sulfurization as described above produced dienol **2** (>70% overall yield from **3**) uncontaminated by over-reduced or isomerized materials.[17] Conversion of **2**, *via* the corresponding allylic bromide, to $C_{17}$ juvenile hormone B or to a number of physiologically active insect juvenile hormone analogs C, can be readily accomplished in satisfactory yields.

**Acknowledgments.** The authors wish to acknowledge support of this research from the Research Corporation and The University of Texas Research Institute. The principal investigator also wishes to express his personal thanks to Dr. J. F. Biellmann for several most pertinent and informative discussions and to Dr. Karl Dahm and Dr. J. B. Siddall for authentic samples and glc data requisite for final identification of our synthetic alcohols. And, finally, the principal investigator thanks earlier coworkers, Dr. S. A. Roman, Dr. V. M. Kobal, and Mr. L. Cain, for their contributions to related studies of sulfur heterocycles.

[17] A mixture of **2** and its three geometric isomers was provided for comparison (nmr and glc) by Dr. John B. Siddall, Director of Research, Zoecon Corporation.

[18] University of Texas Postdoctoral Fellow, 1972.

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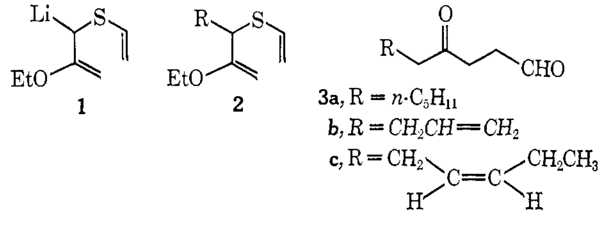
## A New Route to γ-Ketoaldehydes. Application to the Synthesis of *cis*-Jasmone

*Sir:*

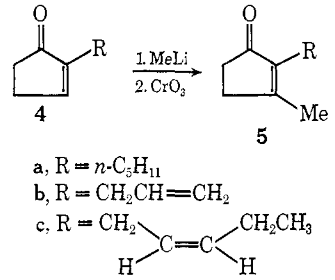
The chain extension of alkyl halides by (1-vinylthio)-allyllithium has previously been applied to the simple synthesis of trans γ,δ-unsaturated aldehydes, including the key intermediate for the naturally occurring sex attractant of propylure.[1] It has now been found that this alkylation–thio-Claisen rearrangement process is also highly effective for the formation of γ-ketoaldehydes, an important class of organic substances for which there exists only a limited synthetic methodology.[2]

Addition of *sec*-butyllithium[1] (1.10 equiv in pentane) to the THF solution of 2-ethoxyallyl vinyl sulfide (1.20 equiv), bp 67° (16 mm),[3,4] under nitrogen at −78° produces the straw yellow solution of the anion **1**, which is stable at this temperature. This anion was alkylated immediately at −78° upon the addition of *n*-amyl bromide (1.00 equiv) to produce high yields of the corresponding sulfide **2** (R = $n$-$C_5H_{11}$). The crude sulfide thus obtained after extractive work-up is suitable for the thio-Claisen rearrangement, which is carried out by dissolving in DME–water (3:1) and heating at reflux for 12 hr[1] to afford, after preparative layer chromatography (plc) on silica gel, the desired 4-oxodecanal (**3a**)[5] in 66% over-all yield. The complete scheme is therefore a two-step operation requiring no purification of intermediates. In a similar experiment, allyl bromide and 1-bromo-*cis*-2-pentene gave the corresponding γ-ketoaldehyde **3b** (70% over-all yield) and **3c** (56% over-all yield), respectively.



The efficiency of this synthetic process depends in part on the fact that the ethoxyl group in **2** does not interfere with the subsequent thio-Claisen rearrangement step,[6] and moreover the hydrolysis of vinyl ether is achieved after rearrangement.[7]

The anion **1** has been shown to serve effectively as an equivalent of the unknown enolate anion, $LiCH_2C({=}O)CH_2CH_2CHO$, and the γ-ketoaldehyde units thus obtained are valuable intermediates for further elaboration into furan, pyrrole, and 2-cyclopentenone derivatives. As an example, we have carried out a simple synthesis of *cis*-jasmone from **3c**. The base catalyzed cyclization of **3c** (10% NaOH in methanol–water (1:1)) at 25° for 2 hr produced the cyclopentenone derivative **4c**[8,9] in 60% yield. Transformation of this cyclopentenone **4c** to *cis*-jasmone (**5c**)[8,10] followed the recorded procedure.[9] By a similar sequence we were able to convert the γ-ketoaldehydes **3a** and **3b** to **4a**[11] (71%) and **4b**[12] (71%), respectively, which in turn were



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[1] K. Oshima, H. Takahashi, H. Yamamoto, and H. Nozaki, *J. Amer. Chem. Soc.*, **95**, 2693 (1973).

