5 H), 6.38 (dd, $J = 6.4$, 1.4 Hz, 1 H), 5.78 (dd, $J = 17.3$, 10.8 Hz, 1 H), 5.17 (dd, $J = 17.3$, 1.1 Hz, 1 H), 5.06 (dd, $J = 10.7$, 1.1 Hz, 1 H), 4.88 (ddd, $J = 6.4$, 2.6, 1.3 Hz, 1 H), 4.54 (AB q, $\Delta\nu = 15.8$ Hz, $J_{AB} = 11.85$ Hz, 2 H), 3.96 (m, 1 H), 2.10 (ddd, $J = 13.4$, 6.0, 1.2 Hz, 1 H), 1.87 (dd, $J = 13.3$, 8.0 Hz, 1 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 143.75, 140.83, 138.72, 128.33, 127.52, 127.46, 112.99, 101.20, 77.22, 69.91, 68.07, 38.27, 26.95 ppm; MS m/z (M^+) calcd 230.1307, obsd 230.1300; $[\alpha]^{25}_D$ -142.3° (c 0.61, $CHCl_3$).

(-)-(2*R*,4*S*,6*R*)-2-Methyl-2-vinyl-4-(benzyloxy)-6-(phenylthio)tetrahydropyran (26). A cold (-78 °C), magnetically stirred solution of **25** (230 mg, 0.88 mmol) in 3 mL of dichloromethane was treated with thiophenol (103 μL, 1 mmol) followed by boron trifluoride etherate (0.16 mL, 1.3 mmol). After 1 h at -78 °C, the reaction mixture was quenched with cold, saturated sodium bicarbonate solution (10 mL) and extracted with ether (3 × 10 mL). The combined organic phases were dried and concentrated, and the residue was purified by silica gel chromatography (elution with 10% ether in petroleum ether). There was isolated 290 mg (97%) of **26** as a clear, colorless oil homogeneous by TLC: IR (neat, cm^{-1}) 3055, 3030, 2970, 2945, 2920, 2860, 1580, 1493, 1478, 1450, 1438, 1410, 1358, 1310, 1210, 1182, 1150, 1125, 1070, 1040, 1025, 970, 928, 878, 806, 740, 695; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55-7.49 (m, 2 H), 7.35-7.21 (m, 8 H), 5.66 (dd, $J = 17.8$, 11.1 Hz, 1 H), 5.08 (d, $J = 11.1$ Hz, 1 H), 4.93 (d, $J = 17.8$ Hz, 1 H), 4.83 (dd, $J = 12.0$, 2.05 Hz, 1 H), 4.52 (AB q, $\Delta\nu = 17.6$ Hz, $J_{AB} = 11.8$ Hz, 2 H), 3.65 (m, 1 H), 2.35-2.20 (series of m, 2 H), 1.62-1.40 (m, 2 H), 1.33 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 141.67, 138.36, 133.85, 132.25, 128.59, 128.34, 127.56, 127.51, 127.48, 127.39, 115.42, 78.56, 71.91, 69.89, 39.81, 37.96, 31.04 ppm; MS m/z (M^+ - SPh) calcd 232.1462, obsd 232.1462; $[\alpha]^{25}_D$ -57.4° (c 1.25, $CHCl_3$).

Anal. Calcd for $C_{21}H_{24}O_2S$: C, 74.08; H, 7.10. Found: C, 74.32; H, 7.10.

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Action of Alkylmagnesium and Alkyllithium Reagents on Some Quaternary Hydrazonium Salts[1]

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Benzophenone *N*-methyl-*N*,*N*-pentane-1,5-diylhydrazonium iodide (**1a**) and its *p*,*p*′-dichloro and *p*,*p*′-dimethoxy analogues undergo loss of CH_3I in boiling ethyl ether or THF, but the fluoroborates are stable. The complexes formed from **1** and Grignard reagents do not undergo incorporation of deuterium when they are hydrolyzed with D_2O. When **1** and analogues are treated with propyl- and decylmagnesium bromide, the corresponding alkane, alkene, and bialkyl are produced, facts that imply formation of alkyl radicals by a single-electron-transfer process. With all alkyl Grignard reagents studied, the overwhelming reaction is reductive cleavage of the N,N bond to form imines unsubstituted on nitrogen; no *N*-alkyl imines were detected. Small amounts of 1,1-diarylalkylamines, formed by addition of R′MgX to the azomethine carbon, were formed in some instances, and *tert*-butylmagnesium chloride formed about 2% of benzhydrylamine in reaction with **1a**. Sodium cyanide reacted with the tetrafluoroborate analogue of **1a** to form acetonitrile by demethylation; neither addition nor reduction was detected. Sodium azide behaved analogously.

The thin stream of literature on quaternary hydrazonium compounds since the first report[2] in 1957 has been mostly concerned with their use as intermediates in synthesis of azirines, an analogue of the Neber rearrangement. Their stereochemistry has been studied by Arseniyadis, Laurent, and Mison,[3] who also showed[4] that reaction of Grignard reagents with quaternary hydrazonium iodides having a hydrogen α to the azomethine carbon is an efficient method for synthesis of aziridines (a second equivalent of RMgX adds to the azirine first formed). They observed that the direction of ring closure with hydrazonium salts derived from unsymmetrical ketones was independent of the stereochemistry about the C=N double bond, and that it occurred highly preferentially to the least hindered α-position, regardless of the relative acidities of the α-hydrogens. Yields were mostly high, and the only competing reaction reported was dealkylation at the quaternary nitrogen to form a dialkylhydrazone (in general, products other than aziridines were not determined, even for those cases in which the yields of aziridine were very low).

In contrast, quaternary benzophenone hydrazonium salts (**1**), which have no α-hydrogens, have been shown by Smith and Tan[5] to react with Grignard reagents through an intermediate of unknown composition (**2**?), formed with evolution of heat, which proceeds to a mixture of products resulting from at least three competing reactions (eq 1-3),

$$\underset{\textbf{1a-f}}{Ar_2C{=}N\text{-}\overset{+}{N}R_3I^-} + R'MgX \rightarrow [\textbf{2}?] \xrightarrow{\Delta} \underset{\textbf{3}}{Ar_2C{=}NMgX} + R_3N + R'{-}R' \quad (1)$$

1a, Ar = Ph, $R_3 = CH_3$ and $(CH_2)_5$

1b, Ar = p-$CH_3C_6H_4$, $R_3 = CH_3$ and $(CH_2)_5$

1c, Ar = p-ClC_6H_4, $R_3 = CH_3$ and $(CH_2)_5$

1d, Ar = Ph, R = CH_3

1e, Ar = Ph, $R_3 = C_2H_5$ and $(CH_2)_5$

1f, Ar = p-$CH_3OC_6H_4$, $R_3 = CH_3$ and $(CH_2)_5$

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[1] From the doctoral dissertation of C. R. Messing.

