fords Ph_3Pb-PQ·, though not so strongly as that obtained by irradiation at 300-350 nm in the absence of TCNE. A charge-transfer process similar to that above, but photochemically pumped, is shown below:

$$Ph_3PbPbPh_3 + TCNE \xrightarrow{650\ nm} [Ph_3PbPbPh_3^{+}\cdot\ TCNE^{-}\cdot] \quad (10)$$

$$[Ph_3PbPbPh_3^{+}\cdot TCNE^{-}] \xrightarrow{fast} [Ph_3Pb\cdot\ Ph_3PbTCNE\cdot] \quad (11)$$

$$[Ph_3Pb\cdot\ Ph_3PbTCNE\cdot] \rightarrow Ph_3Pb\cdot + Ph_3PbTCNE\cdot \quad (12)$$

$$Ph_3Pb\cdot + PQ \rightarrow Ph_3Pb\text{-}PQ\cdot \quad (13)$$

According to this scheme, Ph_3Pb· results from the photoinduced electron transfer from Ph_3Pb-$PbPh_3$ to TCNE in eq 10, followed by the rapid collapse of the ion pair.[7] Furthermore, diffusion of Ph_3Pb· must be sufficiently competitive with cage combination to allow the formation of Ph_3Pb-PQ· in eq 13.

Thus, there is a common theme of charge-transfer interactions, induced thermally and photochemically, leading to facile reactions of organometals. The chemically induced dynamic magnetic polarization studies, both CIDNP and CIDEP, presently in progress will shed further light on the mechanistic details of these interesting processes. Furthermore, in addition to quinones and TCNE, a variety of other compounds, especially organic halides and carbonyl compounds, are known to act as electron acceptors, and many types of organometals other than alkyl metals are also available as electron donors. We hope that these studies will aid in the further development of general concepts related to the activation of organometals, especially as intermediates in reactions with organic substrates.

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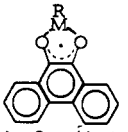
(3) The spin adducts of organometal radicals RM· to 9,10-phenanthroquinone have the general structures shown (K. S. Chen, J. K. S. Wan, and J. K. Kochi,



unpublished work). For the Me_3Sn adduct, $g = 2.0030$ and the hyperfine splittings are 8.75 (^{119}Sn), 8.36 (^{117}Sn), 1.87 (quintet) and 0.43 (quintet) (H) G. For the manganese carbonyl adduct, $g = 2.0028$ and the hfs are 5.50 (^{55}Mn) and 1.72 (quintet) and 0.40 (quintet) (H) G. Both adducts are formed simultaneously from Me_3Sn-$Mn(CO)_5$.
(4) In this experiment energy transfer from PQ* cannot be eliminated since PQ has a weak absorption in this region.
(5) Cf. also N. S. Vyazankin, V. T. Bychkov, O. V. Linzina, L. V. Aleksandrova, and G. A. Razuvaev, *J. Organomet. Chem.*, **31**, 311 (1971). G. A. Abakumov, E. N. Gladyshev, N. S. Vyazankin, G. A. Razuvaev, P. Ya. Bayushkin, and V. A. Muraev, *ibid.*, **64**, 327 (1974).
(6) The maximum is obscured by the end absorption of hexaphenyldilead.
(7) Cation radicals formed in eq 2 and 7 are highly unstable to homolysis. For example, Ph_3Pb-$PbPh_3^{+}\cdot \rightarrow Ph_3Pb\cdot + Ph_3Pb^{+}$ (see A. Peloso, *J. Organomet. Chem.*, **67**, 423 (1974)) and $R_4Sn^{+}\cdot \rightarrow R_3Sn^{+} + R\cdot$ (see H. C. Gardner and J. K. Kochi, *J. Am. Chem. Soc.*, **97**, 1855 (1975)). Consequently the ion pair may collapse to form either a new ion pair as in eq 3 or a radical pair as in eq 8. The latter is favored for dimetals (i.e., $RMMR^{+}\cdot$), whereas the high reactivity of alkyl radicals suggests that an $R_4M^{+}\cdot$ collapses as in eq 3.
(8) We wish to thank the National Research Council of Canada and the National Science Foundation for financial support.