[2] Recently a variety of new synthetic methods for the preparation of 1,4-diketone has been developed; see (a) G. Stork and R. Borch, *ibid.*, **86**, 935 (1964); (b) G. Büchi and H. Wüest, *J. Org. Chem.*, **31**, 977 (1966); (c) E. J. Corey and L. S. Hegedus, *J. Amer. Chem. Soc.*, **91**, 4926 (1969); (d) E. Wenkert, R. A. Mueller, E. J. Reardon, Jr., S. S. Sathe, D. J. Scharf, and G. Tosi, *ibid.*, **92**, 7428 (1970); (e) J. E. McMurry and J. Melton, *ibid.*, **93**, 5309 (1971); (f) T. Mukaiyama, K. Narasaka, and M. Furusato, *ibid.*, **94**, 8641 (1972).

[3] This sulfide was prepared by the sequence 2-ethoxy-2-propen-1-ol [W. Grell and H. Mchleidt, *Justus Liebigs Ann. Chem.*, **699**, 53 (1966)] → 3-bromo-2-ethoxypropene (*n*-butyllithium–methanesulfonyl chloride–lithium bromide in ether: E. J. Corey, H. Yamamoto, D. K. Herron, and K. Achiwa, *J. Amer. Chem. Soc.*, **92**, 6635 (1970)) → 2-ethoxyallyl vinyl sulfide (lithium ethenethiolate in liquid ammonia: L. Brandsma, P. J. W. Schuijl, *Recl. Trav. Chim. Pays-Bas*, **88**, 513 (1969)) (30% over-all yield after distillation). Nmr ($CCl_4$, TMS) δ 1.30 (t, 3 H, *J* = 7.5 Hz), 3.23 (s, 2 H), 3.25 (q, 2 H, *J* = 7.5 Hz), 3.94 and 4.08 (2 d, 1 H each, *J* = 2 Hz), 5.08 (d, 1 H, *J* = 16 Hz), 5.13 (d, 1 H, *J* = 9 Hz), 6.32 (dd, 1 H, *J* = 9 and 16 Hz).

[4] All new compounds encountered in this work were characterized spectrometrically and analytically.

[5] Mass *m/e* 170 ($M^+$); ir (neat) 2735, 1735 (sh, CHO), 1710 $cm^{-1}$ (C=O of ketone); nmr ($CCl_4$, TMS) δ 9.80 (1 H, CHO); homogeneous by tlc assay ($R_f$ 0.30; $SiO_2$–$CH_2Cl_2$).

[6] Recently the Claisen rearrangement of 2-ethoxyallyl ester was reported: R. E. Ireland and R. H. Mueller, *J. Amer. Chem. Soc.*, **94**, 5897 (1972).

[7] α-Vinylthioketone was not detected in the crude reaction mixture after the rearrangement procedure.

[8] Identical in all respects with reported spectrometric data.

[9] (a) G. Büchi and B. Egger, *J. Org. Chem.*, **36**, 2021 (1971); (b) P. A. Grieco, *ibid.*, 37, 2363 (1972).

[10] For references to other syntheses, see (a) ref 9b; (b) H. C. Ho, T.-L. Ho, and C. M. Wong, *Can. J. Chem.*, 50, 2718 (1972).

[11] Mass *m/e* 152 ($M^+$); ir (neat) 1703 (C=O), 1634 $cm^{-1}$ (C=C); nmr ($CCl_4$, TMS) δ 7.19 (bs, 1 H, olefinic proton); homogeneous by tlc.

[12] Mass *m/e* 122 ($M^+$); ir (neat) 1700 (C=O), 1640 (C=C), 1000 and 910 $cm^{-1}$ (terminal olefin); nmr ($CCl_4$, TMS) δ 7.20 (bs, 1 H, olefinic proton); homogeneous by tlc.

transformed to dihydrojasmone (**5a**)[2f,8,9b,13] and allylrethrone (**5b**),[8,14] respectively.

We are currently studying further improvements in the synthetic method here outlined as well as a number of other, quite different approaches to 2-cyclopentenone derivatives.

**Acknowledgment.** We thank Dr. Kiitiro Utimoto for helpful discussions.

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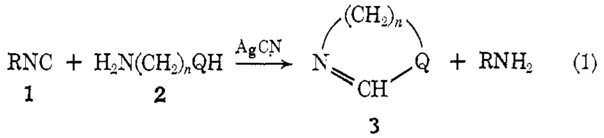
## Synthetic Reactions by Complex Catalysts. XXXI. A Novel and Versatile Method of Heterocycle Synthesis

*Sir:*

To date, the preparation of cyclic imidates (**3**, Q = oxygen) which are unsubstituted in the 2 position has been done with some difficulty. Especially, to our best knowledge, the synthetic method of a six-membered cyclic imidate, 5,6-dihydro-4*H*-1,3-oxazine, has not been known. Now, we wish to report a new general method for the synthesis of heterocycles which include 2-oxazoline[1] and dihydro-1,3-oxazine as well as 2-imidazoline,[2] tetrahydro-2-pyrimidine,[2] and 2-thiazoline.[3] The synthesis is readily accomplished by a single-step reaction of isonitrile (**1**) with amino alcohol, with diamine, or with aminothiol in the presence of a small amount of silver cyanide. The reactions are expressed by the following general equation.