[2] Smith, P. A. S.; Most, E. E., Jr. *J. Org. Chem.* 11957, *22*, 358.

[3] Arseniyadis, S.; Laurent, A.; Mison, P. *Bull. Soc. Chim. Fr.* 1980, *II*, 233.

[4] Arseniyadis, S.; Laurent, A.; Mison, P. *Bull. Soc. Chim. Fr.* 1980, II, 246.

[5] Smith, P. A. S.; Tan, H. H. *J. Org. Chem.* 1967, *32*, 2586.

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$$1 + \mathrm{R'MgX} \rightarrow \underset{\mathbf{5}}{\mathrm{Ar_2C{=}N{-}R'}} + \mathrm{R_3N} \qquad (2)$$

$$1 + \mathrm{R'MgX} \rightarrow \underset{\mathbf{6}}{[\mathrm{Ar_2(R')C{-}\overset{-}{N}{-}\overset{+}{N}R_3}]} \rightarrow \underset{\mathbf{4}}{\mathrm{Ar(R')C{=}N{-}Ar}} + \mathrm{R_3N} \qquad (3)$$

of which reductive cleavage (eq 1) predominated. The other reactions were replacement of the tertiary amine moiety by the aryl group of arylmagnesium halide to form an *N*-aryl imine (**5**) (eq 2) and addition of the aryl group to the azomethine carbon to form a presumed amine *N*-imide intermediate (**6**) (eq 3), which underwent an analogue of the Stieglitz rearrangement[6] to form an imine isomeric to that formed by eq 2. The nature of **2** was not established, but addition of water regenerated the starting hydrazonium compound. Although it appeared to be an addition complex, another possibility was that it might be an ylide formed by abstraction of a proton from one of the *N*-alkyl groups.[4]

The purpose of the present investigation was to determine whether **2** is an ylide or a simple adduct, to test the hypothesis that the ylide **6** is involved in eq 3, and to obtain further information about the three competing reactions and their dependence on structure and conditions. We had hopes (in the event, unrequited) that eq 2 might have potential for a practical method for converting an organometallic reagent into a primary amine, by hydrolysis of the imine **5**, thus providing an alternative to the reaction of organometallic reagents with various O-substituted hydroxylamines,[7] tosyl azide,[8] vinyl azide,[9] and phenylthiylmethyl azide.[10]

Results and Discussion

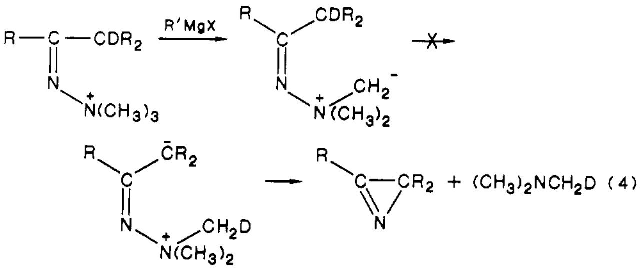
Most of the quaternary hydrazones used in this investigation are methiodides of benzophenone pentane-1,5-diylhydrazones and have been previously described.[5] A tetrafluoroborate (**1a**, with BF_4^- in place of I^-) was prepared by using trimethyloxonium tetrafluoroborate. The lone ethiodide (**1**) was prepared by reaction of benzophenone pentane-1,5-diylhydrazone with ethyl iodide in boiling acetonitrile in the dark; attempts using ethanol or dimethyl sulfoxide as the solvent gave only black oil.

Arseniyadis, Laurent, and Mison[4] observed slow dealkylation of a trimethylhydrazonium salt in boiling toluene. Because dealkylation could affect our subsequent investigations, we examined the subject briefly. The results are recorded in Table I. For the methiodides of benzophenones (**1a–c**), heating in boiling tetrahydrofuran (THF) was sufficient to effect slow but complete demethylation. In ethanol, however, **1a** was stable, even though the temperature was higher. Not unexpectedly, the tetrafluoroborate analogue of **1a** showed no demethylation in THF; however, it was found to be unsatisfactory in the subsequent studies, owing to low reactivity and formation of alcohols corresponding to R'MgX. The ethiodide, **1e**, was more resistant than the methiodides and underwent only partial dealkylation in THF even after 35 h. The *p*-chlorobenzaldehyde analogue of **1a** was even more resistant. We conclude that nucleophilic displacement by iodide at the carbon α to N^+ is facilitated by the strain in the crowded ketone derivatives (in which approach to the α-carbon is nevertheless unhindered) and is a potential competitor with reactions of quaternary hydrazones with organometallic reagents when heated. We therefore avoided solvents having higher boiling points.

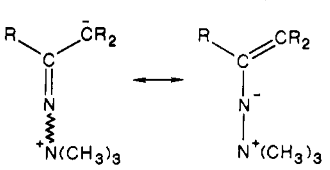
Table I. Thermolysis of Hydrazonium Salts

reactant	X^-	time, h	solvent	$RR'C{=}N{-}N(CH_2)_5$, %	recovd hydrazonium salt, %
1b	I^-	23	THF	95	
1a	I^-	35	EtOH	trace	90
1a	BF_4^-	36	THF		98
1b	I^-	22	THF	96.5	
1c	I^-	22	THF	100	
1e	I^-	34.5	THF	77	22
$p\text{-}ClC_6H_4CH{=}N{-}N^+(CH_3)(CH_2)_5$	I^-	35	THF	33	67

Arseniyadis, Laurent, and Mison[4] investigated the possibility that N,C ylides might be involved in the reaction of Grignard reagents with hydrazonium salts by preparing an example bearing deuterium at the position α to the azomethine carbon (eq 4). Their hypothesis



(eventually rejected) was that the observed regiochemistry might be a consequence of initial formation of an N,C ylide at the quaternary site and subsequent abstraction by the carbanion of a deuteron from the α-position. The trimethylamine eventually evolved was free of deuterium, however. This observation tells us that the proposed intramolecular proton transfer does not occur, but it leaves open the question of whether such N,C ylides are formed. The direct formation of enamide anions (amine vinylimides) (**7**) as intermediates could explain why the direc-



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tion of the ring closure was independent of geometrical isomerism. The choice of the least substituted carbon as the site of the ring closure was reasonably explained[4] as sterically controlled because the attacking base was presumably a cluster, $(RMgX)_n$ (toluene was the solvent in their experiments). This explanation implies that the selectivity is kinetically controlled. Therefore, one can understand why in some examples, such as the hydrazonium salt derived from 3-phenyl-2-butanone, the selectivity was reversed when the base used was sodium hydride in Me_2SO, or butoxide in butanol; thermodynamic control must have come into play because of the possibility of reversible proton transfer.

