with retention of configuration at the α-halo carbon followed by oxidation[8] would produce the *RR,SS* pair of alcohols. Migration with inversion of configuration on the other hand would produce the *RS,SR* pair of alcohols.[9]

Diethylborane was prepared in THF and added to the (*Z*)-vinyl iodide. After 1 h, base was added, the mixture oxidized and the alcohol isolated in 80% yield. Both VPC[10] and NMR[11] analysis indicated that a nearly 1:1 mixture of the diasteriomers had formed. In view of the stereoselectivity normally associated with organoborane reactions, this was a very surprising result. The reaction was then performed using diethylborane prepared from triethylborane and borane–methyl sulfide. An ~3:1 mixture was formed with the product of inversion of configuration predominating. Since the diethylborane contained only 0.3 mol of Me_2S, the reaction was repeated using 1 mol of Me_2S. Again a nearly 1:1 mixture of alcohols was obtained. The Me_2S was evidently causing loss of stereochemistry. Finally, when the vinyl iodide and diethylborane were carefully distilled to remove traces of THF or Me_2S and the reaction was run in the absence of solvent, a >99% selectivity for the product of inversion of configuration was obtained. The organoborane from the (*Z*)-vinyl bromide behaved in a similar manner.

To confirm that there was no stereochemical bias in the system (*E*)-1-iodo-2-methyl-1-butene[12] was subjected to the transfer reaction. Once again THF caused epimerization while the pure material gave >99% *RR,SS* product.

The hydroxide-induced transfer reaction of α-iodo- or α-bromoorganoboranes in the absence of THF or Me_2S thus proceeds in a stereospecific manner to give inversion at the migration terminus (eq 1). The situation is less clear when THF or Me_2S are present. It is reported that α-bromoethyldiethylborane undergoes a THF-induced rearrangement with a half-life of 120 min.[13] Addition of THF to the α-iodoorganoborane gives no apparent loss in the NMR signal for the proton geminal to the iodide (doublet, δ 4.01, J = 10 Hz) even after 48 h. This signal disappears only after the addition of a sodium hydroxide solution. However, the addition of 10 mol excess of THF to the α-iodoorganoborane followed by sodium hydroxide 1 min later causes nearly complete epimerization. (The addition of 3 M sodium hydroxide saturated with THF gives virtually no epimerization.) Even small amounts of THF in the vinyl iodide cause considerable loss of configuration over a period of time.

The THF appears to be causing the epimerization of the borane without causing migration. To test this possibility the ^{13}C spectra of the diastereomeric α-iodoorganoboranes were examined. The organoborane from the (*Z*)- vinyl iodide gave resonances (from Me_4Si) at δ 36.3, 31.5, 18.1, 10.6, and 10.3 (2) ppm, while the organoborane from the (*E*)-vinyl iodide gave resonances at 37.1, 29.5, 22.5, 12.1, and 10.3 (2) ppm. Excess THF was then added to the organoborane from the (*E*)-vinyl iodide. After 1 h the ^{13}C spectrum indicated that a mixture of the two diastereomeric α-haloorganoboranes was present. Oxidation of the NMR sample produced a 1:1 mixture of the diastereomeric alcohols. The α-haloorganoborane thus appears to be configurationally labile in the presence of THF.

The alkyl-transfer reaction of α-iodo- and α-bromoorganoboranes can be controlled to give a stereospecific synthesis at the halogen-bearing carbon. This fact combined with the ready availability of configurationally defined vinyl halides[5,6,12] now makes it possible to stereoselectively prepare a variety of organic products. We are continuing to explore these possibilities.

Acknowledgments. This work was supported in part by a University of California, Riverside, Undergraduate Research Grant. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. The Bruker WH 90-D-18 NMR spectrometer was supported by Biomedical Sciences Grant No. 5 S05 RR07010-19 from the National Institutes of Health and National Science Foundation Grant No. MPS75-06138.

