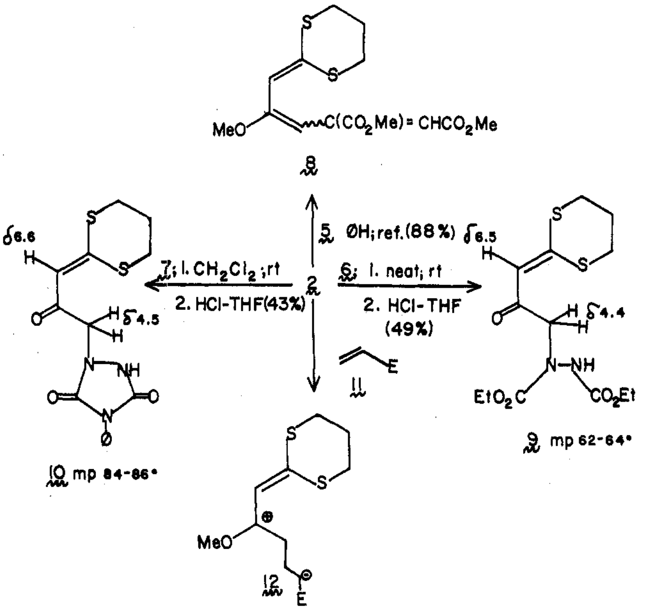
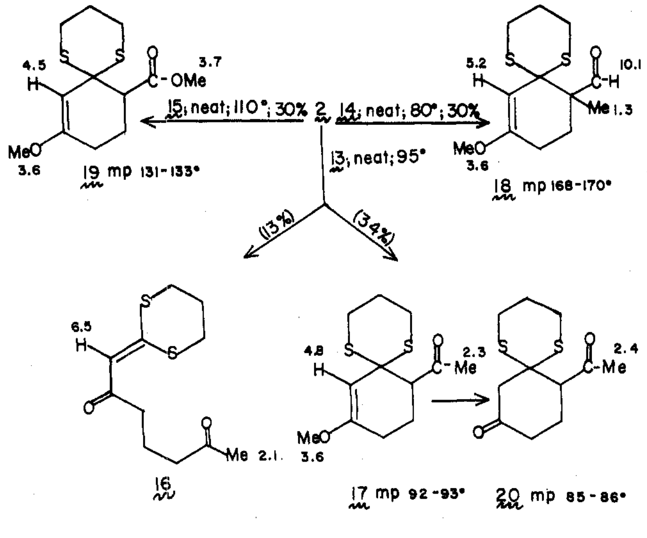
Scheme I



rangements in the alignment of the diene and the dienophile,[14] could be possible if the "electrophile" is of insufficient energy to react via a conjugate addition (one-bond) pathway. The latter process, while less entropically demanding, does, of course, require the sustenance of charged (or radical) intermediates.

While the reasoning advanced above must be regarded as conjectural, in practice *compound 2 does participate in Diels–Alder reactions with methyl vinyl ketone (13), methacrolein (14), and methyl acrylate (15).* In the case of the reaction of **2** + **13**, a 13% yield of Michael-type product **16** was obtained along with the cycloaddition compound, **17**. In the reactions of **14** and **15** no Michael products were detected, though the complexity of the reaction mixtures[13] rules out a definite statement in this regard. The structures of compounds **16–19**[9] are rigorously proven by their infrared, NMR, and mass spectra. Pertinent reaction conditions and yields, as well as diagnostically valuable NMR chemical shifts (as $\delta_{\mathrm{ppm}}^{\mathrm{CDCl_3}}$ from tetramethylsilane) are given in Scheme II. Though

Scheme II



of limited scope, diene **3** may be regarded as a synthetic equivalent of $^{+}C(O)CH_2C(O)C^{-}H_2$.[15] It will be noted that, in products **17**, **18**, and **19**, three carbonyl systems are produced in varying, but differentiated, states of exposure. While the synthetic value of such systems remains to be demonstrated, we note already that compound **17** reacts with aqueous HCl in THF, to give the specifically monoprotected 1,3,5 triketone **20** in 87% yield.