If **2** is, indeed, an ylide, having the function $-{}^+NR_2-CH_2^-$, it should be possible to trap it by reaction with benzaldehyde, in the manner used by Wittig and Polster[11]

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[6] For leading references, see: Smith, P. A. S. *Derivatives of Hydrazine and Other Hydronitrogens Having N-N Bonds*; Benjamin-Cummings: Reading, MA, 1983; pp 266–267.

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[10] Trost, B. M.; Pearson, W. H. *J. Am. Chem. Soc.* **1981**, *103*, 2483.

Table II. Reaction of Hydrazonium Salts with Organometallic Reagents Followed by D_2O

hydrazonium salt (A)	reagent	T, °C	time, h	recovd A, %	% deuterium in recovd A	other product, %
$(p\text{-}CH_3OC_6H_4)_2C{=}N{-}N^+(CH_3)(CH_2)_5I^-$	$n\text{-}C_{10}H_{21}MgBr$	27	15	64	none	$(p\text{-}CH_3OC_6H_4)_2C{=}O$, 20 decane-*d*, 28 decane, 13 1-decene, 3 eicosane, 28
$Ph_2C{=}N{-}N^+(CH_3)_3I^-$	$n\text{-}C_3H_7MgBr$	27	14	47	none	0.1 equiv of gas $Ph_2C{=}O$, 42 $Ph_2C{=}N{-}N(CH_3)_2$, 5
$Ph_2C{=}N{-}N^+(CH_3)_3I^-$	CH_3Li	−40 0	1.5 2.5	90	none	
$Ph_2C{=}N{-}N^+(CH_3)_3I^-$	$n\text{-}C_4H_9Li$	−10 27	9 21	92	none none	

Table III. Reaction of 1a and 1e with Decylmagnesium Bromide

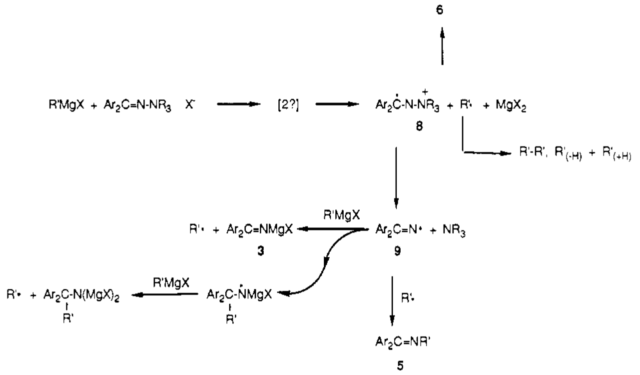
reactant, mmol	$n\text{-}C_{10}H_{21}MgBr$, mmol	products, mmol (yield)[a]					
		$RN(CH_2)_5$	$Ph_2C{=}NH$	$C_{20}H_{42}$	$C_{10}H_{20}$	$C_{10}H_{22}$	$C_{10}H_{21}D$
1a, 50	110	42.4 (85%)	42 (84%)	10.3 (21%)	25.2 (25%)	51 (51%)	
1e, 54	180	39.8 (74%)	34 (63%)	15.5 (29%)	28 (26%)	44 (41%)	11.8[b]

[a] Based on hydrazonium salt, not corrected for blank. [b] Reaction quenched with D_2O.

to trap trimethylammonium methylide. The product **2** formed from **1a** and bromide was inert to benzaldehyde in tetrahydrofuran at room temperature and when heated, it mostly underwent loss of methyl iodide and regeneration of benzophenone pentane-1,4-diylhydrazone. A small amount of gas was, however, evolved and was identified as ethane (rather than butane or ethylene) by its IR spectrum. We therefore tried, instead, to trap the ylide by hydrolysis with D_2O, which would form **1** deuteriated α to the nitrogen atom to the extent that the ylide had been formed. The results with **1a** and **1b**, using propyl- and decylmagnesium bromides and methyl- and butyllithium, are reported in Table II. Because of the nature of **1a**, mass spectrometry was not feasible, but in no case did the recovered quaternary hydrazone show incorporation of deuterium detectable by IR or NMR. We therefore conclude that **2** is not an ylide, but an addition complex, although the presence of a small amount of ylide (<5%) cannot be excluded. Complexation might occur between R_2Mg, RMgX, or MgX_2 and either the azomethine nitrogen or iodide ion. This conclusion is consistent with the fact that the tertiary amine formed by the reactions of **2** is released as such and can be distilled directly from the unhydrolyzed reaction mixture. Were **2** an ylide, a C-metallated tertiary amine or some other type of product would have been subsequently formed, and the tertiary amine would not have been released until after hydrolysis. In contrast, a quaternary hydrazone of acetophenone when treated with butyllithium has been reported to give products that are difficult to explain without invoking an ylide;[12] this observation can be reconciled if a non-ylide adduct, analogous to **2**, is formed, but proceeds to subsequent products through a low, but kinetically significant, concentration of the ylide.

The major reaction reported by Smith and Tan,[5] reduction to unsubstituted imine (eq 1), differs in nature from the reduction of ketones by Grignard reagents; in the former, the C=N double bond is not affected, whereas in the latter, the C=O double bond is reduced, with formation of an alcohol of a pinacol. Convincing evidence has accumulated[13] that the alcohols arise through involvement of a hydrogen on the β-position of the Grignard reagent and that the pinacols arise from ketyls formed by single-electron transfer from RMgX (it has been proposed[14] that even normal addition of Grignard reagents to the carbonyl group proceeds through a single-electron transfer). A path for the reaction of hydrazonium salts can also be envisaged to involve a transfer of a single electron[15] (Scheme I).

Scheme I



In the earlier work,[5] only biaryls or bialkyls were identified to account for the fate of the organometallic reagents. For aryl reagents, biaryls are the only products to be expected, but alkyl reagents should also give rise to some products of disproportionation (alkane and alkene) if alkyl radicals are formed by single-electron transfer. To examine this hypothesis, we carried out experiments with decylmagnesium bromide and **1a** or **1e**.

The experiments were carried out in diethyl ether under nitrogen, using excess Grignard reagent, and heating under reflux for 13–43 h. The volatile products (C_{10} hydrocarbons and tertiary amine) were removed by codistillation with ether repeatedly and then with THF repeatedly until no amine could be detected in the distillate (the attendant heating also served the purpose of driving the reactions toward completion). The amine in the distillate was isolated as its hydrobromide, and the neutral fraction was separated from decomposition products of THF by fractional distillation, weighed, and analyzed by gas chromatography. The nonvolatile part of the original reaction

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(11) Wittig, G.; Polster, R. *Liebigs Ann. Chem.* **1956**, *599*, 1.

