any distortion of the enone from planarity would be expected to *decrease* the reactivity through loss of conjugation.

Our results, in conjunction with Helmchen's work (vide supra), provide strong evidence that the *reactive* geometry of $TiCl_4$–enone complexes may be of an out-of-plane type; further work will be required to establish whether this is a general phenomenon. These results do not, of course, imply that a preference for an out-of-plane reactive geometry exists for other Lewis acids; $TiCl_4$ may be unique in this regard. However, our results do point out the need for caution in basing predictions of reactive geometries on X-ray and spectroscopic data.

Acknowledgment. Financial support by the National Science Foundation (CHEM-8813618) and by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

Supplementary Material Available: Details of the synthesis and characterization of compounds **1–5** as well as the kinetics procedures (13 pages). Ordering information is given on any current masthead page.

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(26) ^{1}H NMR competition experiments employing 1/1/1 **1a**/**1e**/$TiCl_4$ and **2a**/**2e**/$TiCl_4$ indicated a 14/86 ratio of **1a**·$TiCl_4$/**1e**·$TiCl_4$, but that **2a** does not effectively compete with **2e** for $TiCl_4$ (only **2e**·$TiCl_4$ present). We thank a referee for suggesting this experiment.

[1 + 4] Cycloaddition of Vinyl Isocyanates with Alkyl Isocyanides. Formal Total Synthesis of Erysotrine[†]

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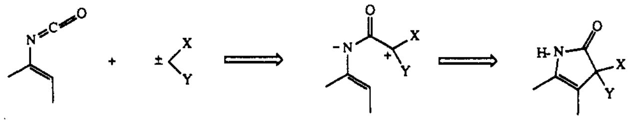
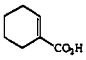
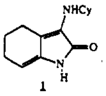
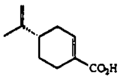
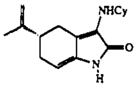
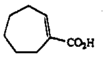
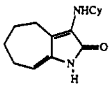
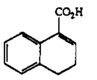
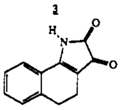
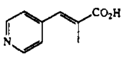
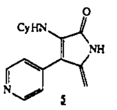
Vinyl isocyanates have emerged as particularly versatile intermediates in combination with various 1,2-dipole equivalents for the construction of structurally elaborate pyridine systems.[1] Employing appropriate 1,1-dipolar reaction partners should permit direct access to highly substituted and functionally rich pyrrolinone derivatives as depicted in eq 1.



(1)

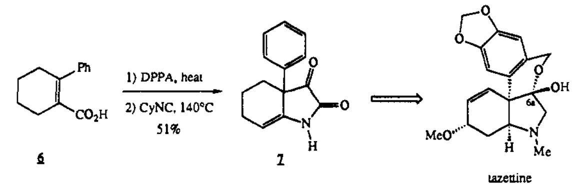
Isocyanides display a unique reactivity profile that is particularly well suited for serving as a 1,1-dipole equivalent in the present context.[2] We report herein that a wide variety of vinyl isocyanates undergo a highly efficient, room temperature [1 + 4] cycloaddition[3] with readily available cyclohexyl isocyanide (CyNC) to produce substituted pyrrolinone derived products. Several examples illustrating the scope of this novel cycloaddition are compiled in Table I.

Table I. Reaction of Vinyl Isocyanates with Cyclohexyl Isocyanide

Entry	Acid	Product[a]	Yield (%)
1		 **1**	84
2		 **2**	68
3		 **3**	75
4		 **4**	82
5		 **5**	81

[a] Each product displays spectral (^{1}H NMR, ^{13}C NMR, IR, MS) and analytical (HRMS and/or combustion analysis) data in complete accord with the assigned structure.

Typically, the isocyanate reaction partner is generated in nearly quantitative yield from the corresponding α,β-unsaturated carboxylic acid by treatment with diphenyl phosphorazidate (DPPA)[4] followed by heating in acetonitrile. This reaction mixture is then cooled, a slight excess of cyclohexyl isocyanide[5] is added, and the resultant mixture is stirred at room temperature for 15 h. In most cases the product precipitates from the reaction mixture and is isolated by filtration and recrystallization.



