# Communications

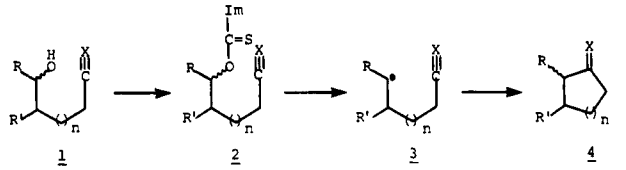
## Synthesis of Ketones by Cyclization of Cyano and Acetylenic Radicals: Use of δ-Hydroxy Nitriles and δ- or ε-Hydroxy Acetylenes

*Summary:* The radical intermediates generated by deoxygenation of alcohols undergo intramolecular ring closure when suitably located triple bonds (C≡C or C≡N) are present; the reaction provides a new synthesis of bicyclic ketones from either monocyclic ketones or cyclic olefins.

*Sir:* Cyclization of ω-acetylenic radicals has not been widely studied[1] although the corresponding process for *olefinic* radicals is extensively documented in the mechanistic literature[2] and is beginning to see use in preparative chemistry.[3,4] The synthetic applications of ω-acetylenic radicals to generate carbocycles[5] have not been properly recognized and only a few examples are known.[5d,6] We report that secondary alcohols **1** (X = C, $n$ = 1, 2; X = N, $n$ = 1) can be converted into cyclic ketones (or their synthetic equivalent) by acylation to the thiocarbonylimidazolide[7] **2** followed by deoxygenation with a tin hydride, **2** → **4**. The intermediate carbon radical **3** is trapped[8] by 5-exo or 6-exo ring closure[9] to produce **4**, which is convertible into a ketone ($n$ = 1, 2) by oxidative cleavage (for X = C) or by hydrolysis (for X = N; $n$ = 1) (Scheme I).

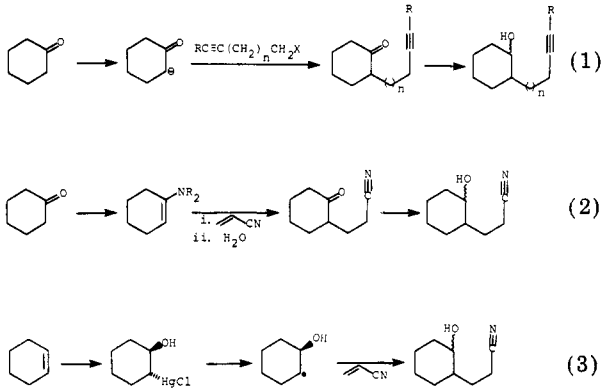
Use of a hydroxyl group (see **1**) to provide the radical **3** was based[10] on the expectation that such a choice would

Scheme I (Im = imidazolyl)



**1** **2** **3** **4**

be a convenient one because several synthetic routes such as those that use alkylation methodology (eq 1) or Michael



(1)

(2)

(3)

addition processes (eq 2[11] and 3[12]) would be available. In the event, the alkylation route (eq 1) was suitable for preparation (62% yield) of **6a** (see Scheme II) by treatment of *N*-cyclohexylidenecyclohexanamine with EtMgBr[13] and 1-phenyl-5-iodopent-1-yne,[14] followed by reduction (LiAlH$_4$). Attempts to use homopropargylic halides (cf. eq 1, $n$ = 1, R = $C_5H_{11}$) led to dehydrohalogenation of the reagent. However, the Michael addition sequence (eq 2) was generally applicable (see Scheme II, **8a**, **10a**, **11a**, **12a**). In each case the starting ketone was converted into its pyrrolidine enamine and treated with acrylonitrile (refluxing dioxane, 12 h). The resulting δ-keto nitrile was reduced (NaBH$_4$, THF), and the crude alcohol was acylated directly by treatment with thiocarbonyldiimidazole (2 equiv, refluxing $CH_2Cl_2$, 19 h).

The cyclization was performed by injecting benzene solutions (0.07–0.1 M) of $Ph_3SnH$ (1.2 equiv) and of azobis(isobutyronitrile) (0.003 M, 0.05 equiv) over 15 h into a refluxing solution (0.015 M) of the thionocarbamate in the same solvent. At the end of the addition refluxing was arbitrarily continued for 5 h. In the case of nitrile cyclizations the crude reaction product was stirred for 1 h in 80% v/v AcOH–$H_2O$ to hydrolize the initially formed imine.

Our results (see Scheme II) show that cyclization of *internal* acetylenes can proceed in good yield, but for the preparation of bicyclic compounds, only ε-hydroxy acety-

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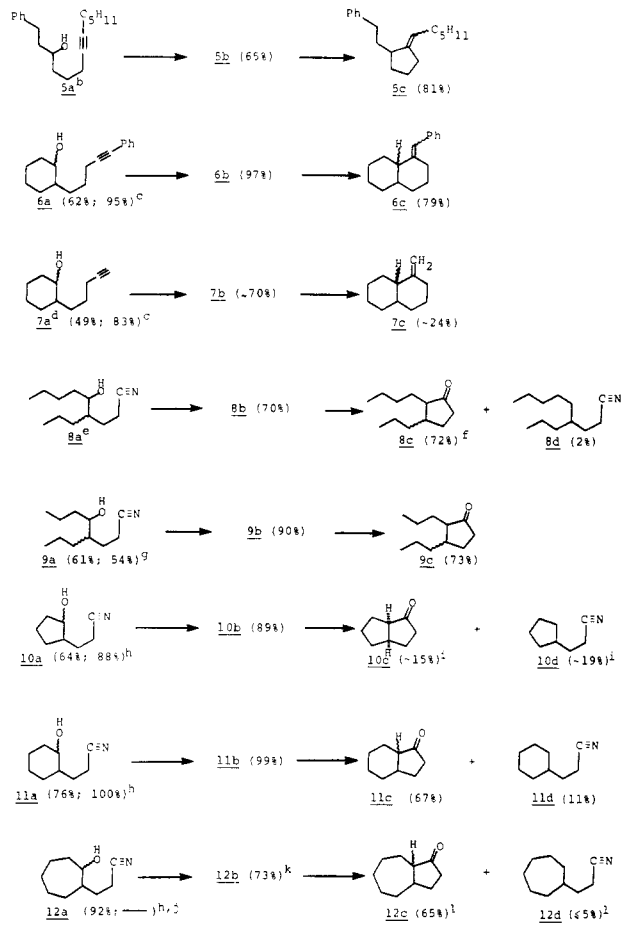
Scheme II[a]