References and Notes

(1) For reviews, see E. Negishi, *J. Chem. Educ.*, **52,** 159 (1975); T. Onak, "Organoborane Chemistry", Academic Press, New York, 1975; H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes", Wiley, New York, 1975; G. M. L. Cragg, "Organoboranes in Organic Synthesis", Marcel Dekker, New York, 1973.
(2) For examples, see (a) T. Leung and G. Zweifel, *J. Am. Chem. Soc.*, **96,** 5620 (1974); (b) H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **91,** 2150 (1969); (c) A. G. Davies and B. P. Roberts, *J. Chem. Soc. C,* 1474 (1968); (d) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83,** 2544 (1961). For reactions which proceed with inversion, see H. C. Brown, N. R. DeLue, G. W. Kabalka, and H. C. Hedgecock, *ibid.*, **98,** 1290 (1976); H. L. Goering and S. L. Trenbeath, *ibid.*, **98,** 5016 (1976).
(3) Pasto has reported that hydride migration occurs with inversion (D. J. Pasto and J. Hickman, *J. Am. Chem. Soc.*, **89,** 5608 (1967)). On the other hand, Brown has found that a 2-*exo*-bromo-2-*endo*-norbornylborane gives syn migration of a methyl group. However, the stereochemistry of the α-bromoborane has not been rigorously proven and the norbornyl system may give a biased stereochemical outcome (H. C. Brown, private communication).
(4) G. W. Kabalka, R. J. Newton, and J. Jacobus, *J. Org. Chem.*, **43,** 1567 (1978).
(5) J. F. Normant, G. Cahiez, C. Chuit and J. Villieras, *J. Organomet. Chem.*, **77,** 269, 281 (1974).
(6) A. B. Levy, P. Talley, and J. A. Dunford, *Tetrahedron Lett.*, 3545 (1977).
(7) Prepared from the redistribution reaction of excess triethylborane and borane–tetrahydrofuran or borane–methyl sulfide (see R. Köster and P. Binger, *Inorg. Synth.*, **XV,** 141 (1974)). Borane–tetrahydrofuran was prepared free of boron trifluoride (H. C. Brown and R. L. Sharp, *J. Am. Chem. Soc.*, **90,** 2915 (1968)). Borane–methyl sulfide was obtained from Aldrich.
(8) Oxidation of organoboranes with basic hydrogen peroxide proceeds with retention of configuration.[2c,d]
(9) The authentic *RR,SS* and *RS,SR* alcohols were prepared by hydroboration–oxidation of (*Z*)- and (*E*)-3-methyl-3-hexene, respectively.
(10) A 10 ft × 1/8 in. 10% TCP column was used for VPC analysis.
(11) The two diasteriomeric alcohols could be differentiated by the CHOH ^1H NMR (90 MHz), although the two signals were not completely resolved after decoupling NMR: *RR,SS,* δ 3.39 (m); *RS,SR,* δ 3.33 (m).
(12) Prepared by iodination of the organometallic obtained from the reaction of 1-butyne with methylmagnesium bromide–cuprous bromide (A. Marfat, P. F. McGuirk, and P. Helquist, *Tetrahedron Lett.*, 1363 (1978)).
(13) H. C. Brown and Y. Yamamoto, *J. Am. Chem. Soc.*, **93,** 2796 (1971).
(14) Alfred P. Sloan Foundation Fellow, 1978–1980.
(15) National Science Foundation Undergraduate Research Participant, 1978.