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(15) Michanisms involving single-electron transfer by Grignard reagents have been reviewed by: Dagonneau, H. *Bull. Soc. Chim. Fr.* **1982**, II, 269. A reductive cleavage of the N,N bond of hydrazines involving radicals has been reported by: Rheinboldt, H.; Kirberg, R. *J. Prakt. Chem.* **1982**, *118*, 1.

Table IV. Reactions of Hydrazonium Salts with Alkylmagnesium Halides

$Ar_2C{=}N{-}N^+R_3I^-$	RMgX (molar equiv)	products, % yield					
		$CH_3N(CH_2)_5$	$Ar_2C{=}O$	$ArRC{=}O$	RNH_2	$ArNH_2$	other
1c	CH_3MgCl (3.4)	94	85	none			$Ar_2C(CH_3)NH_2$?, trace
1b	CH_3MgCl (3.3)	98	91	none	none	none	
1c	CH_3CH_2MgBr (2.2)	23	37	none	none	none	$Ar_2C(Et)NH_2$[a], >16
1c	CH_3CH_2MgBr (3.5)	56	18	none	none	none	$Ar_2C(Et)NH_2$, 34
1f	CH_3CH_2MgBr (2.9)	83	52	3	none	9	$Ar_2C{=}CHCH_3$, 4.6[b]
1f	$(CH_3)_2CHMgCl$ (3.6)	100	66	none	none	none	$Ar(R)C{=}N{=}Ar$[c]?, 1–2
1a	t-C_4H_9MgCl (2.7)	23		none	none	none	$PhCHNH_2$[d], 2
1a	t-C_4H_9MgCl (2.5)	85	77	none	none	none	

[a] Oil, bp 150 °C/0.25 mm; IR (neat) 3380, 3315 cm^{-1}; NMR ($CDCl_3$) δ 0.77 (t, $J \simeq 7$ Hz, 3 H), 1.72 (broad s, 2 H), 2.15 (q, $J \simeq 7$ Hz, 2 H), 7.15 (s, 8 H). Anal. C, H, N. [b] Estimated from the NMR spectrum of its mixture with *p,p'*-dimethoxybenzophenone and *p*-methoxyacetophenone before recrystallization. [c] An impure, basic oil having an IR spectrum consistent with this structure; NMR ($CDCl_3$) δ 1.1 (d, $J = 6$ Hz, 6 H), 2.4 (weak m), 3.8 (s, 6 H), 6.5–7.8 (m, 8 H). [d] Weighed and identified as its benzenesulfonamide, mp 183–185 °C alone and when mixed with authentic material.

mixture was hydrolyzed with aqueous ammonium chloride, and the basic components were separated by precipitation with hydrogen chloride. The product appeared to be essentially pure benzophenoneimine hydrochloride; only benzophenone and ammonium chloride were obtained by hydrolysis, and no decylamine could be detected. The nonbasic fraction was separated into a mixture of decene and decane and a mixture of eicosane and benzophenone by fractional distillation. The latter was separated into its components by recrystallization. The resulting material balance is necessarily imperfect, owing to variable mechanical losses in handling, but the results nevertheless give an acceptable picture of the reactions occurring (Table III). We are confident that no primary amines (derived from eq 2, 3, or 4) were formed in more than trace amounts.

It is significant that most of the decane was obtained before hydrolysis, and thus could not have been derived from unconsumed Grignard reagent. To confirm this point, the reaction of **1e** with decylmagnesium bromide was quenched in D_2O, thus converting unconsumed $C_{10}H_{21}MgBr$ to $C_{10}H_{21}D$. A control experiment on the Grignard reagent without hydrazonium salt produced a C_{10} mixture having a composition of 92.8% $C_{10}H_{21}D$ + 5.7% $C_{10}H_{22}$ and $C_{10}H_{20}$, along with a small amount (4.7% of the original $C_{10}H_{21}Br$) of $C_{20}H_{42}$, inevitably formed during preparation of the Grignard reagent. The results, shown in Table III, clearly show formation of the disproportionation products, decane and decene, expected of decyl radicals. The fact that the amount of alkane exceeded that of alkene can be accounted for by abstraction of H from the solvent by some of the decyl radicals. The amounts of R_3N and imine were roughly equivalent, and the sum of the hydrocarbons slightly exceeds the amount corresponding to the imine, assuming a 2:1 stoichiometry for the reduction.

With ethyl- and *tert*-butylmagnesium halides, no *N*-alkyl imine, $Ar_2C{=}NR'$, was found by Smith and Tan, and eq 2 was not detectable. In contrast, with arylmagnesium halides, small to substantial amounts of *N*-aryl imines, $Ar_2C{=}NAr'$, were formed (a low of 4% when $Ar' = C_6H_5$, and high of 35% when Ar′ = mesityl). Only in the case of ethylmagnesium bromide were any products derived from addition of the Grignard reagent across the C═N double bond (eq 3) observed in more than trace amounts; *p*-anisidine, formed by hydrolysis of **4** arising from the reaction of **1f** (eq 3), was obtained in 23% yield. Since the quaternary hydrazonium compounds are congested, access to the azomethine carbon is likely to be prohibitively difficult for any but the smallest alkyl groups. We are therefore not surprised that the reaction of **1a** with decylmagnesium bromide showed no evidence of the products from eq 3. If bulk is the dominant factor, one might expect eq 3 to be maximized with a methyl reagent and to be much reduced with isopropylmagnesium halides. We therefore examined the action of such Grignard reagents.

