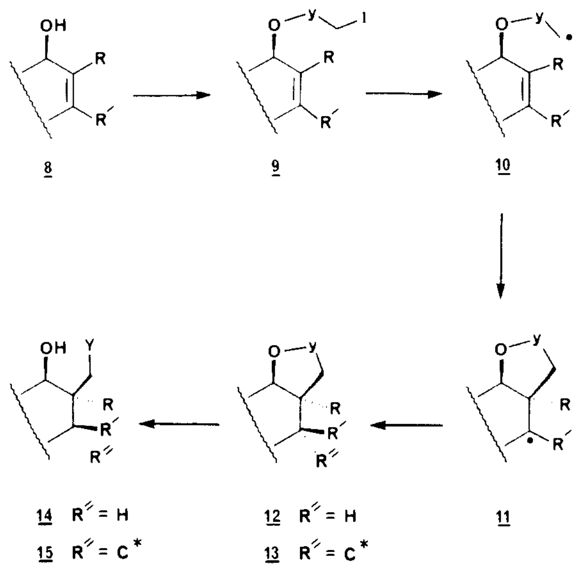
previously described cyano compound **6** in 60% yield.[12] An analogous procedure could be used with a variety of electrophilic olefin traps (10 equiv).[13] Acrylonitrile, methyl acrylate, ethyl vinyl ketone,[14] diethyl vinylphosphonate, methyl vinyl sulfone, and phenyl vinyl sulfone thus gave 55–75% yields of the trapped cyclized products **7**, Z = CN, CO_2Me, COEt, $PO(OEt)_2$, SO_2Me, and SO_2Ph, respectively.[15,16]

We conclude by noting that the cyclization–trapping process forms the final link in a general scheme which, starting with an allylic alcohol system (**8**), controls the structural problems attending formation of two adjacent chiral centers (**8** → **14** or **15** with y = temporary oxygen connection, Y = liberated functionality derived from y, e.g., y = CH(OEt), CMe(OMe),[17] or $SiMe_2$[2c] and Y = CHO, COMe, or OH, respectively). The control of regio- and stereochemistry derives from two factors: (1) The cyclization step (**10** → **11**) achieves regio- and stereospecific attachment of the operational equivalent of a functional carbon or a functional chain, CH_2Y, at the proximal end of the double bond and cis to the controlling allylic oxygen. (2) At the distal position, the cup shape of the cis-fused bicyclic radical intermediate **11** leads to trans delivery with respect to the controlling oxygen, either of a hydrogen (**11** → **12**) via simple radical cyclization or, as we report in this paper, of a functional carbon or a functional chain, C* (**11** → **13**).



8 9 10

14 R″ = H
15 R″ = C*
12 R″ = H
13 R″ = C*
11

The wealth of methods for establishing the required stereochemistry of the controlling hydroxyl, and the ease with which it could eventually be inverted or removed, should make this vicinal substitution scheme especially useful.

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[11] This consisted of addition of methylene chloride, vigorous shaking with 3% aqueous ammonia, addition of brine, separation of the organic phase, two further extractions with methylene chloride, drying, removal of methylene chloride and of *tert*-butyl alcohol (by azeotroping with benzene), and chromatography (silica; 10% ethyl acetate–petroleum ether).

[12] 8% of the easily separable epimeric cyano compound (and a small amount of **5**) was also formed in this reaction. Starting with the mixed iodo acetal from 2-cyclopentenol, the better defined cup shape of the bicyclic radical intermediate results in a 68% yield of the expected trans cyano product accompanied by only 2% of its epimer. Furthermore, trapping is equally successful at a tertiary radical center. Thus, the mixed iodo acetal of 3-methyl-2-cyclohexenol gives 62% of the expected trans cyano product and 5% of its epimer.

[13] In the case of electrophilic olefins, Giese's conditions[5] could be used, but the yields were at least as good, and in some cases much better, under our conditions. Under Giese's conditions, hydride reduction of the radical trap and conjugate addition of ethanol to the radical trap were problems observed in some cases.