(2)

In light of the widespread occurrence of the hydroindole unit as a substructure in numerous alkaloid families, this methodology, which can accommodate substantial structural modifications, should prove of considerable utility for the rapid assembly of a range of target natural products. As a particularly stringent test of the scope of this process for carbon–carbon bond formation in the face of significant steric hindrance and as a model for the construction of the *Sceletium* alkaloids (mesembrine), the isocyanate derived from carboxylic acid **6**[6] was exposed to cyclohexyl isocyanide (CyNC) under normal conditions. While no cycloaddition was detected at room temperature, the cyclization proceeded smoothly in refluxing xylene to give adduct **7**[7] (mp 186–188 °C) in 51% overall yield. The functionalization available in intermediate **7** is particularly significant with regard to the eventual construction of certain Amaryllidaceae alkaloids such as tazettine.[8]

The Amaryllidaceae alkaloid ring system can also be rapidly accessed by employing this [1 + 4] protocol starting from building block **1** (Table I). Chemoselective N-alkylation of the enamide

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[†] Portions of this work were reported at the Symposium on Heterocycles in Synthesis, 200th National Meeting of the American Chemical Society, Washington, DC, August 29, 1990, ORGN 202.

(1) (a) Rigby, J. H.; Qabar, M. *Synth. Commun.* **1990**, *20*, 2699. (b) Rigby, J. H.; Qabar, M. *J. Org. Chem.* **1989**, *54*, 5852. (c) Rigby, J. H.; Holsworth, D. D.; James, K. *Ibid.* **1989**, *54*, 4019. (d) Rigby, J. H.; Balasubramanian, N. *J. Org. Chem.* **1989**, *54*, 224.

(2) (a) Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1991**, *113*, 2127. (b) Morel, G.; Marchand, E.; Foucaud, A.; Toupet, L. *J. Org. Chem.* **1990**, *55*, 1721. (c) Westling, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1987**, *109*, 590. (d) Westling, M.; Smith, R.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 1159. (e) Deyrup, J. A.; Killion, K. K. *J. Heterocycl. Chem.* **1972**, *9*, 1045.

(3) For some recent examples of other 1 + 4 strategies into nitrogen heterocycles, see: (a) Pearson, W. H.; Bergmeier, S. C.; Degan, S.; Lin, K.-C.; Poon, Y.-F.; Schkeryantz, J. M.; Williams, J. P. *J. Org. Chem.* **1990**, *55*, 5719. (b) Padwa, A.; Norman, B. H. *Tetrahedron Lett.* **1988**, *29*, 3041. (c) Bäckvall, J. E.; Renko, Z. D.; Byström, S. E. *Ibid.* **1987**, *28*, 4199.

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

(5) Ugi, I.; Meyr, R.; Lipinski, M.; Bodesheim, F.; Rosendahl, F. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, p 300.

(6) Klein, J.; Levin, G. *J. Am. Chem. Soc.* **1958**, *80*, 1707.

(7) This compound displayed spectral (^{1}H NMR, ^{13}C NMR, IR, MS) and analytical (combustion analysis and/or HRMS) data in complete accord with the assigned structure.

(8) Abelman, M. M.; Overman, L. E.; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959.

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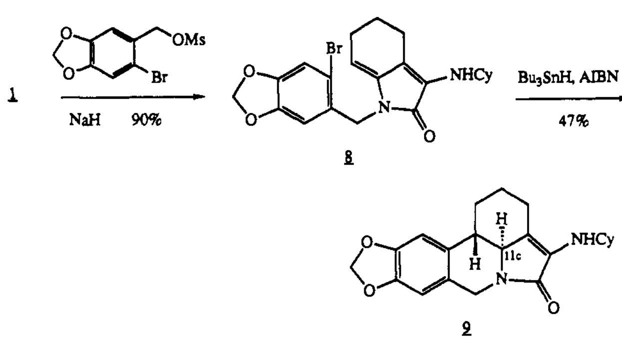
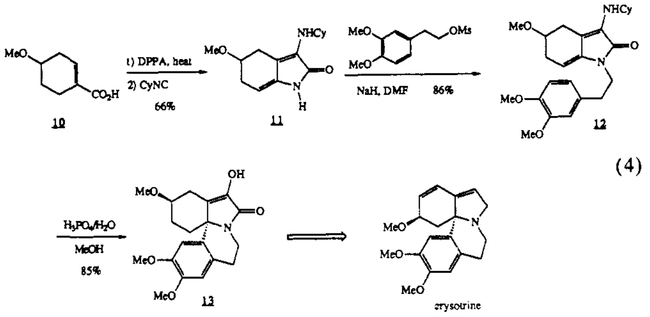