Studies involving the utilization of such systems as well as the exploration of new highly functionalized dienes are in progress and will be described in due course.

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Supplemental Material Available. Experimental procedures for these reactions (4 pages). Ordering information is given on any current masthead.

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(2) S. Danishefsky and T. Kitahara, *J. Org. Chem.*, **40**, 538 (1975).
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(4) F. A. Carey and A. J. Court, *J. Org. Chem.*, **37**, 4474 (1972).
(5) D. J. Peterson, *J. Org. Chem.*, **33**, 780 (1968).
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(7) (a) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 1926 (1972); (b) D. Seebach, B. Th. Gröbel, M. Braun, and K. H. Geiss, *Angew. Chem., Int. Ed. Engl.*, **11**, 443 (1972); (c) F. Jones and M. F. Lappert, *J. Chem. Soc., Chem. Commun.*, 526 (1972).
(8) The NMR spectrum indicates a few percent of impurity containing a trimethylsilyl group.
(9) The structure of this compound is in accord with its infrared, NMR, and high resolution mass spectra.
(10) D. Seebach, M. Kolb, and B.-Th. Gröbel, *Angew. Chem., Int. Ed. Engl.*, **12**, 69 (1973).
(11) (a) S. M. McElvain and E. L. Engelhardt, *J. Am. Chem. Soc.*, **66**, 1077 (1944); (b) S. M. McElvain, E. R. Degginger, and J. D. Behun, *ibid.*, **76**, 5736 (1954); (c) J. Banville, J. L. Grandmaison, G. Long, and P. Brassard, *Can. J. Chem.*, **52**, 80 (1974).
(12) R. C. Cookson, S. S. H. Gilani and I. D. R. Stevens, *Tetrahedron Lett.*, 615 (1962).
(13) Many of the reactions of compound **2** with electrophiles are characterized by the formation of intense colors and apparently high molecular weight products. The possibility of direct electron transfer from **2** to give cation and anion radical intermediates and extensive polymerization seems likely.
(14) For a recent discussion, see K. N. Houk, *Acc. Chem. Res.*, **8**, 371 (1975). We thank Professor Houk for a useful exchange of correspondence on our work.
(15) Compound **2** appears to be the first 3-oxygenated vinylketene equivalent for Diels–Alder reactions. For simple vinylketene equivalents in Diels–Alder reactions, see (a) E. J. Corey and A. P. Kozikowski, *Tetrahedron Lett.*, 2389 (1975); (b) E. Sonveaux and L. Ghosez, *J. Am. Chem. Soc.*, **95**, 5417 (1973).

