competitive alkali-metal cation solvent extractions. A further increase in ring size to the 15-crown-4 derivative **9** produced a much lower selectivity for lithium extraction.

The outstanding lithium selectivity obtained with the lipophilic 14-crown-4 carboxylic acids **7** and **8** encourages the application of these and closely related complexing agents for the recovery of lithium from natural sources and waste streams.

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A New Pyridine Synthesis

T. Ross Kelly* and Hshiou-ting Liu

Department of Chemistry, Boston College
Chestnut Hill, Massachusetts 02167
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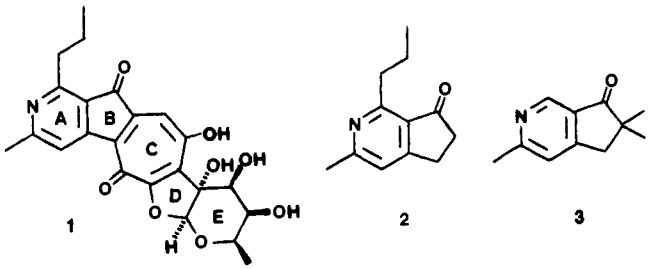
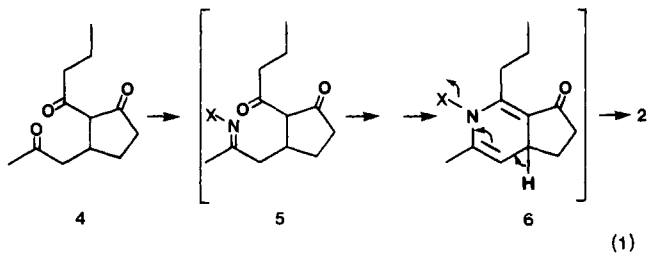
In conjunction with a projected synthesis of the unusual red pigment rubrolone (**1**),[1] we had need of an expeditious route to



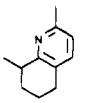
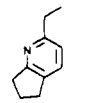
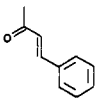
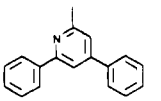
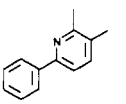
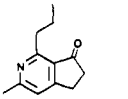
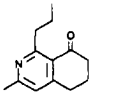
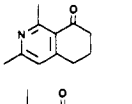
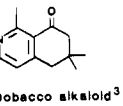
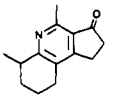
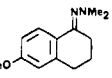
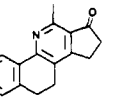
the AB unit **2**. Examination of the literature[2] revealed that available methods would require a lengthy synthesis: the reported[3] synthesis of **3**, which was the compound most structurally related to **2** then known, requires seven[4] steps. We now describe a conceptually new, highly convergent method of pyridine synthesis which not only affords **2** in a *one-pot* operation but also provides general and simple access to a diverse spectrum of complex pyridines.

The method results from an amalgamation of classical pyridine synthesis with new enolate technologies. As applied to **2**, the classical Knoevenagel[2,5] route would first require construction of the triketone **4** followed by reaction with hydroxylamine and cyclization. Formation of the pyridine ring in this fashion would presumably[6a] proceed along the general mechanistic lines shown in eq 1 (X = OH), the driving force being elimination of water



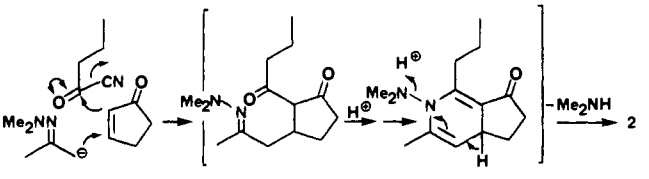
(1)

Table I

	Hydrazone[15]	Enone	Acylating Agent	Pyridine	Yield[a] (mp)
1	 11	 12	—		82
2			—		65
3			—		38 (71-72°)
4		 13[16]	—		55
5					31 (56-57°)
6	 14	 15			14
7					14 (93-94°)
8		 16[17]		 Burley tobacco alkaloid[3]	16
9					45 (125-126°)
10	 17				23 (189-190°)

[a] Isolated overall yield (based on enone) of chromatographically pure material.

from **6** with generation of an aromatic system. Conventionally, X is an OH group, but in principle any moiety capable of functioning as a leaving group should suffice. Therefore, generation of any compound equivalent to **5** should serve to set the stage for pyridine ring formation. In practice, as illustrated for the preparation of **2**, this can be achieved as shown in eq 2.



