]
2				65	231–33
3				64	280–82
4				61[d]	>300
5				57[d]	289–91
6				30[d]	244–45
7				43[d]	228–29
8				52	248–50

[a] Reference 5. [b] Yields of recrystallized 2-pyridones are calculated from the starting vinyl acids. [c] Lit. mp 296–98 °C. Montgomery S. R. U.S. Patent 3 291 801, Dec 12, 1966. [d] Yields are not optimized. Oligomerization of starting vinyl isocyanate is a competing side reaction. [e] Yield of 2-pyridone based on isolated vinyl isocyanate.

temperature, the reaction mixture is heated at reflux for several hours. Formation of the vinyl isocyanate can be monitored by IR or evolution of N_2. When all of the azide has disappeared, the solution is cooled to room temperature, 10 mmol of the enamine is added, and the mixture is refluxed for 48 h. The product is recrystallized from 95% ethanol. Solvent exchange on addition of the enamine occasionally gave improved yields.

Exposure of isocyanate **1** to enamine **2** at room temperature resulted in the formation of a moderately labile species to which structure **4** has been assigned.[8] This material could be smoothly transformed into pyridone **3** on heating neat or in refluxing toluene.[9,10] Similar thermal and photochemical electrocyclic bond reorganizations in related systems are precedented.[11] It is envisioned that the reaction of the enamine with the isocyanate initially generates a zwitterionic C-acylated iminium intermediate **5**. This species may undergo direct cyclization to **6** which



can then lose the elements of pyrrolidine to give the observed pyridone. Alternatively, **5** may tautomerize to diene amide **4**. The rate of formation of **4** appears to be dependent on solvent polarity. Polar aprotic solvents such as acetonitrile greatly accelerate the formation of diene–amide **4** and seem to minimize detrimental side reactions such as isocyanate oligomerization.

Table I illustrates representative substituted 2-pyridones which have been prepared by using the vinyl isocyanate–enamine cyclocondensation. The generality and efficiency with which the hydrophenanthridinone nucleus can be assembled suggests the potential utility of this process for the construction of members of the amaryllidaceae[12a] and chelidonine[12b] alkaloids, as well as for certain azasteroid

(8) IR (KBr) ν_{max} 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.7 (b s, 1 H), 5.3 (b s, 1 H), 3.8–3.3 (m, 4 H), 3.0–2.6 (m, 8 H), 2.2–1.8 (m, 12 H); MS, m/e (relative intensity) M$^+$ 274 (9), 179 (11), 178 (100), 150 (12).

(9) In some instances increased yields of 2-pyridones could be realized if the reactants were initially stirred at room temperature in acetonitrile followed by solvent exchange to toluene and refluxing for 48 h.

(10) Interestingly, this cyclization can also be effected at room temperature by acid catalysis. Treatment of intermediate **4** with TFA resulted in the rapid disappearance of the vinyl proton at δ 5.3. This was followed shortly by the appearance of the characteristic NMR signals of the pyridone **3**.

(11) (a) MacMillan, J. H.; Washburne, S. S. *J. Org. Chem.* **1973**, *38*, 2982. (b) Mallory, F. B.; Mallory, C. W. *Org. React.* (N.Y.) **1984**, *30*, 1.

(12) (a) Wildman, W. C. *Alkaloids* **1968**, *11*, 307. (b) Takao, N.; Bessho, N.; Kamigauchi, M.; Iwasa, K.; Tomita, K.; Fujiwara, T.; Fujii, S. *Tetrahedron Lett.* **1979**, 495.

systems. Entries 4 and 5 illustrate that one-step access to the 12-azasteroid nucleus can be achieved by employing a commercial enamine and readily accessible isocyanates as reaction partners. Entries 3 and 7 demonstrate that various functionalized enamines and isocyanates can also participate effectively in the ring-forming process. The relatively modest yield observed in entry 6 reflects the propensity of the isocyanate derived from cinnamic acid to suffer oligomerization in competition with acylation during reaction with enamines. This side reaction occurred to a lesser extent with some of the other examples as well. The pyridone moieties generated by using the transformation described in this paper are potentially versatile intermediates for synthesis, particularly in terms of their role in facilitating further carbon–carbon bond formation and oxidation level manipulation.[13]

Work is currently underway to exploit the considerable potential of this methodology for natural product synthesis.

Acknowledgment. We thank the Research Corporation and the National Science Foundation (CHE 83-10538) for their generous support of this research.