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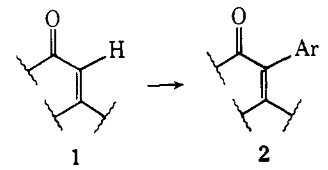
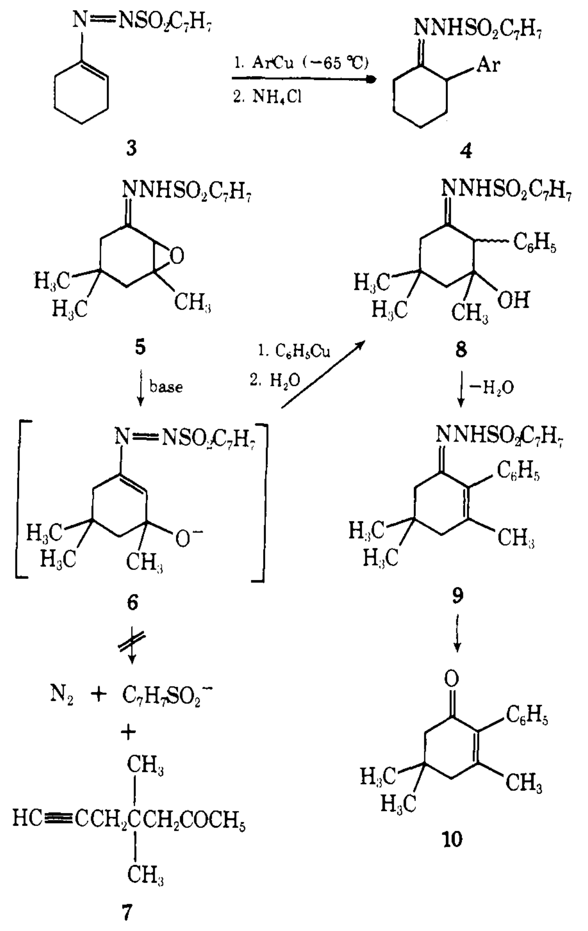
α-Arylation of α,β-Unsaturated Ketones. Utilization of the α-Epoxytosylhydrazone Functional Group as a Δ²-Enonium Synthon

Summary: The sequential reaction of α-epoxytosylhydrazones (easily available in two steps from α,β-unsaturated ketones) with *n*-butyllithium (1.0 equiv) followed by phenylcopper (1.2 equiv) yields α-aryl-β-hydroxytosylhydrazones which may be dehydrated and hydrolyzed to produce α-aryl α,β-unsaturated ketones.

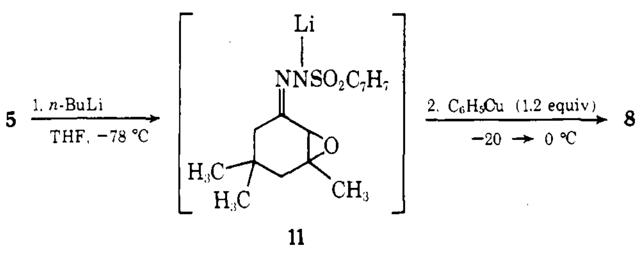
Sir: In connection with a synthetic project, we required methodology for the α-arylation of α,β-unsaturated ketones (**1** → **2**).[1,2]



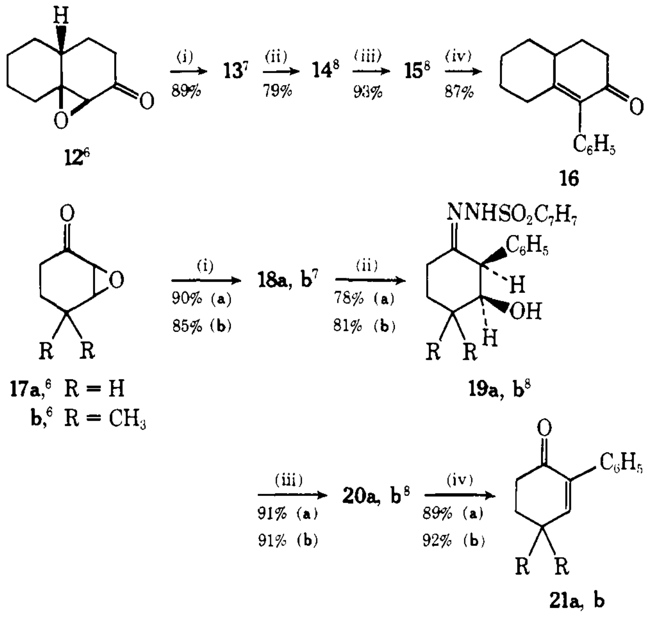
Our previous observation that the reaction of arylcopper reagents with tosylazoenes (**3**) resulted in a facile synthesis of α-aryltosylhydrazones (**4**) suggested a possible solution to this problem.[3] It is well known that the base- (and acid-) catalyzed fragmentation reaction of α-epoxytosylhydrazones (**5** → **7**) proceeds via an azoene intermediate (**6**);[4,5] therefore, if azoene intermediates could be generated *in the presence* of an arylcopper reagent, they should be smoothly intercepted to yield an α-aryl-β-hydroxytosylhydrazone (**8**). Dehydration (to **9**) and hydrolysis should, in turn, produce the desired enone **10**.