(3)

provided compound 8[7] (mp 158–160 °C) in 90% yield. Radical-mediated cyclization[9] followed uneventfully to provide the tetracycle 9[7] (mp 188–190 °C), as a single diastereomer. The exclusive formation of the requisite trans B–C ring fusion in this cyclization is particularly noteworthy since this stereochemical arrangement is often encountered in Amaryllidaceae alkaloids.[10]



(4)

A very concise, formal total synthesis of the *Erythrina* alkaloid, erysotrine, has also been achieved by employing the new methodology.[11] The normal [1 + 4] cycloaddition protocol conducted on 4-methoxy-1-cyclohexenecarboxylic acid (**10**)[12] gave hydroindole **11**[7] in 66% overall yield. Chemoselective N-alkylation at the enamide nitrogen followed by smooth acid-mediated cyclization (presumably via the corresponding *N*-acyliminium ion)[13] produced compound **13**[7] (mp 185–187 °C; lit.[14a] mp 187 °C) as a single diastereomer displaying a fully intact *Erythrina* carbon skeleton. This material has been carried on to erysotrine by Mondon and co-workers and as such constitutes a formal total synthesis of this natural product.[14b]

It is clear from the examples provided that this novel [1 + 4] cycloaddition chemistry is a versatile and powerful method for constructing a wide range of alkaloid systems, and additional applications to total synthesis are underway.

Acknowledgment. We thank the National Science Foundation (CHE-9021206) for their generous support of this work.

Supplementary Material Available: Typical experimental procedures and full characterizations of all new compounds including melting points, ^{1}H and ^{13}C NMR, IR, and mass spectral data, and HRMS and/or combustion analyses (8 pages). Ordering information is given on any current masthead page.

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[9] Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072.

[10] The proton at C_{11c} in compound **9** appeared as a doublet at δ 3.13 with $J = 11$ Hz. Typical trans J values for similar protons in naturally occurring alkaloids range between 10 and 12 Hz: (a) Torssell, K. *Tetrahedron Lett.* **1974**, 623. (b) Kotera, K.; Hamada, Y.; Tori, K.; Aono, K.; Kuriyama, K. *Ibid.* **1966**, 2009.

[11] For a recent review of the *Erythrina* alkaloids, see: Dyke, S. F.; Quessy, S. N. In *The Alkaloids*; Rodrigo, R. G. A., Ed.; Academic Press: New York, 1981; Vol. XVIII, p 1.

[12] Prepared from commercially available 4-methoxycyclohexanecarboxylic acid via a selenenylation–selenoxide elimination sequence: Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

[13] Tamura, Y.; Maeda, H.; Akai, S.; Ishibashi, H. *Tetrahedron Lett.* **1982**, *23*, 2209.

[14] (a) Mondon, A.; Hansen, K. F.; Boehme, K.; Faro, H. P.; Nestler, H. J.; Vilhuber, H. G.; Böttcher, K. *Chem. Ber.* **1970**, *103*, 615. (b) Mondon, A.; Nestler, H. J. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 588.