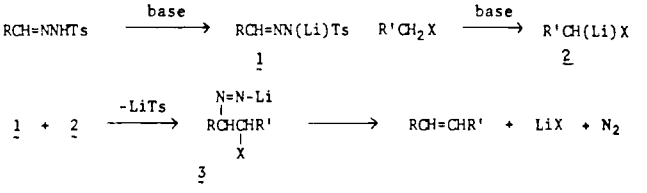
M. Mark Midland,*[14] Andrew R. Zolopa
Ronald L. Halterman[15]
Department of Chemistry, University of California
Riverside, California 92521
Received August 17, 1978

A New Olefin Synthesis: Condensation of Aldehyde Tosylhydrazones with Stabilized Carbanions

Sir:

We report a synthesis of alkenes from aldehyde tosylhydrazones which provides a simple and inexpensive alternative to the Wittig reaction. In the new reaction, anionic species **1** and **2** undergo an unusual condensation–fragmentation process as illustrated in Scheme I. The intimate mechanistic details are unknown, but formation of intermediate **3** seems essential to explain the overall results.[1,2]

Scheme I



0002-7863/79/1501-0249$01.00/0

A variety of carbanions **2** can be used for the condensation–fragmentation process provided that X is an anion-stabilizing group which is also a potential leaving group. Successful alkene synthesis have been achieved with α-lithio sulfides, sulfones, thioacetals, hemithioacetals, and nitriles (Table I). For practical reasons, it is most convenient to employ low molecular weight dialkyl sulfones as the carbanion precursors in a one-pot reaction (method B). A mechanically stirred solution of sulfone (45 mmol, ~0.2 M) and tosylhydrazone (32.5 mmol) in THF (−20 °C) is treated with lithium diisopropylamide (LDA) (75 mmol) in THF (~1.5 M) under a nitrogen atmosphere.[3] Copious nitrogen evolution begins as soon as >33 mmol of LDA has been added and the reaction is typically complete within an hour at −20 °C (no further N_2 evolution). After warming to 20 °C, simple aqueous workup removes lithium sulfinates, water-soluble sulfone, and traces of unreacted *N*-lithio tosylhydrazone. If desired, bulb-to-bulb distillation can then be employed to purify the alkene, usually the only easily volatile product in the examples studied (Table I).

The one-pot method can also be used with nitriles as carbanion precursors. However, side reactions[4] are minimized if the nitrile anion is formed separately (LDA/THF) and is then added by cannula to a solution of preformed *N*-lithio tosylhydrazone (from BuLi or LDA) in THF (method A). Method A is recommended for all anion precursors other than sulfones, and is essential for the weakly acidic sulfides or acetals.

Based on the several examples of disubstituted alkene synthesis studied, cis–trans mixtures are to be expected from *n*-alkyl sulfone or nitrile anions. The clean formation of *trans*-β-methylstyrene (entry 15) is unusual.

The condensation–fragmentation process does not lead to alkene products with certain substrates: (1) tosylhydrazones derived from α,β-unsaturated aldehydes (cinnammaldehyde, 2-hexenal); (2) sterically hindered and/or more highly stabilized carbanions, ($Ph_3CCH(Li)CN$, $PhCH(Li)CN$, $CH_3S(O)CH(Li)SCH_3$, *p*-tolyl-$SO_2CH(Li)CH{=}C(CH_3)_2$, $CH_3CH(Li)PO(OC_2H_5)_2$.

Enolizable ketone tosylhydrazones are also not suitable substrates for alkene synthesis. In a typical example, combination of monolithiated 2-phenylcyclohexanone tosylhydrazone with $LiCH_2SO_2CH_3$ or $CH_3CH(Li)CN$ results in the formation of an intense red color at −22 °C. This color is apparently due to the tosylhydrazone dianion, as evidenced by the formation of Shapiro elimination products (1- and 3-phenylcyclohexenes) upon warming to >0 °C.[5] None of the desired 2-phenylalkylidenecyclohexanes could be detected.