We are pleased to report that this is indeed the case. Reaction of isophorone oxide[6] with a suspension of tosylhydrazine (18 h, room temperature) in ether produces the insoluble crystaline α-epoxytosylhydrazone **5**[7] (95%). Addition of **5** to a tetrahydrofuran (THF) solution of phenylcopper (2.5 equiv, solubilized as its diisopropyl sulfide complex) at −20 °C, followed by warming to 0 °C (over 1.5 h), produces the α-phenyl-β-hydroxytosylhydrazone **8** (80%).[8] Since this procedure has the attendant disadvantage of being wasteful with respect to the phenylcopper reagent and since our eventual application demands the use of a more highly functionalized arylcopper species, we required an alternate procedure (see Experimental). α-Epoxytosylhydrazone **5** (THF, −78 °C) is treated with *n*-butyllithium (1.0 equiv, dipyridyl indicator[9]) to produce a solution of the α-epoxytosylhydrazone anion **11** (−78 °C). The soluble phenylcopper reagent is added to this solution (−78 °C) and the reaction is allowed to warm to 0 °C (−20 → 0 °C, 1.5 h)[10] in order to again produce the phenylated product **8** (85%). Dehydration of **8** (C_6H_6, reflux, 0.5 h) produces α,β-unsaturated tosylhydrazone **9**[8] (95%) which can be smoothly converted to enone **10**[11] (94%) via carbonyl exchange.[12,13]

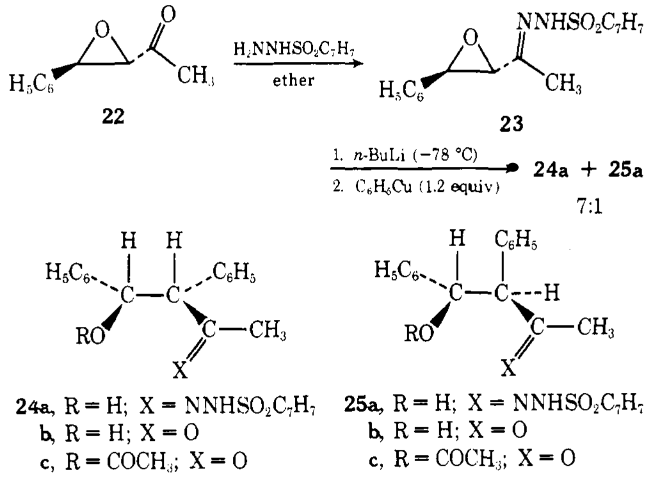


Epoxy ketones **12**, **17a**, and **17b** are also easily transformed to α-arylenones **16**, **21a**, and **21b** by application of the above methodology. The α-phenyl-β-hydroxytosylhydrazones (**8**, **14**, **19a**, **19b**) are all isolated as a single isomer in the four cases examined. Although the stereochemistry of **8** or **14** has not yet been established, **19a** and **19b** appear to have the hydroxyl and phenyl groups in a cis relationship ($J_{2,3}$ = 2.5 Hz).[14]



Reagents: (i) $H_2NNHSO_2C_7H_7$/ether; (ii) (1) *n*-BuLi (−78 °C), (2) C_6H_5Cu (1.2 equiv), −20 °C; (iii) C_6H_6, Δ; (iv) $BF_3 \cdot Et_2O$, H_2O, $(CH_3)_2CO$.

