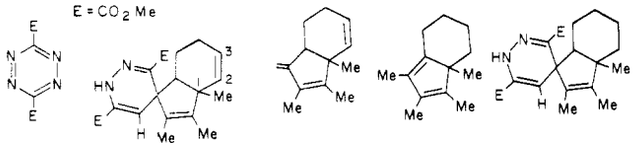
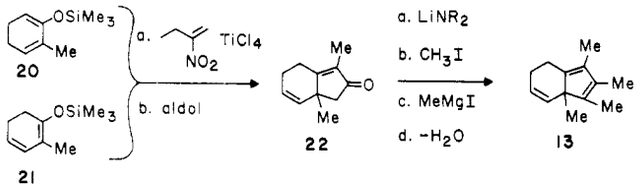
Preparative-scale flow pyrolysis[2] of **12** at 345 °C (0.04 Torr) led to partial conversion to a single product, X; more complex mixtures were obtained at higher temperatures. Product X was isolated by preparative GLC and found to show ^{1}H NMR, IR, and mass spectral data[12] consistent with either structure **13** or **14.** In order to define the structure of X, a crystalline adduct (mp 166–166.5 °C) was prepared by reaction (25 °C, 12 h, dichloromethane solution) with 3,6-dicarbomethoxytetrazine (**15**). Our expectation that the adduct arose via Diels–Alder reaction, with **15** as the diene component, followed by loss of dinitrogen[13] was supported by the elemental composition ($C_{19}H_{24}N_2O_4$), but was clearly inconsistent with the ^{1}H NMR spectrum of the adduct.[14] Therefore an X-ray diffraction study was undertaken.

Crystals formed in the triclinic space group $P\bar{1}$ with a = 8.085 (3), b = 10.326 (4), and c = 12.207 (5) Å, α = 109.83 (1), β = 88.53 (1), and δ = 109.70 (1)°, and one molecule of $C_{19}H_{24}O_4$ in the asymmetric unit. A total of 2379 unique intensity data ($2\theta \leq 114°$, Cu K_α radiation) were measured and 1530 (64%) were judged observed after correction for Lorentz, polarization, and background effects. Solution via a weighted, multiple solution sign determining procedure[15] and refinement[16] were uneventful. The final crystallographic residual is 0.095 for the observed reflections and metric details agree well with generally accepted values.[17] The structure of the adduct is **16.**



While **16** is formally the [4 + 2] adduct (loss of dinitrogen) of tetrazine **15** with the *exo*-methylene isomer (**17**), the actual mechanim of the formation of **16** is not clear. It is clear that the structural relationship between the isolated double bond (C_2–C_3) and the quaternary methyl group (at C_1) is the same in **13** and **16.** There remains the possibility, however, that the isolated double bond started out as in **14** and migrated to the observed position in **16** during reaction with the tetrazine. The fact that the saturated analogue[18] **18** reacts with tetrazine **15** in a precisely parallel way (to give **19**)[20] shows that the isolated double bond in **13** is not necessarily involved in this type of reaction.

Further evidence for the structure of X was provided by rational synthesis. Reaction of 2-methylcyclohex-2-en-1-one with chlorotrimethylsilane and triethylamine in dimethylformamide at reflux led to a mixture of sensitive products, tentatively characterized as enol ethers **20** and **21.** Reaction



of this mixture with 2-nitro-1-butene according to the method of Yoshikoshi,[19] followed by aldol condensation, led to a single distillable product (**22**) in low overall yield.[20] Methylation of the kinetic enolate anion of **22,** followed by addition of methylmagnesium bromide and spontaneous elimination of water, afforded a hydrocarbon identical[21] with the pyrolysis product (X = **13**).