A successful route to trisubstituted alkenes is available from the condensation of α-branched nitrile anions with aldehyde tosylhydrazones (Table II, entries 19, 20, 23). Curiously, the analogous reaction of branched sulfones is an inefficient process (entry 21) owing to competing Shapiro elimination of the aldehyde tosylhydrazone.[6]

By comparison with the Wittig reaction, the sulfone version of anionic condensation–fragmentation is more convenient for preparation of terminal olefins. The nitrile anion variation is best for synthesis of trisubstituted olefins from α-branched nitriles. Large-scale reactions are performed without difficulty, an important advantage in cases where the Wittig reaction is complicated by low solubility and high molecular weight of the starting phosphonium salt or the product phosphine oxide. Disubstituted olefins are easily prepared by our method, but the Wittig reaction allows greater stereochemical control

Table I

$$RCH{=}NNHTs + R'CH(Li)X \rightarrow RCH{=}CHR'$$

R	R′	X	method[a]	% yield[b]	temp, °C	cis:trans	entry
$C_6H_5CH_2CH_2$	H	SO_2CH_3	B	73	−20[c]		1
$C_6H_5CH_2CH_2$	CH_3	$SO_2C_2H_5$	B	80	0[c]	2:1	2
$C_6H_5CH_2CH_2$	CH_3O	$SO_2C_6H_5$	A	43	−45	1:1	3
$C_6H_5CH_2CH_2$	C_6H_5	SC_6H_5	A	74	−78[c]	*d*	4
$C_6H_5CH_2CH_2$	C_6H_5S	SC_6H_5	A	58	−45[c]	*d*	5
$C_6H_5CH_2CH_2$	CH_3O	SC_6H_5	A	76	−78[c]	1:3	6
$C_6H_5CH_2CH_2$	H	CN	A	60	−20[c]		7
$C_6H_5CH_2CH_2$	CH_3	CN	A	77	−20[c]	1:1	8
$C_6H_5CH_2CH_2$	CH_3CH_2	CN	B	70	−20[c]	1:1	9
$C_6H_5CH_2CH_2$	$(CH_3)_2CHCH_2$	CN	B	60	−20[c]	45:55	10
$C_6H_5CH_2CH_2$	c-$C_6H_{13}CH_2$	CN	B	65	−78[c]	1:2	11
$C_6H_5CH_2CH_2$	$C_6H_5CH_2$	CN	A	55	−78[c]	2:3	12
$C_6H_5CH_2CH_2$	Me_3SiCH_2	CN	A	72	−78[c]	*d*	13
C_6H_5	CH_3	$SO_2C_2H_5$	A	73	−20[c]	14:86	14
C_6H_5	CH_3	CN	A	35	−20[c]	<5:95	15
n-$C_9H_{19}CH(CH_3)$	H	SO_2CH_3	B	68	−20[c]		16
n-$C_9H_{19}CH(CH_3)$	CH_3	$SO_2C_2H_5$	B	75	0[c]	2:1	17
c-C_6H_{13}	$C_6H_5CH_2CH_2$	CN	C	48	−20[c]	1:2	18

[a] Method A: anions preformed separately and carbanion added by cannula to tosylhydrazone anion. Method B: LDA added to solution of tosylhydrazone and $R'CH_2X$. Method C: solution of $RCH{=}NNHTs + R'CH_2X$ added to LDA. [b] Yields refer to distilled or chromatographed (PLC) product. [c] Spontaneous nitrogen evolution. [d] Cis–trans mixture, ratio not determined. [e] Temperature of initial mixing of reagents; reaction allowed to warm slowly to initiate nitrogen evolution (ca. −40 °C).

Table II. Trisubstituted Alkenes

	method	temp, °C	% olefin yield[a]	entry
$C_6H_5CH_2CH_2CH{=}NN(Li)Ts + (CH_3)_2C(Li)CN$	C	−78[b]	70	19
$C_6H_5CH_2CH_2CH{=}NN(Li)Ts$ + c-$(CH_2)_5C(Li)CN$	B	−78[b]	75	20
$C_6H_5CH_2CH_2CH{=}NN(Li)Ts + (CH_3)_2C(Li)SO_2$-*i*-Pr	A	−78[b]	36	21
$C_6H_5CH_2CH_2CH{=}NN(Li)Ts$ + c-$(CH_2)_2C(Li)SPh$	A	−78[b]	20	22
n-$C_9H_{19}CH(CH_3)C{=}NN(Li)Ts + (CH_3)_2C(Li)CN$	B	−78[b]	73	23