The experiments were carried out in THF, using methylmagnesium chloride (commercial), ethylmagnesium bromide, and isopropylmagnesium chloride in reaction with quaternary hydrazones of benzophenone, *p,p'*-dichlorobenzophenone, and *p,p'*-dimethoxybenzophenone. The results are summarized in Table IV. Surprisingly, the methyl reagent brought about reduction exclusively;[16] no more than a trace, too small to purify and identify conclusively, of a 1,1-diarylalkylamine (**10**) (eq 5) was

$$\mathbf{1} \xrightarrow{R'MgX} [Ar_2(R')C\text{-}\overset{-}{N}\text{-}\overset{+}{N}R_3] \xrightarrow[2.\ H_2O]{1.\ 2R'MgX} \underset{\mathbf{10}}{Ar_2(R')C\text{-}NH_2} + NR_3 \quad (5)$$

detected. With ethylmagnesium bromide, eq 5 became a major competitor with eq 1 when **1c** was used, whereas **1f** gave products from reduction (eq 1) and addition plus Stieglitz-type rearrangement (eq 3). This difference in behavior between the two hydrazonium salts is understandable in consideration of the known migratory aptitudes of the aryl groups in migrations to electron-deficient centers; a *p*-chloro substituent retards migration of a phenyl group, whereas a *p*-methoxy group markedly promotes it. With **1c**, therefore, eq 3 would be suppressed, and the reduction of **6** (eq 5) would be able to compete; with **1f**, eq 3 would be accelerated and could predominate over the evidently slower eq 5. The reaction of ethylmagnesium bromide with **1f** also produced a 1,1-diarylpropene in small amount; this is formally an elimination product from **6** to **8** (although it could in principle also be derived by elimination of water from 1,1-diarylpropanol formed by addition of the Grignard reagent to *p,p'*-dimethoxybenzophenone, we do not believe that such a contaminant was present in the hydrazonium salt).

The reaction of isopropylmagnesium bromide with **1f** followed eq 1 almost exclusively; only a very small amount of an imine like **4** was found, and no **7**. We also confirmed the report of Smith and Tan that *tert*-butylmagnesium chloride brought about only reduction of **1a**, although a trace (2%) of benzhydrylamine, a type of reduction product not encountered in any other case, was obtained in one experiment.

Cyanide, having smaller steric requirements even than methyl, might be thought to be a reasonable candidate for

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(16) In retrospect, we cannot rule out the possibility that traces of transition metals, such as iron, may have been present in the methylmagnesium chloride that we used; such contamination has been shown to favor reduction: Ashby, E. C.; Bubler, J. D.; Lopp, I. G.; Wiesemann, T. L.; Bowers, J. S., Jr.; Laemmlie, J. T. *J. Am. Chem. Soc.* **1976**, *98*, 6561.

addition to the azomethine carbon. In our experiment, sodium cyanide in anhydrous ethanol was used, conditions necessarily very different from those with Grignard reagents. Neither addition nor reduction was detected; the sole reaction seemed to be nucleophilic displacement at a saturated carbon, giving acetonitrile (47.7%), a trace of *N*-methyl-*N*-(5-cyanopentyl)hydrazone, demethylated hydrazone (49%), and recovered hydrazonium salt (11%). With sodium azide, recovered hydrazonium salt (62%) was the principal result, accompanied by a 10% yield of demethylated hydrazone and 1.5% of the ring-opened compound, benzophenone *N*-methyl-*N*-(5-azidopentyl)hydrazone. No 1,5-diphenyltetrazole, which could be expected if an analogue of the Beckmann rearrangement had taken place, could be detected.

In order to substantiate the hypothesis that amine *N*-imides (**6**) are intermediates in some of the foregoing reactions, we attempted to prepare an example by an independent route. *N*-Aminopiperidine was easily alkylated with triphenylmethyl bromide to produce a stable, crystalline product, *N*-(triphenylmethyl)-*N'*,*N'*-pentane-1,5-diylhydrazine, $Ph_3CNHN(CH_2)_5$. However, all attempts to convert it to a quaternary salt (or the conjugate base, the amine *N*-imide) by alkylation with methyl iodide or trimethyloxonium tetrafluoroborate failed (only dark oils and nitrogen-free compounds were obtained).

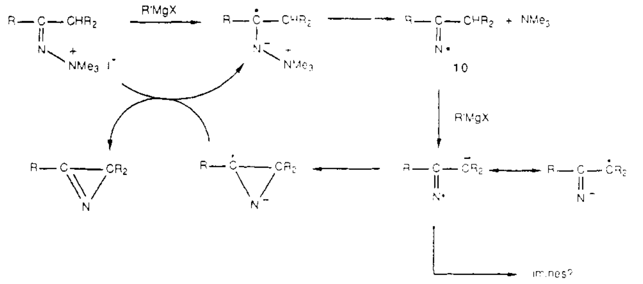
It is not possible to make firm conclusions about the reasons for the partitioning of the hydrazonium salts among the several reactions according to the nature of the alkyl group of the Grignard reagent, in part because the composition of the addition complexes (**2**) is not known. However, it appears that simple steric bulk, although of dominant influence, is not by itself sufficient to account for the observed behavior. If the *N*-aryl imines obtained by Smith and Tan from aryl Grignard reagents are the consequence of single-electron transfer and collapse of the resulting pair of radicals (**9** and R'• in Scheme I), the fact that the parallel reaction with alkyl Grignard reagents is not observed with primary, secondary, or tertiary alkyl groups requires explanation. A possibility is that either disproportionation, not available to aryl radicals, or subsequent single-electron transfer by a second alkyl group of "R'MgX", converting **9** to the imine anion, $Ar_2C{=}N^-$, is overwhelmingly faster. Such a situation could occur if reaction of alkyl Grignard reagents takes place through a complex **2** in which R'_2Mg (or alkyllithium oligomer) is the complexing species, with the azomethine N as ligand.

The major difference in products in our experiments from those of Arseniyadis, Laurent, and Mison is an obvious and necessary one, because the benzophenone derivatives that we used have no acidic α-hydrogens. However, reduction to imine should be possible with the aliphatic hydrazonium salts as well as those of benzophenones. The paper by Arseniyadis, Laurent, and Mison does not comment on the fate of those substrates, such as the hydrazonium salt from cyclopentanone, that give only very low yields of aziridine, and it is possible that reductive cleavage of the N–N bond occurred. There is a possible path for the formation of azirines through the same initial step, single-electron transfer, as occurs with benzophenone derivatives (Scheme II). Only a small amount of electron transfer from the Grignard reagent would be required to initiate a chain reaction, which would be feasible if the imine radical (**10**) has a more acidic α-hydrogen than the parent hydrazonium salt.

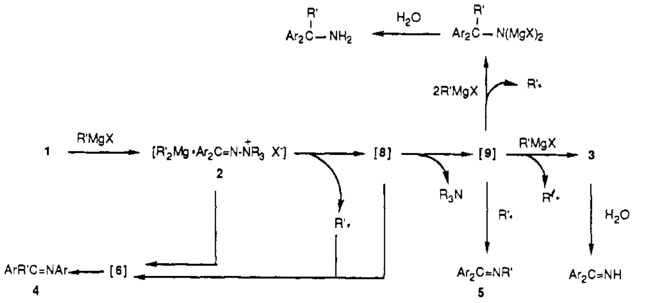
Conclusion

The most consistent interpretation of the evidence is that quaternary hydrazonium salts (1) and Grignard reagents from an addition complex (**2**) that gives rise to the observed products by Scheme III, in which the predominant path leads to *N*-magnesioimines (**3**) by two single-electron transfers. In structurally favorable cases, the intermediates **2**, **8**, and **9** may be diverted to products having R' attached to the C or N of the erstwhile azomethine portion of 1; otherwise, R'• undergoes dimerization or disproportionation to form hydrocarbons.