Registry No. 1, 5041-27-0; 2, 1125-99-1; 3, 13689-45-7; *trans*-PhCH=CHNCO, 33066-20-5; *trans*-PhCH=CHCO$_2$H, 140-10-3; 4-(1-methylethenyl)-1-isocyanatocyclohexene, 92525-48-9; 8-isocyanato-1,4-dioxaspiro[4.5]dec-7-ene, 92525-49-0; 1-isocyanatocyclopent-1-ene, 92525-50-3; 2-(pyrrolidin-1-yl)-3,4-dihydronaphthalene, 21403-95-2; 4-[2-(ethoxycarbonyl)-1-methyl-(*E*)-ethenyl]morpholine, 55212-82-3; 2-(pyrrolidin-1-yl)-3-methyl-1-cyclohexene, 75337-00-7; (−)-2-(1-methylethenyl)-1,2,3,4,5,6,7,8,9,10-decahydro-6-oxophenanthridine, 92525-51-4; 1,3,4,5,7,8,9,10-octahydro-2,6-phenanthridinedione 2,2-ethanediyl acetal, 92525-52-5; 7,8,9,10,11,12-hexahydrobenzo[*i*]phenanthridin-5(6*H*)-one, 92525-53-6; 6,7,8,9,10,11-hexahydrobenzo[*h*]-cyclopent[*c*]isoquinolin-5-one, 92525-54-7; 4-phenyl-5,6,7,8-tetrahydroisoquinolin-1(2*H*)-one, 92525-55-8; ethyl 4-methyl-2-oxo-5,6,7,8-tetrahydroquinoline-3(1*H*)-carboxylate, 92525-56-9; 10-methyl-1,3,4,5,7,8,9,10-octahydro-6(2*H*)-phenanthridinone, 92525-57-0; 1-cyclohexenecarboxylic acid, 636-82-8; 4-(1-methylethenyl)-1-carboxy-1-cyclohexene, 92525-58-1; 1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylic acid, 92525-59-2; 1-cyclopentenecarboxylic acid, 1560-11-8.

Supplementary Material Available: Table of spectral and analytical details for the 2-pyridones in Table I (2 pages). Ordering information is given on any current masthead page.

(13) (a) Domagala, J. M. *J. Org. Chem.* **1984**, *49*, 126. (b) Kuzuya, M.; Mano, E; Adachi, M.; Noguchi, A.; Okuda, T. *Chem. Lett.* **1982**, 475.

James H. Rigby,* N. Balasubramanian
Department of Chemistry
Wayne State University
Detroit, Michigan 48202
Received August 14, 1984

Nucleophilic Addition of Silyl Enol Ethers to Aromatic Nitro Compounds: A Facile Synthesis of α-Nitroaryl Carbonyl Compounds†

Summary: Silyl enol ethers and silyl ketene acetals add to aromatic nitro compounds in the presence of fluoride ion sources (e.g., tris(dimethylamino)sulfonium difluorotrimethylsilconate (TASF)) to give, after oxidation, α-nitroaryl carbonyl compounds.

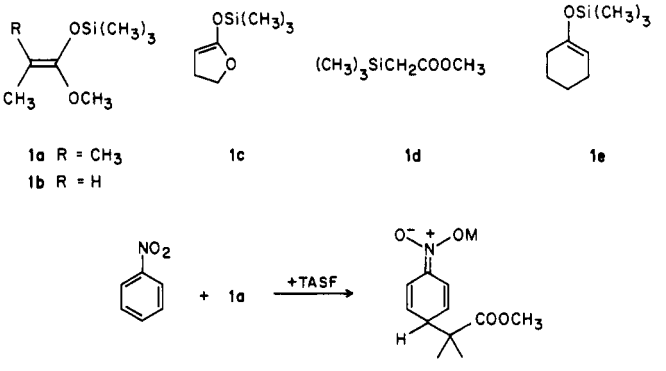
Sir: The synthetic utility of organosilicon reagents has been raidly expanding in the last few years.[1] Recently, we have reported that potent carbon nucleophiles with low basicity can be generated from silyl enol ethers and Lewis bases such as tris(dimethylamino)sulfonium difluorotrimethylsiliconate (TASF) or bifluoride (TASHF$_2$).[1g] Thus, this reagent combination is compatible with Michael acceptors bearing active hydrogen atoms[2] and initiates "group transfer polymerization" of acrylic monomers.[3] In this communication we record our initial findings on the reactions of aromatic nitro compds. with silyl ketene acetals and silyl enol ethers.[4] In spite of the ready availability of aromatic nitro compounds, an efficient and general method to introduce alkyl side chains with useful functional groups to these compounds has not been developed.

Table I. Synthesis of α-(2-Nitroaryl) Carbonyl Compounds 5, from Nitroaromatics 4 and Silyl Reagents 1

		nitro compound		silyl reagent and yield of 5				
entry		X	Y	1a	1b	1c	1d	1e
1	4a	CH_3	H		44	43		
2	4b	Cl	H	51	58	55	50	50
3	4c	F	H		77	79		
4	4d	Cl	Cl		61			
5	4e	Cl	OCH_3	65				
6	4f	$C(CH_3)_2Cl$	H		31			
7	4-NITRO-2,1,3-BENZOTHIADIAZOLE[a]			64				
8	1-NITRONAPHTHALENE[a]				51	41		

[a] Addition occurs at positon ortho to the nitro group.

We find that nitrobenzene reacts with trimethylsilyl ketene acetal **1a** in THF/CH_3CN in the presence of 1 equiv of TASF.[5] The NMR spectrum of an equimolar mixture



1a R = CH_3 1c 1d 1e
1b R = H

2

M = TMS or TAS

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