The chemistry of an acyclic example further documents the utility of this arylation reaction. Although acyclic α-epoxytosylhydrazones cannot be prepared in polar solvents owing to intramolecular pyrazoline formation,[7b] the conversion of **22** to **23**[7c] using ether/tosylhydrazine[7a] presents no difficulties

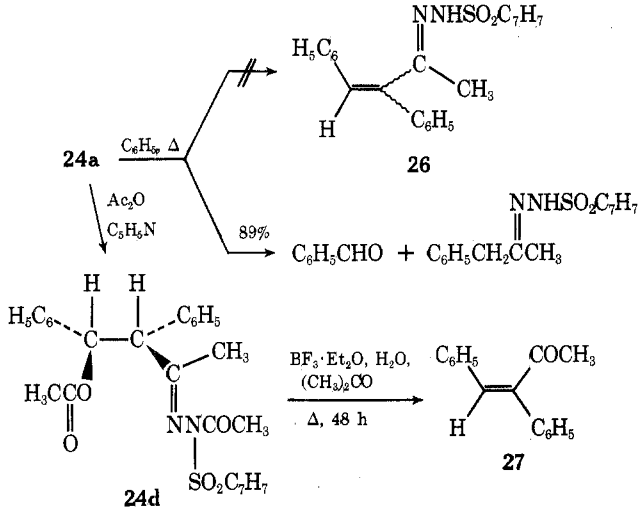


24a, R = H; X = $NNHSO_2C_7H_7$
b, R = H; X = O
c, R = $COCH_3$; X = O

25a, R = H; X = $NNHSO_2C_7H_7$
b, R = H; X = O
c, R = $COCH_3$; X = O

(85%). Sequential reaction of **23** with *n*-butyllithium and phenylcopper provides *erythro*-α-phenyl-β-hydroxytosylhydrazone (**24a**,[8] 60%). Hydrolysis[12] of **24a** provides *erythro*-β-hydroxy ketone **24b**[8,15] (60%), which can be converted to acetate **24c**[8] [$(CH_3CO)_2O/C_5H_5N$, 98%] for the purpose of spectral assignment.[16] The isomeric *threo*-tosylhydrazone **25a** has not been directly isolated from this reaction, but its presence (~10%[17]) has been inferred by isolation of *threo*-β-hydroxy ketone **25b**[8] (6%) by hydrolysis[12] and chromatography of the **24a** reaction residues (7% **24b** also isolated). This places the value of the **24a**:**25a** ratio for the phenylation reaction at ~7:1.

An additional complication exists with the acyclic example. Attempted dehydration of **24a** (C_6H_6, reflux, 6 h) produces no unsaturated tosylhydrazone (**26**), but, instead, **24a** undergoes retro-aldol reaction. This difficulty is overcome by conversion of **24a** to the bisacetyl derivative **27d**[7] ($(CH_3CO)_2O/C_5H_5N$, 98%) which, in turn, can be converted to the thermodynamically more stable enone **27** by a single-step hydrolysis–elimination reaction (80%).[18]



Although the primary goal of this investigation was to provide methodology for the α-arylation of α,β-unsaturated ketones, the α-aryl-β-hydroxytosylhydrazones and α,β-unsaturated tosylhydrazones produced via the azoene route should serve equally well as precursors for previously established tosylhydrazone transformations.[19]

Acknowledgment. I wish to thank Eli Lilly and Co. for a Young Faculty Grant.

Supplementary Material Available. General experimental, characterization information, and spectral data (1 page). Ordering information is given on any current masthead page.

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(6) Prepared from the corresponding enone by the method of R. L. Wasson and H. O. House, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 552.

(7) (a) This mild procedure appears to be generally applicable for the preparation of high-purity α-epoxytosylhydrazones in excellent yields. Difficulties associated with preparation of this compound class in polar solvents or in the presence of acid catalysts are well documented.[4,7b] α-Epoxytosylhydrazones are best kept in the freezer for extended storage. (b) A. Padwa, *J. Org. Chem.*, **30**, 1274 (1965). (c) Melting points (°C, all with decomposition, $-N_2$): **5**, 90–91; **12**, 86–87; **17a**, 117–118.5; **17b**, 89–90; **23**, 123–125.