Scheme II



Scheme III



Experimental Section[17]

Quaternary hydrazonium iodides were prepared according to Smith and Tan,[5] unless otherwise mentioned.

Benzophenone *N*-methyl-*N*,*N*-pentane-1,5-diylhydrazonium tetrafluoroborate was prepared from 198 g (0.75 mol) of benzophenone *N*,*N*-pentane-1,5-diylhydrazone and trimethyloxonium tetrafluoroborate obtained by the method of Meerwein[18] from 123.5 g (1 mol) of triethyloxonium tetrafluoroborate. The reactants were allowed to stand in dichloromethane solution under nitrogen at ambient temperature for 4 days. Addition of an excess of dry ether to the solution precipitated the crude salt, which was recrystallized from ethanol: yield, 236.8 g (0.67 mol, 90%); mp 172–174 °C dec; IR and NMR spectra essentially identical with those recorded for the corresponding iodide (**1a**).

Anal. Calcd for $C_{19}H_{23}N_2BF_4$: C, 62.32; H, 6.33; N, 7.65. Found: C, 62.34; H, 6.33; N, 7.64.

Benzophenone *N*-Ethyl-*N*,*N*-pentane-1,5-diylhydrazonium Iodide. A mixture of 95.25 g (0.36 mol) of benzophenone *N*,*N*-pentane-1,5-diylhydrazone, 84.0 g (0.54 mol) of ethyl iodide, and 150 mL of acetonitrile (reagent grade, dried by passing through alumina) was refluxed for ca. 48 h with protection from light and moisture. The mixture was then chilled in ice and diluted with several volumes of dry ether. The resulting solid was collected, washed several times with ether, and allowed to dry in air; yield 110.0 g (0.26 mol, 72%); mp 175–180 °C dec; NMR ($CDCl_3$) δ 7.5 (m, 10 H), 4.0 (q, broad s, 6 H), 2.0 (broad s, 6 H), 1.5 (t, 3 H); IR spectrum essentially the same as that[5] of **1a**. An analytical sample, obtained by recrystallization from methanol, was pale yellow: mp 178–180 °C dec.

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[17] Infrared spectra were determined on a Perkin-Elmer Model 237-B instrument; NMR spectra were recorded on a Varian A-60 instrument. Mass spectrometric determinations were carried out by Anne P. Rowe, and microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI.

[18] Meerwein, H. *Org. Synth.* 1966, *46*, 120.

Anal. Calcd for $C_{20}H_{25}N_2I$: C, 57.15; H, 6.00; N, 6.66. Found: C, 57.13; H, 5.93; N, 6.65.

Stability of Hydrazonium Salts to Heat. The results recorded in Table I were obtained according to this representative procedure. Compound **1a** (0.0500 g, 1.23 mmol) and 50 mL of THF were boiled under reflux with stirring in a nitrogen atmosphere for 23 h. Examination of the cooled solution (there was no precipitate) by TLC showed only benzophenone *N*,*N*-pentane-1,5-diylhydrazone. Evaporation of the solution left an oil: 0.31 g (95%); IR spectrum identical with that of benzophenone *N*,*N*-pentane-1,5-diylhydrazone. In those experiments in which dealkylation of the hydrazonium was not complete, unconsumed salt crystallized from the cooled solution before evaporation.

Reaction of 1a·BF$_4$ with Cyanide and with Azide. A mixture of 3.54 g (9.65 mmol) of the tetrafluoroborate corresponding to **1a**, 0.52 g (11.0 mmol) of sodium cyanide, and 25 mL of absolute ethanol was boiled under reflux for 22 h; it rapidly became bright yellow. Examination of the cooled solution by TLC showed the presence of benzophenone *N*,*N*-pentane-1,5-diylhydrazone, benzophenone, and two slower moving components; there was no spot with an R_f value corresponding to α-(phenylimino)acetonitrile (benzoyl cyanide anil). Fractional distillation of an aliquot (30%) of the filtered solution: the first fraction had bp 73 °C (the azeotrope of acetonitrile and ethanol has bp 72.9 °C). After ~5 mL had been collected (weight 4.10 g), the boiling point had leveled off at 77 °C. Analysis by GLC (6-ft 10% glycerol column at 50 °C) gave peaks only for ethanol and acetonitrile; the relative areas corresponded to 0.19 g of acetonitrile in the total reaction mixture (47.7%), which also showed IR absorption at 2260 cm^{-1} (C≡N stretching). The distillation residue was an oil, which was dissolved in chloroform, washed with water, dried (K_2CO_3), and again evaporated. Extraction of the oily residue with petroleum ether (bp 30–60 °C) left 0.40 g (11%) of recovered hydrazonium salt. Chromatography of the petroleum ether extract on an alumina column gave 1.24 g (4.7 mmol, 49%) of benzophenone *N*,*N*-pentane-1,5-diylhydrazone (TLC R_f and IR spectrum identical with those of authentic material), 0.67 g (3.66 mmol, 38%) of benzophenone (mp 47–48 °C), and ca. 0.1 g of an oil that appeared to be a mixture of benzophenone and a component having weak IR bands at 2220 and 2240 cm^{-1}. The high-amplitude NMR spectrum of the oil showed weak peaks at δ 2.8 (br s), 2.63 (s), and 1.5 (br s), which may have been due to benzophenone *N*-methyl-*N*-(5-cyanopentyl)hydrazone.

In a similar experiment using sodium azide instead of sodium cyanide, recovery of starting material was 62% after 7 days at the boiling point of ethanol, and benzophenone *N*,*N*-pentane-1,5-diylhydrazone was isolated in 10% yield. No attempt was made to isolate methyl azide, but a bright yellow oil, identified as benzophenone *N*-methyl-*N*-(5-azidopentyl)hydrazone, was separated in 1.5% yield by chromatography on alumina after elution of the pentanediylhydrazone; IR spectrum very similar to that of the pentanediylhydrazone except for a strong absorption at 2100 cm^{-1} ($-N_3$); NMR ($CDCl_3$) δ 1.5 (m, 6 H), 2.12 (s, 3 H), 2.77 (t, J = 6.5 Hz, 2 H), 3.14 (t, J = 6.5 Hz, 2 H), 7.02 (m, 10 H); MS m/e 321 (calcd for $C_{19}H_{23}N_5$, 321). Benzophenone (1.9%) was eluted last. Examination of the original reaction mixture by TLC showed no spot having an R_f value matching that of 1,5-diphenyltetrazole.