We conclude that 1,5-vinyl shifts are favored over 1,5-alkyl migrations in the spirocycles, and that subsequent hydrogen shifts are not rate determining. It is now appropriate to focus on the central question: Why does the vinyl group migrate easily?[22]

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(12) ^{1}H NMR (90 MHz, CCl_4) δ 5.30–5.75 (m, 2 H), 2.00–2.80 (m, 4 H), 1.75 (s, 9 H), 0.95 (s, 3 H); IR 3010 (w), 2940 (m), 2900 (s), 2850 (m), 1630 (w); mass spectrum *m/e* 174.
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(17) Full experimental details can be found in ref 7.
(18) Compound **18** was prepared according to the general scheme shown for preparation of **13** (**20** + **21** → **22** → **13**) starting from 2-methyl-1-(trimethylsilyloxy)-1-cyclohexene; the general method and the specific first steps are reported.[19]
(19) M. Miyashita, T. Yanami, and A. Yoshikoshi, *J. Am. Chem. Soc.*, **98,** 4679 (1976).
(20) Compounds **13, 16, 18, 19,** and **22** showed ^{1}H NMR, IR, UV, and mass spectral data consistent with the proposed structures. Crystalline derivatives were prepared which gave either satisfactory microanalyses or exact mass spectra.
(21) Compound **13** prepared from **22** showed ^{1}H NMR and IR spectral data and GLC retention time identical with parallel measurements for **13** obtained from pyrolysis, and reacted with **15** to give **16.**
(22) We are pleased to acknowledge support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.
(23) Recipient of a Camille and Henry Dreyfus Teacher–Scholar Grant.
(24) Department of Chemistry, Cornell University, Ithaca, N.Y. 14853.

M. F. Semmelhack,*[23] H. N. Weller
Department of Chemistry, Cornell University, Ithaca, New York 14853

Jon Clardy[23,24]
Department of Chemistry, Iowa State University Ames, Iowa 50010
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Homologation–Alkylation of Carbonyl Compounds via Regiospecifically Generated Metallo Enamines

Summary: A novel and efficient synthetic strategy for effecting the geminal substitution at a carbonyl center has been

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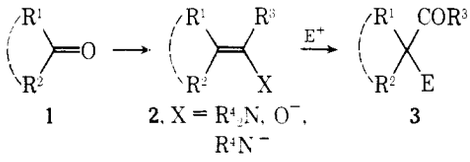
developed which features a one-pot procedure for the regiospecific conversion of carbonyl compounds into the metallo enamines of the homologous aldehydes or ketones via intermediate 2-aza dienes; subsequent trapping of these metallo enamines with a variety of electrophiles occurred with a high degree of regioselectivity.

Sir: The nucleophilic properties of enamines,[1] enolates,[2] and metallo enamines[3,4] have long played a commanding role in processes involving the formation of new carbon–carbon bonds by alkylation, hydroxyalkylation, and acylation reactions. Since most of the procedures for the generation of these important synthetic intermediates commence with the corresponding aldehyde, ketone, or a suitable derivative thereof, the use of these nucleophiles in organic synthesis is restricted by the availability of the parent carbonyl compound. Unfortunately, the requisite carbonyl compounds are not always readily accessible, and therefore the development of an efficient procedure for the regioselective construction of enamines, enolates, or metallo enamines by the carbonyl olefination of less complex aldehydes or ketones, **1 → 2,** would constitute an important addition to the arsenal of synthetic reactions. If these carbonyl derivatives were subsequently treated in situ with assorted electrophiles, the α-substituted, homologous carbonyl compounds 3 would be produced. The combination



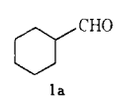
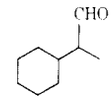
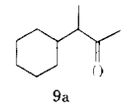
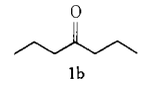
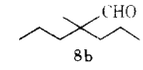
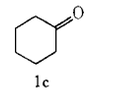
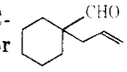
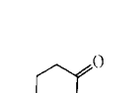
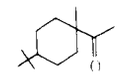
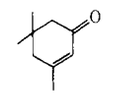
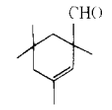
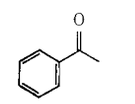
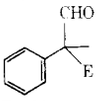
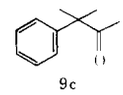
1 **2**, X = R^4_2N, O^-, R^4N^- **3**

of these two steps in tandem would result in a simple process for geminal substitution via a sequence that features the initial nucleophilic acylation[5] of a carbonyl compound, followed by the formation of an additional carbon–carbon or a carbon–heteroatom bond at the original electrophilic center.