[14] In this case, the solvent was THF, initiation was by photolysis (254 nm; quartz) at room temperature for 10 h, and 0.2 equiv of Bu_3SnCl was used.

[15] The products **7** were adequately characterized by spectral means after workup and purification as for **6**. Variable amounts of simple cyclization product **5** and of telomers were generally produced in addition of the desired products.

[16] It appears that electron-deficient olefins respond to stearic bias similarly to *tert*-butyl isocyanide. For instance, using acrylonitrile as the radical trap, **7**, Z = CN, is produced in 70% yield accompanied by 8% of its epimer.

[17] A procedure similar to that of ref 9 appears satisfactory for the synthesis of mixed iodo ketals: from 2-cyanohexenol and 2-methoxypropene we obtained a >90% yield of mixed iodo ketal which was then successfully submitted to cyclization-trapping.

Deprotonation of Chelating Enamines. Direct Formation of β-Lithio Enamines

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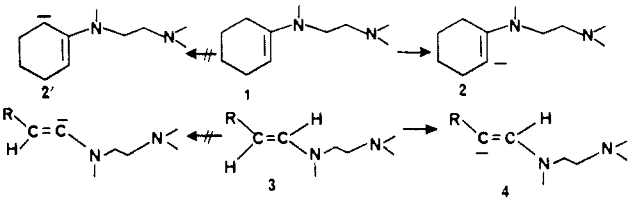
We report here that deprotonation of the chelating enamine **1** derived from cyclohexanone and *N,N,N′*-trimethylethylenediamine leads to complete formation of the *vinyl* carbanion **2** rather than of the expected[1] *allyl* carbanion **2′**. We further report the equally surprising result that chelating enamines (derived from aldehydes unbranched at the α-position) in which the competition now involves removal of either the α- or the *β-vinyl* hydrogen (**3**) lead to β-(**4**) rather than the expected α-deprotonation.[2]



2′ 1 2

3 4

These results are in striking contrast with the observations that chelation-mediated deprotonation of the related **5**[3] gives the anticipated allyl anion and that deprotonation of the simple vinylamine **6** (in the presence of tetramethylethylenediamine) takes place at the α position (arrows),[4] the normal result of deprotonation of heterosubstituted ethylenes.[5]

5 6

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[1] Morton, A. A.; Finnegan, R. A. *J. Polym. Sci.* **1959**, *38*, 19. Broaddus, C. D.; Much, D. L. *J. Am. Chem. Soc.* **1967**, *89*, 6533. Crawford, R. J.; Erman, W. F.; Broaddus, C. D. *J. Am. Chem. Soc.* **1972**, *94*, 4298. Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1976**, *59*, 453. The greater stability of the allylic vs. the vinyl carbanion is well established: See, inter alia: Dessy, R. E.; Kitching, W.; Psarras, T.; Salinger, R.; Chen, A.; Chivers, T. *J. Am. Chem. Soc.* **1966**, *88*, 460. Butin, K. P. Beletskaya, I. P.; Kashin, A. N.; Reutov, O. A. *J. Organomet. Chem.* **1967**, *10*, 197. Shatenshtein, A. I. *Adv. Phys. Org. Chem.* **1963**, *1*, 155.

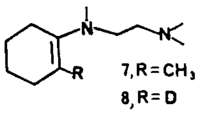
[2] Varying amounts of β-deprotonation competition with α-deprotonation have been reported with enol ethers as early as 1952: Paul, R.; Tchelitcheff, S. Bull. Soc. Chim. Fr. **1952**, 208. See also: Soderquist, J. A.; Hsu, G. J. H. *Organometallics* **1982**, *1*, 830. Less obviously relevant cases include preferential β- vs. γ-deprotonation in certain vinyl ethers: McDougal, P. G.; Rico, J. R. *Tetrahedron Lett.* **1984**, *25*, 5977. For preferential α-deprotonation vs. allylic deprotonation in enol ethers, see: Rossi, A. R.; Reuillard, B. D.; Gould, S. J. *Tetrahedron Lett.* **1978**, 4357. For an interesting case involving vinyl vs. allyl deprotonation in an allyl alcohol system, see: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315.