Reactions of Grignard Reagents with Quaternary Hydrazone Salts. The general procedure described by Smith and Tan[5] for reactions in THF was followed, with minor variations as circumstances required. Methylmagnesium chloride in THF was bought from Alfa Inorganics; other Grignard reagents were prepared by standard procedures. The titer of Grignard reagents was determined against standard hydrochloric acid before use. Those reactions that were carried out in diethyl ether differed in that after the ether was distilled, THF or benzene was added in portions and each portion was distilled off to codistill tertiary amine. In most experiments, tertiary amine (*N*-methylpiperidine) was converted to its hydrobromide, mp 184–186 °C, with dry HBr, concentrated aqueous HBr, or HBr in glacial acetic acid. Precipitation appeared to be complete or nearly so; only when decylmagnesium bromide was used was a condensable neutral material (decane or decene) distilled along with the amine. Gaseous neutral products were collected in gas burettes and were examined by IR spectroscopy or were passed into a solution of bromine in CCl_4 in order to convert alkene to *vic*-dibromoalkane. In the experiments with decylmagnesium bromide, the decane and decene that were formed were only incompletely distilled with the solvents and tertiary amine; a substantial part remained behind and was separated from the other neutral component, eicosane, by fractional distillation. Eicosane was isolated from the distillation residue by crystallization from absolute ethanol: mp 36.5–37 °C (lit.[19] mp 36.7 °C); IR spectrum identical with that of authentic material. The C_{10} distillates, bp 72–74 °C/24 mm, were analyzed by gas–liquid chromatography, using an 8-ft column containing 5% Carbowax 1500 or 1% SE30, with benzene as internal standard (relative responses were determined with pure decane, decene, eicosane, and benzophenone). Benzophenone imines were in most cases isolated as hydrochlorides, precipitated from ether with dry HCl; identity was confirmed by hydrolysis (aqueous HCl) to the corresponding benzophenone and ammonium chloride, both of which were isolated and weighed. Results are summarized in Tables III and IV.

Reactions of Hydrazonium Salts with Alkylmagnesium Halides or Alkyllithium Followed by D$_2$O. Oven-dried apparatus was used, and experiments were carried out in an atmosphere of dry nitrogen until D_2O was added. A representative example is that of decylmagnesium bromide with **1f**.

A solution of decylmagnesium bromide in ether was prepared from 22.12 g (0.10 mol) of 1-bromodecane and 2.43 g (0.10 mol) of magnesium turnings. Finely powdered **1f** (43.44 g, 0.093 mol) was added in portions from a flask attached by a Gooch tube, with magnetic stirring, and the mixture was allowed to stand at room temperature for 15 h. The supernatant liquid gave a positive test for Grignard reagent with Michler's ketone. With vigorous stirring, 3.0 g (0.15 mol) of D_2O (99.6%) was added dropwise; after 3 h, the mixture was filtered and the light yellow solid was washed with hexane. The solid was then treated with 500 mL each of chloroform and cold, dilute hydriodic acid and quickly went into solution. The chloroform layer was separated and the aqueous layer was extracted several times with fresh chloroform. The dried (K_2CO_3), combined, chloroform solutions were concentrated and then diluted with ethyl acetate and ether and allowed to stand. The resulting precipitate of recovered **1f** weighed 27.70 g (0.0595 mol, 64%); mp 159–161 °C, undepressed when mixed with authentic material; IR spectrum identical with that of authentic **1e** (no absorption in the 2000–2400-cm^{-1} region); NMR spectrum identical with that of **1e** qualitatively and quantitatively (seven integration sweeps).

The filtrate and hexane washings from the treatment with D_2O were dried and distilled through a column packed with glass helices, yielding 6.42 g (0.045 mol, 45%) of C_{10} hydrocarbon; bp 54–56 °C/10 mm; IR spectrum nearly identical with that of decane, except for a band at 2180 cm^{-1} (C–D) and weak bands at 3075 and 1645 cm^{-1} (decene); the NMR spectrum showed only feeble signals in the olefinic region. Mass spectrometric analysis showed 6% 1-decene, 27% $C_{10}H_{22}$, and 65% $C_{10}H_{21}D$. The distillation residue (3.90 g, 0.014 mol, 28%) was eicosane, identified by IR spectroscopy; recrystallization from hexane gave crystalline material, mp 36–37 °C. The filtrate from the recovered **1e** upon evaporation gave 4.60 g (0.019 mol, 20%) of crystalline *p*,*p*′-dimethoxybenzophenone, mp 140–142 °C (lit.[20] mp 144 °C) after recrystallization from chloroform/petroleum ether. The results are summarized in Table II.

A similar experiment with 0.05 mol of propylmagnesium bromide in THF and 0.05 mol of benzophenone trimethylhydrazonium iodide very slowly evolved 60 mL of gas after the hydrazonium salt was added (uncorrected for temperature or vapor pressure of THF). After 12 h, the supernatant gave no test for Grignard reagent (test repeated five times). After treatment with D_2O followed by dilute hydriodic acid, a one-third aliquot of the chloroform extract yielded 1.45 g of oil by chromatography on alumina; analysis by NMR showed it to consist of benophenone and benzophenone dimethylhydrazone in 7/1 ratio. Petroleum ether precipitate 2.85 g (0.0078 mol) of crude recovered starting material, mp 145–160 °C, raised to 168–170 °C by recrystallization from ethanol. Its IR spectrum showed no detectable absorption

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[19] Krafft, F. *Ber. Detsch. Chem. Ges.* **1886**, *19*, 2220.

[20] Schnackenberg, H.; Scholl, R. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 654.

in the 2000–2400-cm^{-1} region; the NMR spectrum was identical with that of the original hydrazonium salt, and seven integration sweeps showed 8.97 methyl protons to 10.0 phenyl protons (indistinguishable from the original salt).