In accordance with this general strategy, we have recently described an approach to geminal alkylation in which ketones were converted directly into the enamines of the homologous aldehydes, **1 → 2** (R^3 = H; X = R^4_2N).[6-8] The subsequent reaction of these enamines with a variety of electrophiles, including allyl bromide,[6] methyl vinyl ketone,[7] and 2,3-dibromopropene,[8] resulted in several effective procedures for the formation of quaternary carbon centers.[9] Enamines are, however, relatively weak nucleophiles which may also suffer irreversible N-alkylation, and thus there are some inherent limitations in the above methods which may attenuate their general application in organic synthesis. On the other hand, since metallo enamines exhibit a high reactivity toward electrophiles coupled with a low propensity to suffer proton transfer, they are frequently superior to both enamines and enolates for the introduction of new substituents α to a carbonyl group. In order to circumvent the limitations attendant to our previous procedures for the geminal alkylation of a carbonyl group involving enamines as the key intermediates,[6-8] we initiated a search for an efficient means of transforming aldehydes or ketones into metallo enamines by carbonyl homologation operations.[10] As a result of these investigations, we have discovered a facile, one-pot procedure for the homologation–alkylation of carbonyl compounds via metallo enamine intermediates, **1 → 2** (X = R^4N^-) **→ 3.**

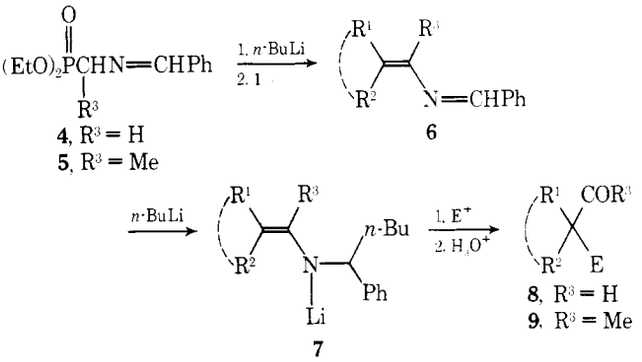
This new strategy for carbonyl homologation with α substitution (Scheme I) was based upon the prediction that the 2-aza dienes **6** would react smoothly with organometallic reagents such as *n*-butyllithium to give the metallo enamines **7.**[11] The synthesis of the requisite 2-aza dienes **6** (R^3 = H) was easily achieved by allowing diethyl lithio-*N*-benzylideneaminomethylphosphonate, prepared by metalation of **4**[12]

Table I. Homologation–Alkylation of Carbonyl Compounds 1

carbonyl compd	phosphonate	electrophile	product	overall yield, %[a]
 **1a**	**4**	MeI	 **8a**	43
1a	**5**	MeI	 **9a**	41
 **1b**	**4**	MeI	 **8b**	58
 **1c**	**4**	CH_2=C-HCH_2Br	 **8c**	51
 **1d**	**4**	MeI	 **8d**, E = Me[b]	63
		CH_2=C-HCH_2Br	**8e**, E = CH_2CH=CH_2[b]	51
		$(MeS)_2$	**8f**, E = SMe	40
1d	**5**	MeI	 **9b**	60
 **1e**	**4**	MeI	 **8g**	80
 **1f**	**4**	MeI	 **8h**, E = Me	77
		CH_2=C-HCH_2Br	**8i**, E = CH_2CH=CH_2	81
1f	**5**	MeI	 **9c**	63

[a] Yields are of distilled product, but have not been optimized. [b] Obtained as a mixture of diastereomers.