(2)

Thus conjugate addition of the cuprate[7] derived from the anion of acetone dimethylhydrazone to cyclopentenone followed first

(1) Palleroni, N. J.; Reichelt, K. E.; Mueller, D.; Epps, R.; Tabenkin, B.; Bull, D. N.; Schüep, W.; Berger, J. *J. Antibiotics* **1978**, *31*, 1218-1225. Schüep, W.; Blount, J. F.; Williams, T. H.; Stempel, A. *Ibid.* **1978**, *31*, 1226-1232.

(2) For reviews, see: (a) Brody, F.; Ruby, P. R. In "Pyridine and its Derivatives"; Klingsberg, E., Ed.; Interscience: New York, 1960; pp 99-589. (b) Boodman, N. S.; Hawthorne, J. O.; Masciantonio, P. X.; Simon, A. W. In "Pyridine and Its Derivatives: Supplement, Part One"; Abramovitch, R. A., Ed.; Wiley: New York, 1974; pp 183-308. For a more recent survey, see: Jones, G. In "Comprehensive Heterocyclic Chemistry"; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 2 (Boulton, A. J., McKillop, A., Eds.), Chapter 2.08.

(3) Demole, E.; Demole, C. *Helv. Chem. Acta* **1975**, *58*, 523-531.

(4) From 5,5-dimethylcyclopent-2-enone.

(5) Knoevenagel, E. *Justus Liebigs Ann. Chem.* **1894**, *281*, 25-126.

(6) See ref 2a: (a) p 279; (b) p 274.

(7) The conjugate addition of dimethylhydrazone enolate derivatives to enones (including **11** + **12** and **14** + **15**) has been reported as part of a synthesis of 1,5-diketones: (a) Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1362-1383. (b) Gawley, R. E.; Termine, E. J.; Aube, J. *Tetrahedron Lett.* **1980**, *21*, 3115-3119. (c) See also: Corey, E. J.; Boger, D. L. *Ibid.* **1978**, 4597-4600.

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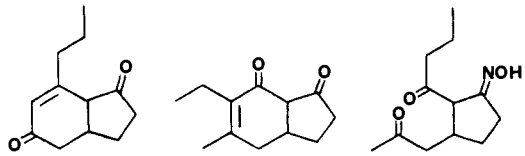
by trapping of the resulting enolate with butyryl cyanide[8,9] and then cyclization with glacial acetic acid gives **2**.

The scope of the method is evident from the entries in Table I. While the yields are not uniformly high,[10] this deficiency is more than offset by the facility with which a high degree of complexity can be straightforwardly assembled from quite simple starting materials. In particular, the method provides a means for assembling on a pyridine nucleus up to five different substituents in one operation with full regiochemical control. We note also that the regiospecific incorporation of the dimethylhydrazone unit as in **7** serves to avoid a number of competing[6b] side reactions (such as those leading to or passing through **8-10**)



8 **9** **10**

which could be anticipated to beset a synthesis of **2** proceeding via **4**. As is apparent from the first four entries in Table I, trapping of the initial Michael adduct with an acylating agent is optional, depending on the structure of the target molecule. A representative experimental procedure is provided.[11]

Acknowledgment. Support of this work by the National Institutes of Health (Grant GM30696) is gratefully acknowledged. We thank Dr. A. S. Magee and M. C. Connelly for ancillary studies, Professor R. E. Gawley[7] for sharing information, and Professor G. Stork for suggesting the use of acyl cyanides.[9]