(8) (a) This material exhibits spectra (ir, NMR) and analysis (CHNS or CH) in accord with its assigned structure. (b) Melting point and TLC R_f values for these compounds can be found in the microfilm version.

(9) S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967).

(10) The solution of anion **11** appears to be stable at temperatures below *ca.* −30 °C (TLC analysis). The temperature (−20 °C) at which the phenylation reaction proceeds appears to be the same temperature at which epoxide fragmentation occurs *in the absence of phenylcopper*. This observation is consistent with the epoxide fragmentation being the rate-determining step for the overall process. (Simpler azoenes are phenylated within 1 min at −65 °C[3].)

(11) (a) This material exhibits spectra (ir, NMR, mass) and analysis (exact mass) in accord with its assigned structure. (b) Melting points (°C): **2**, 86–87; **16**, 77–78; **21a**, 94–95 (lit.[11c] 94–95); **21b**, oil (lit.[11c] oil); **27**, 54–55 (lit.[11d] 55–556). (c) H. Born, R. Pappo, and J. Szmuszkovicz, *J. Chem. Soc.*, 1779 (1953). (d) H. E. Zimmerman, L. Singer, and B. S. Thyagarajan, *J. Am. Chem. Soc.*, **81**, 108 (1959).

(12) C. E. Sacks and P. L. Fuchs, *Synthesis*, in press.

(13) Direct hydrolysis[12] of **8** is less satisfactory. Several other minor uncharacterized products contaminate a mixture of β-hydroxy ketone and enone **10**.

(14) The Corey[1] and Stork[2] procedures give products of trans stereochemistry. The synthetic and mechanistic consequences of this observation are under further investigation.

(15) Benzaldehyde and phenylacetone (20–25% each) are also produced in this reaction.

(16) See supplimentary material for the spectral assignments.

(17) This estimation is based on the assumption that the hydrolysis reaction[12] is equally efficient (~60%) for both isomers.

(18) If this reaction is conducted for shorter periods of time or at a lower temperature, significant amounts (40–50%) of acetate **24c** may be isolated in addition to enone **27**.

(19) (a) For example, tosylhydrazones **9** and **15** serve as excellent substrates for the Dauben–Shapiro diene synthesis.[19b] Treatment of **9** and **15** (in THF, −78 °C) with lithium diisopropylamide[19c,d] (2.5 equv), followed by warming to room temperature (1.5 h), produces 2-phenyl-1,5,5-trimethyl-1,3-cyclohexadiene (90%) and 1-phenyl-4,4a,5,6,7,8-hexahydronaphthalene (85%), respectively. (b) W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *J. Am. Chem. Soc.*, **90**, 4762 (1968). (c) G. E. Gream, L. R. Smith, and J. Meinwald, *J. Org. Chem.*, **39**, 3461 (1974). (d) E. Vedejs and R. A. Shepherd, *J. Org. Chem.*, **41**, 742 (1976).

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α-Alkylation and Arylation of α,β-Unsaturated Ketones

Summary: The *N,N*-dimethylhydrazones of α,β-epoxy ketones react with aryl and alkyl Gringnard reagents to produce intermediates β-hydroxyhydrazones which are dehydrated to α-aryl or α-alkyl enones; the scheme represents a method for the introduction of alkyl and aryl groups on the α carbon of an α,β-unsaturated ketone.

Sir: The introduction of carbon substituents on the α carbon of an α,β-unsaturated ketone, with preservation of the α,β unsaturation (**1** → **2**), can often be carried out by formation of the thermodynamic enolate ion, followed by treatment with an alkyl halide.[1] The method is not applicable, however, inter alia, (a) when the α,β-unsaturated ketone is incapable of