[a] See Table I, footnote *b*. [b] See Table I, footnote *e*.

where this is an important consideration. An especially important advantage of the new alkene synthesis is that numerous sulfones and nitriles are commercially available at minimal cost by comparison with phosphonium salts. Although our method requires prior isolation of the tosylhydrazone, this step is generally trivial and often provides a convenient means for purification of commercially available aldehydes. Finally, we note that synthetic intermediates of current interest such as vinyl sulfides (entry 5), vinyl ethers (entry 6), and allylic silanes (entry 13) can be prepared from appropriate precursors.

Acknowledgment. This work was supported by the National Science Foundation (CHE77-04658 A01).

References and Notes

(1) For addition of alkyllithium reagents to aldehyde tosylhydrazones, see E. Vedejs and W. T. Stolle, *Tetrahedron Lett.*, 135 (1977).
(2) A similar intermediate is apparently formed in the reaction of CH_3Li + $PhCH_2CH_2CH(OCH_2OCH_3)CH{=}NNHTs \rightarrow PhCH_2CH_2CH{=}CHCH_3$ (~20%): E. Vedejs and J. Dolphin, unpublished results.
(3) Low molecular weight sulfone anions occasionally precipitate under the standard conditions. Nitrile anion condensations are homogeneous throughout.
(4) Addition of >1 equiv of LDA to the tosylhydrazone will cause some fragmentation to a nitrile (see ref 1): $RCH{=}NNHTs \rightarrow RCN$. If the resulting nitrile has acidic α protons, the derived anion will form and will attack starting tosylhydrazone to afford alkene products of "self-condensation". This side reaction is seen in trace amounts with most reactions in Tables I and II.
(5) R. H. Shapiro, *Org. React.*, **23**, 405 (1976).
(6) Shapiro elimination is not normally observed when aldehyde tosylhydrazones are treated with LDA or alkyllithium reagents.[1]

E. Vedejs,* J. M. Dolphin, W. T. Stolle
McElvain Laboratory of Organic Chemistry
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706
Received August 13, 1978

Efficient Guaiazulene and Chamazulene Syntheses Involving [6 + 4] Cycloadditions

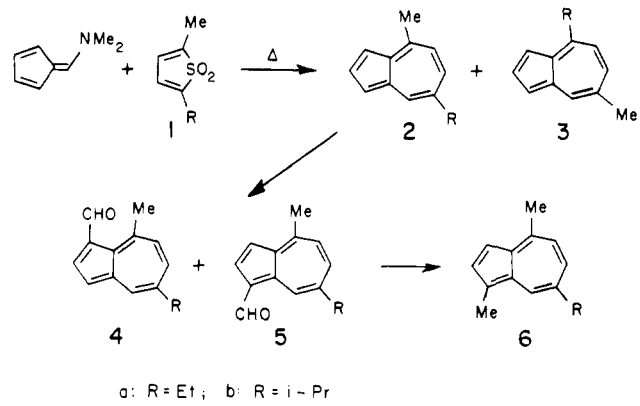
Sir:

Guaiazulene[1] and chamazulene[2] are obtained from natural sources by the degradation of hydroazulene sesquiterpenes.[3] The best azulene syntheses[4] are not generally applicable to the ready preparation of these compounds, so that only extremely lengthy and low yield total syntheses of both of these azulenes have been reported.[5] We report the application of two new azulene syntheses involving [6 + 4] cycloadditions[6,7] to the synthesis of these substances.