Registry No. 2, 97235-08-0; **7**, 97235-13-7; $Me_2C{=}NNMe_2$, 13483-31-3; $MeC(O)CH{=}CH_2$, 78-94-4; $EtC(O)CH{=}CH_2$, 1629-58-9; $MeC(O)CH{=}CHPh$, 122-57-6; $MeC(O)C(CH_3){=}CH_2$, 814-78-8; $PrC(O)CN$, 38576-58-8; $MeC(O)CN$, 631-57-2; 2-methylcyclohexanone dimethylhydrazone, 5758-08-7; cyclopentanone dimethylhydrazone, 14090-60-9; acetophenone dimethylhydrazone, 13466-32-5; 2-cyclopentenone, 930-30-3; 6-methoxy-1,2,3,4-tetrahydronaphthan-1-one dimethylhydrazone, 16388-08-2; 2-cyclohexenone, 930-68-7; 5,5-dimethyl-2-cyclohexenone, 4694-17-1; 2,8-dimethyl-5,6,7,8-tetrahydroquinoline, 75031-41-3; 6,7-dihydro-2-ethyl-5*H*-1-pyrindine, 30564-54-6; 2,4-diphenyl-6-methylpyridine, 1912-16-9; 2,3-dimethyl-6-phenylpyridine, 27068-61-7; 1-propyl-3-methyl-8-oxoisoquinoline, 97235-09-1; 1,3-dimethyl-8-oxoisoquinoline, 97235-10-4; 1,3,6,6-tetramethyl-8-oxoisoquinoline, 55713-38-7; 4,6-dimethyl-2,3,6,7,8,9-hexahydro-1*H*-cyclopenta[*c*]quinolin-3-one, 97235-11-5; 2-methoxy-6-methyl-10,11-dihydro-9*H*-benzo[*h*]cyclopenta[*c*]quinolin-7-one, 97235-12-6; 2-(2-oxobutyl)-6-methylcyclohexanone dimethylhydrazone, 58911-64-1; 2-(3-oxopentyl)cyclopentanone dimethylhydrazone, 97235-14-8; 2,6-dioxo-5,6-diphenylhexane dimethylhydrazone, 97235-15-9; 2,6-dioxo-3-methyl-6-phenylhexane dimethylhydrazone, 97235-16-0; 2-butanoyl-3-(2-oxopropyl)cyclohexanone dimethylhydrazone, 97235-17-1; 2-acetyl-3-(2-oxopropyl)cyclohexanone dimethylhydrazone, 97235-18-2; 2-acetyl-3-(2-oxopropyl)-5,5-dimethylcyclohexanone dimethylhydrazone, 97235-19-3; 2-methyl-6-(2-acetylcyclopentanon-3-yl)cyclohexanone, 97235-20-6; 2-(2-acetylcyclopentanon-3-yl)-6-methoxy-1-naphthalenone dimethylhydrazone, 97235-21-7.

(8) Normant, J. F.; Piechucki, C. *Bull. Soc. Chim. Fr.* **1972**, 2402-2403.

(9) Use of butyryl chloride gave O-acylation. For the use of acyl cyanides to circumvent this problem, see: Howard, A. S.; Meerholz, C. A.; Michael, J. P. *Tetrahedron Lett.* **1979**, 1339-1340 and references therein.

(10) In general the yield-limiting step is the ring closure (e.g., **7** → **2**). We believe this is partly due to the tautomeric composition of the diketone intermediate (e.g., **7**).

(11) Preparation of **2**:[12a] To a solution of 6.50 g (65.0 mmol) of acetone dimethylhydrazone in 130 mL of THF under Ar at −78 °C (Neslab cryocool) was added over ca. 40 min 68.2 mmol of *n*-butyllithium (~2.5 M in hexane). After stirring at −78 °C for another 30 min the milky white suspension was added dropwise over 20-30 min via cannula[12a] to a −78 °C solution of 11.2 g (65 mmol) of PhSCu[12b,13] in 180 mL of THF. The mixture was stirred at −78 to −65 °C until (ca. 3 h) a *clear* orange-red solution formed. To this was added over 30 min at −78 °C a solution of 4.2 mL (50 mmol) of cyclopent-2-enone in 15 mL of THF. The reaction was stirred at −70 °C for 12 h, gradually warmed to 0 °C over 8 h, and recooled to −78 °C. A precooled (−78 °C) solution of 6.3 mL (65 mmol) of butyryl cyanide[8] in 30 mL of THF was then added rapidly via cannula. After 0.5 h the cooling bath was removed and the reaction was allowed to warm to room temperature. Solvent and volatiles were removed under vacuum and the residue was suspended in 275 mL of glacial HOAc and heated at reflux for 4 h. The reaction was cooled to room temperature and solid material filtered off and washed with 10% HCl. The filtrate and wash were neutralized at 0 °C with 3 N NaOH, made basic with saturated aqueous $NaHCO_3$ and extracted 5× with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give 10.4 g of a brown oil. Flash chromatography (45:55:3 EtOAc/petroleum ether/Et_3N) gave **2** in 31% overall yield based on cyclopentenone.