Yields of Excited Carbonyl Species from Alkoxyl and from Alkylperoxyl Radical Dismutations

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Recently Niu and Mendenhall reported that the yields of singlet *molecular oxygen* from the self-reactions of simple alkylperoxyl radicals averaged about 0.1 and did not change much with changes in alkyl structure.[2] In this communication we show that the yields of excited *carbonyl* species, generated from reactions 1–3, are 10^3–10^4 less and vary by about 1 order of magnitude with changes in alkyl group.

$$t\text{-BuON}{=}\text{NO-}t\text{-Bu} \rightarrow 2\,t\text{-BuO}^{\bullet} + \text{N}_2 \qquad (1)$$

$$\text{R}_1\text{R}_2\text{CHOOH} + t\text{-BuO}^{\bullet} \rightarrow \text{R}_1\text{R}_2\text{CHOO}^{\bullet} + t\text{-BuOH} \qquad (2)$$

$$2\text{R}_1\text{R}_2\text{CHOO}^{\bullet} \rightarrow\rightarrow \text{R}_1\text{R}_2\text{C}{=}\text{O}(\text{S}_0,\text{S}_1,\text{T}_1) + \text{R}_1\text{R}_2\text{CHOH} + \text{O}_2(\text{T}_0,\text{S}_1) \qquad (3)$$

The yields of excited states were determined from the initial chemiluminescence emission from solutions 0.01–0.03 M in alkyl hydroperoxide[3] and *tert*-butyl hyponitrite initiator (BHN), by titration with 2-*tert*-butyl-9,10-dibromoanthracene (tDBA) (physical trap):

$$\text{R}_1\text{R}_2\text{C}{=}\text{O}(\text{T}_1) + \text{tDBA}(\text{S}_0) \rightarrow\rightarrow \text{R}_1\text{R}_2\text{C}{=}\text{O}(\text{S}_0) + \text{tDBA}(\text{S}_1) \qquad (4a)$$

$$\rightarrow \text{R}_1\text{R}_2\text{C}{=}\text{O}(\text{S}_0) + \text{tDBA}(\text{T}_1,\text{S}_0) \qquad (4b)$$

$$\text{tDBA}(\text{S}_1) \rightarrow \text{tDBA}(\text{S}_0) + h\nu \qquad (5)$$

Plots of 1/[tDBA] vs 1/(chemiluminescence intensity) were obtained, from which the product of the rate of energy transfer to fluorescer and the carbonyl excited-state lifetime, $k_{et}\tau$, and the relative yields of excited carbonyl species were calculated from the slope and intercept ($1/I_\infty$) by well-established procedures.[4]

For each carbonyl product, values of Φ_{TS}, defined as the ratio $k_{4a}/(k_{4a} + k_{4b})$, were independently obtained by analysis of the double-exponential decay curves of tDBA fluorescence, obtained by the single photon counting method following pulse excitation of degassed solutions of tDBA and the carbonyl compound.[5] The resulting values, along with current and corrected data from previous studies, appear in Table I. The lifetime of triplet benzaldehyde in *t*-BuPh was too short to obtain Φ_{TS}, and solutions of formaldehyde in organic solvents are too unstable to make reliable measurements.[6]

The values of $k_{et}\tau$ correspond to excited-state lifetimes on the order of 100 ns, consistent with triplet lifetimes in aerated solutions.

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* Author to whom correspondence should be addressed. This work was presented at the symposium in honor of Frank Mayo, 198th Meeting of the American Chemical Society, Miami Beach, FL, Sept 1989.

[1] This work taken in part from the Masters Thesis of X. C. Sheng, Michigan Technological University, 1990.

[2] Niu, Q.; Mendenhall, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 1656–7. Niu, Q.; Mendenhall, G. D. *J. Am. Chem. Soc.*, manuscript in press.

[3] Free-radical initiation with BHN in air-saturated ethylbenzene afforded PhCHMeOO$^{\bullet}$ radicals directly (Table I).

[4] Wilson, T.; Golan, D. E.; Harris, M. S.; Baumstark, A. L. *J. Am. Chem. Soc.* **1976**, *98*, 1086–91 and references therein.

[5] Catalani, L. H.; Wilson, T. *J. Am. Chem. Soc.* **1987**, *109*, 7458–62.

[6] Walker, J. F. *Formaldehyde*; 3rd ed.; Reinhold: New York, 1964; p 52.

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