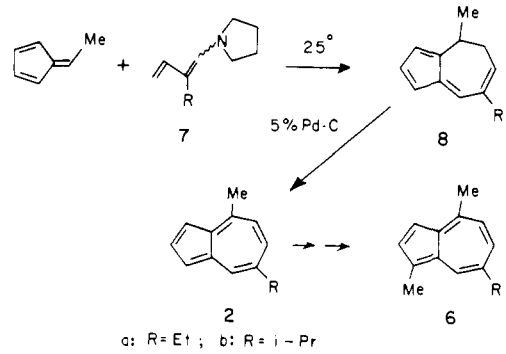
Model studies showed that the 1,4,7-trisubstitution pattern present in guaiazulene and chamazulene could not be produced directly owing to the incorrect regioselectivity of the cycloadditions in the five-membered ring.[8] However, either [6 + 4] cycloaddition sequence selectively gives the 4,7-disubstituted azulenes, and the 1-methyl substituent could be introduced selectively utilizing the propensity of azulenes to undergo electrophilic substitution at the 1 (or 3) position and the greater hindrance to attack of the 3 position in the 4,7-disubstituted azulene.

Although high regioselectivity was not anticipated for the aminofulvene, thiophene dioxide route (Scheme I), in practice this sequence proved quite efficaceous. The appropriate thiophene dioxides (**1a** and **1b**) were prepared from 2-acetyl-5-methylthiophene[9] as follows. Wolff-Kishner reduction (hydrazine hydrate, KOH, diethylene glycol, 210 °C, 3 h) gave 2-ethyl-5-methylthiophene, bp 150–152 °C (72%), which was oxidized (*m*-chloroperbenzoic acid, $NaHCO_3$, CH_2Cl_2, 10 °C, 2 days) in 69% yield to **1a** (viscous oil). The use of solid sodium bicarbonate to neutralize the chlorobenzoic acid formed represents a considerable improvement over the one-phase oxidation of Melles and Backer, which gives low yields and tarry byproducts.[10]

Scheme I



Scheme II



Addition of methyl Grignard to 2-acetyl-5-methylthiophene, followed by dehydration of the crude product with $KHSO_4$ at 200 °C, gave 2-methyl-5-(2-propenyl)thiophene (42%). Hydrogenation of the propenyl group over 5% $Pd/BaSO_4$ proceeded quantitatively to give 2-isopropyl-5-methylthiophene, which was oxidized as before to give the thiophene dioxide (**1b**, 71%).

Reaction of **1a** (1.3 g) with 6-dimethylaminofulvene (1.2 g) in refluxing benzene, and workup as described previously,[6] gave a mixture of 7-ethyl-4-methylazulene (**2a**) and 4-ethyl-7-methylazulene (**3a**) in a total yield of 11%. By carrying out this and related cycloadditions in refluxing pyridine, the yield can be improved to a more tolerable 20%.[11] NMR spectra (for example, the ratio of the 4-methyl resonance in **2a** at δ 2.79 to the 7-methyl resonance in **3a** at δ 2.49)[12] indicated that the desired isomer (**2a**) and the undesired one (**3a**) were formed in a ratio of 4:1. Steric effects must control the regioselectivity of these cycloadditions: the most nucleophilic site (C-2) of the aminofulvene becomes attached to the less hindered site of the thiophene dioxide, even though the final adduct may be more crowded.[6]

The methyl group at C-1 was introduced by Vilsmeier formylation ($POCl_4$, DMF, 0 °C), which gave a mixture of the 1,5,8-trisubstituted azulene (**4a**) and the 1,4,7 isomer (**5a**), which were easily separated by column chromatography (alumina, benzene) in isolated yields of 13 and 68%, respectively. The anisotropy of the aldehyde makes identification by NMR of the isomers simple: in **4a**, Me_8 resonates at δ 3.13 and H_4 at 8.32, while, in **5a**, Me_4 resonates at δ 2.78 and H_4 at 9.53. Wolff-Kishner reduction of **5a** gave chamazulene (**6a**, 50%) as a purple oil.[13]

The synthesis of guaiazulene proceeded similarly. The cycloaddition of **1b** (1.3 g) with 6-dimethylaminofulvene (1 g) gave **2b** and **3b** in a ratio of 4:1 (NMR), from which 60 mg of **2b** could be isolated by column chromatography. Vilsmeier

0002-7863/79/1501-0251$01.00/0