Scheme I



4, R^3 = H
5, R^3 = Me

6

7

8, R^3 = H
9, R^3 = Me

with *n*-butyllithium, to react with aldehydes or ketones **1.**[13] Although the 2-aza dienes **6** (R^3 = H) could be isolated, it was more convenient and efficient to treat them in situ with *n*-butyllithium at −78 °C, thereby generating the metallo enamines **7** (R^3 = H). Subsequent addition of various electrophiles such as methyl iodide, allyl bromide, or methyl disulfide

followed by aqueous acid completed the synthetic sequence, affording the aldehydes 8 (E = Me, CH_2=$CHCH_2$, and MeS, respectively) in generally good to very good overall yields (Table I).[14]

An important variant of the above method entails the use of homologous *N*-benzylideneaminoalkylphosphonates such as **5**.[15] For example, treatment of cyclohexanecarboxaldehyde (**1a**) with the anion obtained by metalation of **5**, followed by the sequential addition of *n*-butyllithium, methyl iodide, and then aqueous acid cleanly produced the methylated ketone **9a**. Since the methyl ketone **9a** appeared to be formed exclusively, the generation and trapping of the metallo enamines **7** (R^3 = Me) occurred with a high degree of regioselectivity. The attainment of a similar degree of regiocontrol in the production of metallo enamines such as **7** (R^3 = alkyl) by the simple deprotonation of the corresponding ketimines is not generally feasible. Thus, by appropriately varying the carbonyl precursor and the alkyl substituent on the phosphonates **4** (R^3 = alkyl), it should now be possible to effect the regioselective generation and trapping of *either* of the two possible metallo enamines of an unsymmetrical, acyclic ketone.

The efficiency and particular ease with which the entire reaction sequence may be executed in one pot is illustrated by the following general procedure. A solution of diethyl *N*-benzylideneaminomethylphosphonate (**4**)[12] (12.0 mmol) in anhydrous THF (5 mL) was added to a stirred solution of *n*-butyllithium (12.0 mmol, 3.3 N hexane) in anhydrous THF (50 mL) at −78 °C. After 1 h, a solution of the carbonyl compound **1** (10.0 mmol) in anhydrous THF (5 mL) was added, and the reaction mixture was allowed to warm to room temperature. After heating the reaction at reflux for 3 h, the solution of 2-aza diene was cooled to −78 °C, whereupon *n*-butyllithium (20.0 mmol, 3.3 N hexane) was added. The reaction mixture was stirred at −78 °C for 1 h, the resulting metallo enamine was treated with the appropriate electrophilic reagent (50.0 mmol), and the mixture was then allowed to warm to room temperature. Following the hydrolysis of the intermediate imine with 1 N hydrochloric acid (2 h at room temperature), extractive workup afforded the crude product **8** or **9**, which was purified by vacuum distillation.

As clearly evidenced by the entries in Table I, this new synthetic strategy for the efficient homologation–alkylation of the carbonyl function via metallo enamines, some of which were heretofore inaccessible, is applicable to a variety of carbonyl compounds and alkylating agents. Furthermore, these intermediate metallo enamines may also be sulfenylated to give β-oxo sulfides, which are known precursors of, inter alia, α,β-unsaturated carbonyl compounds[16] and 1,2-dicarbonyl compounds.[17] The applications of this procedure for geminal substitution to other synthetic transformations, including annelation operations and directed aldol processes, are under active investigation and will be reported independently. The feasibility of extending this methodology to the enantioselective construction of quaternary carbon centers is also being examined.

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Supplementary Material Available: Characterization of all new compounds together with representative experimental details (3 pages). Ordering information is given on any current masthead page.

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Stephen F. Martin,* Gerald W. Phillips
Department of Chemistry
The University of Texas at Austin
Austin, Texas 78712
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Deprotonations with Potassium Diisopropylamide–Lithium *tert*-Butoxide. Alkylation of 1-(Phenylseleno)alkenes and Bis(phenylseleno) Acetals[1]

Summary: A readily prepared, nonnucleophilic, strongly basic mixture of potassium diisopropylamide–lithium *tert*-butoxide (KDA) rapidly deprotonates both 1-(phenylseleno)alkenes (**1**) and bis(phenylseleno) acetals (**3**); in contrast, neither lithium diisopropylamide nor potassium bis(trimethylsilyl)-amide were able to deprotonate these compounds at a perceptible rate. The deprotonation–alkylation of both **1** and **3** is described.

Sir: Nonnucleophilic, strong bases such as lithium diisopropylamide (LDA) have been of invaluable utility in organic chemistry.[2] Although the *rate* of deprotonation of weakly acidic compounds may be changed by several orders of magnitude simply by altering the cation accompanying the amide

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