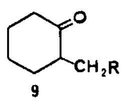
[3] Beak, P.; Kempf, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 4550.

[4] Bates, R. B.; Beavers, W. A.; Blacksberg, I. R. *Abstr. Pap.—Am. Chem. Soc.* **1975**, *169th*. See also: Schmidt, R. R.; Talbiersky, J.; Russeger, P. *Tetrahedron Lett.* **1979**, 4273 and papers cited therein.

[5] Special structural features can result in allylic γ-deprotonation of certain types of enamines related to **1** and to **3**: Ahlbrecht, H. *Chimia* **1977**, *31*, 391. Thompson, H. W.; Huegi, B. S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1603.

The use of chelating enamines, such as **1** and **3**,[6] suggested itself[7,8] after we failed to deprotonate the pyrrolidine enamine of cyclohexanone with *tert*-butyllithium, even in the presence of hexamethylphosphoramide (HMPA). In fact, treatment of enamine **1** (0.2 M in pentane or hexane) with 1.1 equiv of *tert*-butyllithium (8 h at room temperature) led to quantitative deprotonation. Addition of an equal volume of THF and 1.2 equiv of methyl iodide (0 °C), followed by hydrolysis (CH_3OH; aqueous HCl or $CuSO_4$; room temperature) gave ~95% yield of 2-methylcyclohexanone (**9**, R = H). This is, of course, the same product that would be obtained from either anion **2** or **2′**. The proof that the unexpected **2** is actually the correct structure came from examination of the methylated enamine **7** itself: MS (CI, methane), *m/e* 197 (M + 1); bp (Kugelrohr) 90 °C (2 mm); NMR 1.65 (3 H, s, $C{=}CCH_3$; no vinyl hydrogen); IR 1675 cm^{-1}. Similarly, deuteration of the enamine anion (3 equiv of D_2O, −40 °C) gave only **8**: no vinyl hydrogen in NMR; IR 2260 cm^{-1} ($C{=}C{-}D$), no absorption at 3060 cm^{-1} ($C{=}CH$).


7, R = CH$_3$
8, R = D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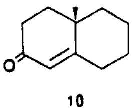
Final confirmation of structure **2** was obtained by X-ray analysis,[9] after we succeeded in isolating the lithium salt of the propanediamine analogue of **2** in a suitable crystalline form.

Deprotonation of the chelating dienamine obtained from the methyloctalone **10** gave, as with **1**, the vinyl anion **11** rather than the anion from allylic deprotonation. Alkylation of **11** then gave the alkylated enones **12** (R = methyl or *n*-decyl) in 75% yield. This constitutes a rather novel, albeit limited, solution to the problem of α-monoalkylation of certain α,β-unsaturated ketones.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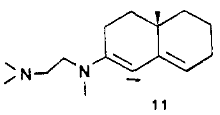
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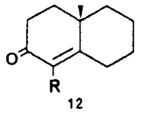
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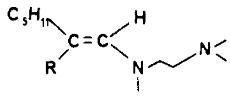
The structure of the β-lithio enamine derived from heptaldehyde **4** (R = C_5H_{11}) follows from the disappearance of the absorption at δ 4.15 of the parent enamine upon deuteration and also from alkylation with methyl iodide to give **13** (R = CH_3, 80% yield; NMR δ 1.63 (br s, $C{=}CCH_3$)) and with decyl iodide to give **13** (R = $C_{10}H_{21}$, 87% yield). These alkylated enamines were easily hydrolyzed to 2-methylheptanal and 2-pentyldodecanal, respectively.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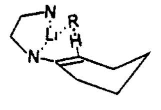
It seems very likely that these remarkable deprotonations of chelating enamines arise from geometric constraints in the relevant transition states. One intriguing possibility is that there may be a preferred collinear arrangement in the transition state for proton abstraction[10,11] by the alkyllithium. Since formation of the allylic anion would presumably require removal of a pseudoaxial hydrogen, correct positioning of the chelated *tert*-butyl carbanion would result in very considerable strain. No such strain is involved in the case of **15** because of the presence of one more atom between the vinyl carbon and the allylic hydrogen to be removed.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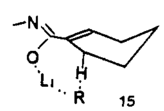
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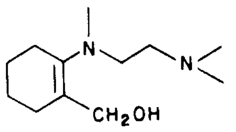
The β-selectivity observed in the deprotonation of **3** also could be a reflection of the somewhat looser transition state for the β- than for the α-proton removal which a collinearity requirement would imply. It is also possible that the chelated lithium may begin to bind to the enamine double bond[12] at the transition state, thus facilitating removal of the β-proton.