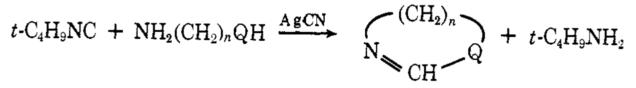


$$\underset{\mathbf{1}}{\mathrm{RNC}} + \underset{\mathbf{2}}{\mathrm{H_2N(CH_2)_nQH}} \xrightarrow{\mathrm{AgCN}} \underset{\mathbf{3}}{\mathrm{N{=}CH{-}Q(CH_2)_n}} + \mathrm{RNH_2} \quad (1)$$

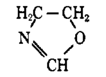
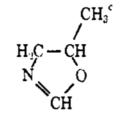
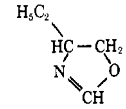
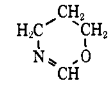
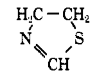
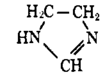
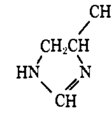
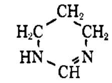
(Q = O, NH, S)

The efficiency and generality of the reaction coupled with the ready availability of the starting materials render it very useful in the preparation of heterocycles containing the –N=CHQ– unit. A typical experimental procedure is illustrated by the reaction of $\gamma$-aminopropanol with *tert*-butyl isocyanide in the presence of silver cyanide leading to the formation of 5,6-dihydro-4*H*-1,3-oxazine. A mixture of 1.5 g (20 mmol) of $\gamma$-aminopropanol, 1.7 g (20 mmol) of *tert*-butyl isocyanide, and 0.13 g (1 mmol) of silver cyanide was heated at 90° for 12 hr with stirring under nitrogen. The reaction mixture was subjected to distillation directly. 5,6-Dihydro-4*H*-1,3-oxazine, bp 85° (70 mm), was obtained in 66% yield (ir (neat) 1650 cm$^{-1}$ ($\nu_{C=N}$), 1150 ($\nu_{C-O}$); nmr (CDCl$_3$) $\tau$ 8.18 (m, 2 H), 6.72 (t, 2 H), 5.87 (t, 2 H), 3.15 (s, 1 H)). As a by-product, *tert*-butylamine (bp 45°) derived from the isonitrile component was isolated and identified. Some results are summarized in Table I. Spectral data and elemental analyses supported the assigned structures of all products. The nmr of all cyclic products exhibited a singlet in the region of $\tau$ 2–3 which is characteristic of a –N=CHQ– unit. Cuprous chloride can also be employed as a catalyst which is, however, less effective than silver cyanide.

**Table I.** Preparation of Heterocycles by the Reactions of Isonitrile with Amino Alcohol, Diamine, and Aminothiol



$$t\text{-}\mathrm{C_4H_9NC} + \mathrm{NH_2(CH_2)_nQH} \xrightarrow{\mathrm{AgCN}} \mathrm{N{=}CH{-}Q(CH_2)_n} + t\text{-}\mathrm{C_4H_9NH_2}$$

| $NH_2(CH_2)_nQH$ | Reaction[a,b] Temp, °C | Reaction[a,b] Time, hr | Product (%) |
|---|---|---|---|
| $NH_2CH_2CH_2OH$ | 90 | 13 |  (67) |
| $NH_2CH_2CH(CH_3)OH$ | 90 | 13 |  (72) |
| $NH_2CH(C_2H_5)CH_2OH$ | 90 | 12 |  (63) |
| $NH_2CH_2CH_2CH_2OH$ | 90 | 12 |  (66) |
| $NH_2CH_2CH_2SH$ | 90 | 19 |  (88) |
| $NH_2CH_2CH_2NH_2$ | 90 | 11 |  (80) |
| $NH_2CH_2CH(CH_3)NH_2$ | 90 | 23 |  (80) |
| $NH_2CH_2CH_2CH_2NH_2$ | 90 | 15 |  (94) |

[a] Reaction: $NH_2(CH_2)_nQH$ 20 mmol, isonitrile 20 mmol, and silver cyanide 1 mmol. [b] The optimum conditions have not been explored. [c] When cyclohexyl isocyanide was employed instead of *tert*-butyl isocyanide, the product of 5-methyl-2-oxazoline was produced in 70% yield.

The present reaction is also applied to *o*-aminophenol,[4] *o*-phenylenediamine,[5] and *o*-aminothiophenol,[4] resulting in the formation of benzoxazole (54%), benzimidazole (64%), and benzothiazole (93%), respectively.

The present synthesis of heterocycles is closely related to the formimidation reaction in which isonitrile is inserted into a heteroatom–hydrogen linkage of

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(3) H. Wenker, *J. Amer. Chem. Soc.*, **57**, 1079 (1935).

(4) G. L. Jenkins, A. M. Knevel, and S. S. Davis, *J. Org. Chem.*, **26**, 274 (1961).

(5) (a) E. C. Wagner and W. H. Millett, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 65; (b) E. C. Taylor and W. Ehrhart, *J. Amer. Chem. Soc.*, **82**, 3138 (1960).