(12) (a) See ref 7b for experimental caveats. (b) In entries 2-4, 6-8, and 10 in Table I the homocuprate (from CuI and Me_2S) was used (see: Heathcock, C. H.; Kleinman, E. F.; Binkley, E. S. *J. Am. Chem. Soc.* **1982**, *104*, 1054-1068).

(13) Posner, G. H.; Brunelle, D. J.; Sinoway, L. *Synthesis* **1974**, 662-663.

(14) All new compounds gave satisfactory combustion analyses and spectra consistent with the structure assigned.

(15) For general method of preparation, see: Wiley, R. H.; Slaymayer, S. C.; Kraus H. *J. Org. Chem.* **1957**, *22*, 204-207. See also: Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1337-1361. To simplify purification **14** was prepared in the absence of solvent; **17** was separated from unreacted tetralone by precipitation of its hydrochloride salt from ether.

(16) Cook, K. L.; Waring, A. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 529-537.

(17) Dauben, W. G.; Shaffer, G. W.; Vietmeyer, N. D. *J. Org. Chem.* **1968**, *33*, 4060-4069.

Synthesis of *sec*-Alkylacetylenes. Reduction of Cobalt Carbonyl Complexes of Acetylenic Alcohols

Kenneth M. Nicholas*[1a]

Department of Chemistry, Boston College
Chestnut Hill, Massachusetts 02167

Jay Siegel*[1b]

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

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Due to competition from elimination reactions, standard acetylene coupling methods are inefficient for the synthesis of secondary alkylacetylenes. Other methods for the preparation of such acetylenes suffer either from poor product yields or inconvenient large-scale preparations.[2] We present here a facile route to secondary alkylacetylenes on a preparative scale through the reduction of the corresponding cobalt complexed α-acetylenic alcohols with sodium borohydride and trifluoroacetic acid in dichloromethane.[3] This method, which takes advantage of the remarkable stability of propargyldicobalt hexacarbonyl cations,[4] is shown to be useful in the preparation of general building block acetylenes (e.g., diisopropylacetylene) as well as those of specific synthetic interest (e.g., 17-deoxy-17-ethynyl steroids).[7] Furthermore this procedure is readily adapted to allow incorporation of deuterium α to an acetylenic unit, the resulting products being

(1) (a) Fellow of the Alfred P. Sloan Foundation, 1980-1984. Present address: University of Oklahoma, Norman, OK 73019. (b) Present address: University of California, San Diego, La Jolla, CA 92093.

(2) For excellent critiques of existing acetylene syntheses, see: Iverson, D. J. Ph.D. Dissertation, Princeton University, Princeton, NJ, 1981. Viehe, H. G. "Chemistry of Acetylenes"; Marcel Dekker: New York, 1969.

(3) Precedence for this method can be found in the report by Gribble et al. that benzyl alcohols that form stable carbenium ions[4] can be reduced with $NaBH_4$ in neat TFA.[5]

(4) Previously it has been shown that $Co_2(CO)_6{\cdot}R_2C(OH)C{\equiv}CC(OH)R_2$ complexes yield stable α-cations while retaining the integrity of the triple bond.[6]

(5) Gribble, G. W.; Leese, R. M.; Evans, B. E. *Synthesis* **1977**, 172.

(6) (a) Connor, R. E.; Nicholas, K. M. *J. Organomet. Chem.* **1977**, *125*, C45. (b) Nicholas, K. M.; Pettit, R. *J. Organomet. Chem.* **1972**, *44*, C21. (c) Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1977**, 3475.

(7) (a) Van Dijck, L. A.; Lankwerden, B. J.; Vermeer, J. G. C. M. *Recl. Trav. Chim. Pays-Bas* **1977**, *96*, 200. (b) Krubiner, A. M.; Gottfried, N.; Oliveto, E. P. *J. Org. Chem.* **1969**, *34*, 3502.

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