We end with a few observations on the chemistry of β-lithio enamines which extend earlier reports[13,14] on a class of anions originally made by halogen–lithium[13,15] or tin–lithium[14] exchange. Alkylation of lithio enamines such as **2** and **4** proceeds[16] in 80–95% yield with primary alkyl iodides. A reactive halide such as benzyl chloromethyl ether works well (90%) but benzyl halides are unsuitable under the usual conditions (e.g., dibenzyl is formed from benzyl bromide).[17] Benzyl and allyl halides, however, give satisfactory results in alkylation (70–85%) in the presence of 1 equiv of cuprous iodide[17] (−40 °C to room temperature). Acylation is also feasible: Treatment of **2** with benzoyl chloride and dimethylformamide gave (−78 °C; inverse addition) the benzoyl and formyl enamines in 90% and 78 yields, respectively, while methyl chloroformate and acetyl chloride (−100 °C; inverse addition) afford 2-carbomethoxy- (79%) and 2-acetylcyclohexanone (56%). Reaction of **2** and **4** with aldehydes gave directly (75% yield) the α,β-unsaturated carbonyl compounds arising from dehydration of the intermediate carbinols during usual workup. The reaction with formaldehyde is of interest because the resulting hydroxymethyl enamine **16** can further react with $RCu.BF_3$ reagents[18] and thus leads to 2-alkylcyclohexanones, e.g., **9**, R = butyl, and **9**, R = *tert*-butyl (76% and 54% yields, respectively).


16

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for the financial support of this work.

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[8] For a comprehensive review of chelation-controlled deprotonation, see: Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1.

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[10] For a recent discussion of preferred geometry in possibly related intramolecular proton abstractions by alkoxide ions, see: Menger, F. M.; Chow, J. F.; Kaiserman, H.; Vasquez, P. C. *J. Am. Chem. Soc.* **1983**, *105*, 4996. See also, inter alia: Gandour, R. D. *Tetrahedron Lett.* **1974**, 295. A collinear geometry has often been intuitively assumed. For a recent example: Meyer, F. K.; Pellerite, M. J.; Brauman, J. I. *Helv. Chim. Acta* **1981**, *64*, 1058.

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[13] Duhamel, L.; Poirier, J.-M. *J. Am. Chem. Soc.* **1977**, *99*, 8356; *Bull. Soc. Chim. Fr.* **1982**, II-297.

[14] Ficini, J.; Falou, S.; Touzin, A.-M.; d'Angelo, J. *Tetrahedron Lett.* **1977**, 3589.

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[16] Alkylation times varied from 5 (CH_3I) to 60 min. Isolation of the alkylated enamines themselves was achieved by filtration through a plug of grade V alumina, followed by rinsing with hexane, solvent removal, and distillation. Hydrolysis of the alkylation products from **11** was done with the usual[6] sodium acetate–acetic acid buffer. Identification of the various products was by spectral data and comparison with authentic compounds.

[17] Wollenberg, R. H.; Albizati, K. F.; Peries, R. *J. Am. Chem. Soc.* **1977**, *99*, 7365.

[18] Yamamoto, Y.; Maruyama, K. *J. Organomet. Chem.* **1978**, *156*, C9.