[a] Yields refer to isolated material unless otherwise stated. The intermediate compounds **5b-12b** are the thiocarbonylimidazolides (cf. Scheme 1) corresponding to the alcohols **5a-12a**. Stereochemistries for **5c-9c, 11c** and **12c** were not established. [b] Prepared by Grignard reaction ($PhCH_2CH_2Br/Mg$) with undec-6-ynal [Svirskaya, P. I.; Leznoff, C. C.; Weatherston, J.; Laing, J. E. *J. Chem. Eng. Data* **1979**, *24*, 152.] Yield from undec-6-ynol, 59%. [c] First yield refers to alkylation of *N*-cyclohexylidenecyclohexanamine; second yield to carbonyl reduction ($LiAlH_4$). [d] Prepared by route analogoue to that used (see text) for **6a**. [e] The preparation of **8a** from the pyrrolidine enamine of 5-nonanone proceeded in poor yield: acyclic hydroxynitriles are better made from olefins: see ref 12 and Scheme II, **9a**. [f] >95% of one isomer. **8c** and **8d** were not separated; combined yield 74%; individual yields calculated by GLC. [g] First yield refers to hydroxymercuration product from (*Z*)-oct-4-ene (see ref 12); second yield refers to alkylation with acrylonitrile. [h] First yield refers to alkylation using a pyrrolidine enamine (cf. eq 2); second yield refers to carbonyl reduction ($NaBH_4$; THF or, for **8a**, 95% EtOH). [i] **10c** and **10d** were not separated: combined yield 39%; individual yields calculated by GLC. [j] The keto nitrile was processed directly to thiocarbonylimidazolide without purification of the intermediate alcohol. [k] Overall yield from keto nitrile. [l] **12c** and **12d** were not separated: combined yield 77%; individual yields calculated by GLC.

lenes (such as **6a**) are easily made by enolate alkylation (eq 1). Suitable hydroxy nitriles are readily accessible by the method of eq 2 and are also available[12] from olefins (eq 3; Scheme II, **9a**), so that the cyclization process constitutes a method for the potentially valuable transformation summarized in eq 4 ($n \geq 1$).

(4)

Reactions corresponding to eq 1 and Scheme I but involving hydroxy *olefins* are also feasible[8,15] and we have studied several examples. In such trigonal cyclizations functionality is destroyed; in contrast, the 5- and 6-exodigonal ring closures (Scheme I) provide compounds readily convertible into cyclic ketones and offer, therefore, numerous possibilities for further manipulations based on carbonyl chemistry.[16]

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**Registry No.** **5a**, 88854-20-0; **5b**, 88854-21-1; **5c**, 88854-22-2; **6a**, 88854-23-3; **6b**, 88854-24-4; **6c**, 88854-25-5; **7a**, 88854-26-6; **7b**, 88854-27-7; **7c**, 57662-70-1; **8a**, 88854-28-8; **8b**, 88854-29-9; **8c**, 88854-30-2; **9a**, 88854-31-3; **9b**, 88854-32-4; **9c**, 88854-33-5; **10a**, 88904-01-2; **10b**, 88867-01-0; **10c**, 32405-37-1; **10d**, 1123-04-2; **11a**, 21197-34-2; **11b**, 88854-34-6; **11c**, 29927-85-3; **11d**, 41010-09-7; **12a**, 88854-35-7; **12b**, 88854-36-8; **12c**, 10407-30-4; **12d**, 4448-80-0; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; 1-(1-pyrrolidinyl)cyclopentene, 7148-07-4; 1-(1-pyrrolidinyl)cyclohexene, 1125-99-1; 1-(1-pyrrolidinyl)-cycloheptene, 14092-11-6; *N*-cyclohexylidenecyclohexanamine, 10468-40-3; 1-phenyl-5-iodopent-1-yne, 34886-50-5; thiocarbonyldiimidazole, 6160-65-2.

**Supplementary Material Available:** Experimental and spectroscopic details for compounds **9a-c** (3 pages). Ordering information is given on any current masthead page.

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(18) In part.

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## Efficient One-Step Synthesis of a Cis Vicinal Tertiary Diamine and Its Complexation to a Lithium Carbanion Salt

*Summary:* *cis*-*N,N,N′,N′*-Tetramethyl-1,2-diaminopentane, obtained by reductive ($NaBH_4$) amination of 2-(dimethylamino)cyclopentanone, forms a 1:1 complex with the tight ion pair of a peralkylcyclohexadienyllithium salt.

*Sir:* The unique efficacy of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), compared to ethers, tertiary amines, and even 1,3-tertiary diamines, in catalyzing the metalation and addition reactions of alkyllithium compound[1] has been ascribed to its predilection to form five-membered bidentate chelates with lithium.[2]

One might imagine that a truly cis vicinal tertiary diamine would form strong complexes with organolithium compounds and spectacularly increase their reactivities.

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