Registry No. **1a**·BF$_4$, 114595-46-9; **1a**·I, 13134-23-1; **1b**, 114583-43-6; **1c**, 13134-25-3; **1d**, 114583-47-0; **1e**, 114583-42-5; **1f**, 13134-24-2; **10** (Ar = p-$\mathrm{ClC_6H_4}$, R = $\mathrm{CH_2CH_3}$), 114583-46-9; p-$\mathrm{ClC_6H_4CH{=}NN^+(CH_3)(CH_2)_5}$, 16994-36-8; ($p$-$\mathrm{H_3CC_6H_4)_2C{=}NN(CH_2)_5}$, 114583-48-1; ($p$-$\mathrm{ClC_6H_4)_2C{=}NN(CH_2)_5}$, 13134-22-0; $\mathrm{Ph_2C{=}NN(CH_2)_5}$, 13134-20-8; p-$\mathrm{ClC_6H_4CH{=}NN(CH_2)_5}$, 13134-29-7; $\mathrm{C_{10}H_{21}MgBr}$, 17049-50-2; $\mathrm{C_3H_7MgBr}$, 927-77-5; $\mathrm{Ph_2C{=}O}$, 119-61-9; $\mathrm{Ph_2C{=}NN(CH_3)_2}$, 24398-55-8; $\mathrm{Ph_2C{=}NH}$, 1013-88-3; $\mathrm{H_3CN(CH_2)_5}$, 626-67-5; (p-$\mathrm{ClC_6H_4)_2C{=}O}$, 90-98-2; ($p$-$\mathrm{H_3CC_6H_4)_2C{=}O}$, 611-97-2; ($p$-$\mathrm{H_3COC_6H_4)_2C{=}O}$, 90-96-0; ($p$-$\mathrm{H_3COC_6H_4)_2C{=}CHCH_3}$, 4663-13-2; $\mathrm{Ph_2CHNH_2}$, 91-00-9; $\mathrm{(CH_3)_2CHMgCl}$, 1068-55-9; t-$\mathrm{C_4H_9MgCl}$, 677-22-5; decane-d, 71941-72-5; decane, 124-18-5; 1-decane, 872-05-9; eicosane, 112-95-8; benzophenone N,N-pentane-1,5-diylhydrazone, 13134-20-8; acetonitrile, 75-05-8; benzophenone N-methyl-N-(5-cyanopentyl)hydrazone, 114583-44-7; benzophenone N-methyl-N-(5-azidopentyl)hydrazone, 114583-45-8.

Transannular Cyclization of Glaucolide A[†]

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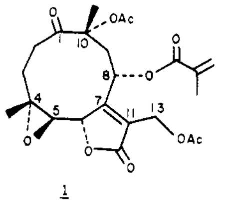
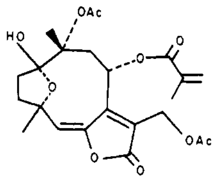
Treatment of glaucolide A with boron trifluoride etherate yielded 10-acetyl-8α-(methacryloyloxy)-2-epivernomargolide 1,4-semiacetal and 8α-(methacryloyloxy)vernomargolide 1,4-semiacetal as a result of a transannular cyclization reaction. Their structures were deduced from spectral data and X-ray diffraction analysis of 5,10-diacetyl-8α-(methacryloyloxy)-2-epivernomargolide 1,4-semiacetal. The 8α-(tigloyloxy)-2-epivernomargolide 1,4-semiacetal had been previously isolated from *Vernonia marginata*.

Transannular cyclization reactions of 1(10),4-germacradienolides and their epoxide derivatives have been studied by several groups.[1] The in vitro transformations of these compounds into eudesmanolides, elemanolides, guaianolides, and cadinolides strongly suggest that cyclodeca-1,5-diene derivatives are biogenetic precursors of a number of sesquiterpene lactones.[1-3]

Glaucolides and hirsutinolides are common sesquiterpene constituents of plants of the genus *Vernonia*[4] (Compositae, tribe Vernonieae). These lactones are characterized by a 7(11)-double bond and an oxygen function at C-13. The biogenetic relation between glaucolides (A, **1**) and hirsutinolides (**2**) has been proposed.[5] Recently, the isolation of cadinanolides **3a**,**b** from plants of the *Vernonia* genus has been reported. The formation of cadinanolides on treatment of a methanolic solution of glaucolide A (**1**) with silica gel suggests that they could be artifacts.[6] This paper deals with the boron trifluoride catalyzed transannular cyclization of glaucolide A (**1**).



1



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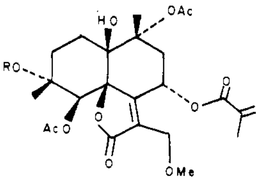
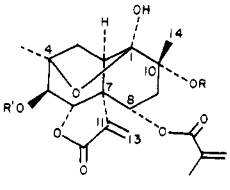


3a, R = H
3b, R = Ac



4a, R = R' = H
b, R = Ac, R' = H
c, R = H, R' = Ac
d, R = R' = Ac

Results and Discussion

Treatment of glaucolide A (**1**) with boron trifluoride etherate in dichloromethane yielded a mixture of products **4a** and **4b** in a ratio that varied with reaction conditions (see Experimental Section). The structures of products **4a** and **4b** were deduced from spectral data.

Product **4b** had a molecular weight of 422 by chemical ionization mass spectrometry. Its IR spectrum showed bands due to hydroxyl groups (3540 cm^{-1}), the α,β-unsaturated γ-lactone function (1770 cm^{-1}), and ester carbonyl (1735 cm^{-1}). The ^{1}H NMR spectrum (Table I) indicated the presence of a new exocyclic methylene conjugated to the carbonyl group of a γ-lactone function (δ 5.65 and 6.43 as sharp singlets, H-13 and H-13′), and the absence of coupling of these signals indicated that C-7 must be quaternary. This was confirmed by the ^{13}C NMR spectrum (Table II), in which a singlet at δ 50.69 could be assigned to C-7 by comparison with the ^{13}C NMR spectra for similar structures.[4,5] The chemical shift found for C-7 indicated that this carbon atom is not bound to oxygen. The ^{1}H NMR spectrum of **4b** also showed a signal due to an acetoxy methyl group (δ 1.96, s, 3 H), which must be bound to a fully substituted carbon atom as there is no signal in the spectrum that can be attributed to a proton geminal to this ester group; therefore it should be bound to C-10. A triplet (J = 3 Hz) observed at δ 4.8 is assigned to the proton geminal to the methacrylate function, H-8. The proton bound to the γ-lactone closure, H-6, is observed as a doublet (J = 5 Hz) at δ 4.28; double-resonance experiments showed that it is coupled to H-5, which appears as a doublet (J = 5 Hz) at δ 3.52, a chemical shift

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[†] Contribution No. 898 of the Instituto de Química, UNAM.

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(4) Jakupovic, J.; Schmeda-Hirschmann, G.; Schuster, A.; Zdero, C.; Bohlmann, F.; King, R. M.; Robinson, H.; Pickardt, J. *Phytochemistry* **1986**, *25*, 145.

(5) Bohlmann, F.; Brindöpke, G.; Rastigi, R. C. *Phytochemistry* **1978**, *17*, 475.

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