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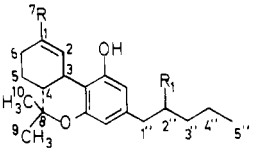
A Terpenic Synthon for Δ^1-Cannabinoids[1]

Sir:

The reversal of the reactivity (i.e., umpolung) of carbonyl compounds when masked as dithioacetals has been shown to be of use for the elaboration of organic molecules.[2] We have applied this principle to the synthesis of metabolites of Δ^1-tetrahydrocannabinol (THC, **1**) by preparing the novel *cis*-



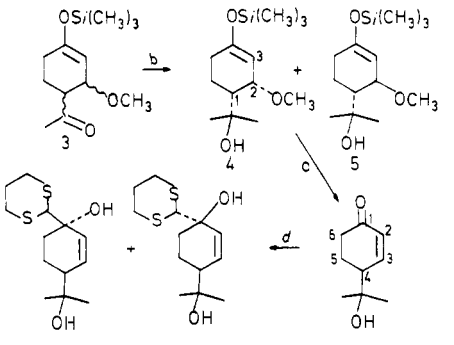
1	R = CH_3	R_1 = H
2	R = COOH	R_1 = OH
14	R = CHO	R_1 = H
15	R = CH_2OH	R_1 = H

and *trans*-terpenes **7** and **8**, which contain the dithiane masking group, and condensing them with olivetol under acid catalysis. Interestingly, by introducing the dithiane moiety into the THC structure, isomerization of the normally[3] labile Δ^1 unsaturation to the Δ^6 isomer is effectively inhibited. In light of the fact that the metabolites of Δ^1-THC also possess this unstable double bond, these versatile dithiane-containing terpenes have great potential as synthons for a variety of hitherto inaccessible metabolites that have been oxidized at C_7 and on the C_5 side chain (e.g., **2**).[3] The synthesis and transformation of these terpenes and the nature of the interactions between the dithiane nucleus and the neighboring double bond are described below.

Treatment of the Diels-Alder adduct[4] (**3**, Scheme I) of *trans*-1-methoxy-3-trimethylsiloxy-1,3-butadiene and methyl vinyl ketone with a 10% molar excess of CH_3MgI afforded, after chromatography (1:1 ether-petroleum ether), equal amounts of compounds **4** and **5** as colorless liquids (99%).[5]

The unsaturated ketone (**6**, 43%)[6] was obtained by hydrolyzing a mixture[7] of **4** and **5** with 2% trichloroacetic acid in CCl_4 at reflux.[8] Addition of the lithium anion of 1,3-dithiane to this ketone occurred exclusively in a 1,2 fashion[9] and furnished a mixture[10] of the desired terpenes **7** and **8**, which were separated by gradient elution on Florisil (ethyl acetate-benzene). The first of these isomers to elute (41%, mp 116-117 °C)[11a] was allowed to react with 1.1 equiv of olivetol in the presence of 0.1 equiv of *p*-toluenesulfonic acid (*p*-TSA) in refluxing benzene for 15 min (Scheme II).[11b] A mixture was obtained from which THCs **9** (20%) and **10** (30%) were isolated by chromatography (graded ether-petroleum ether

Scheme I[a]



[a] All compounds are racemic. [b] CH_3MgI (1.1 equiv). [c] Cl_3CCOOH/CCl_4, reflux. [d] 1,3-Dithiane, BuLi, THF, −30 °C.

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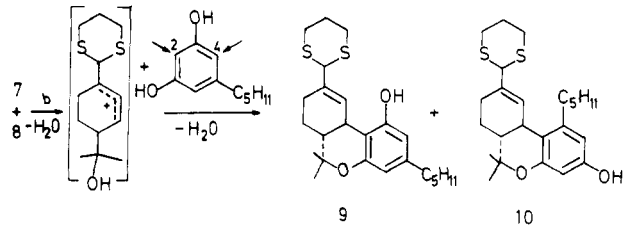
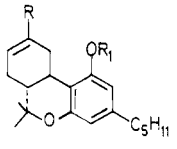
Scheme II[a]

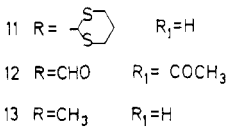


[a] All compounds are racemic. [b] p-TSA, refluxing benzene.

mixtures).[12] The reaction probably proceeds via a common terpenic intermediate that condenses at either the 2 or 4 position of olivetol.[13]

No evidence was found for the formation of Δ^6 analogues of compounds **9** and **10**, even after prolonged treatment with p-TSA (benzene, 70 °C).[14] Furthermore, when THC **11**,[15] the Δ^6 counterpart of **9**, was treated in the same way, it was recovered unchanged. These findings contrast with the fact[3,17]





11 R= R_1=H

12 R=CHO R_1= $COCH_3$

13 $R=CH_3$ R_1=H

that under identical conditions Δ^1- and Δ^6-THC (**1** and **13**, respectively) rapidly equilibrate, with only 3% of the Δ^1 isomer remaining at equilibrium. The Δ^1 unsaturation in THCs **9** and **10** may derive its remarkable stability to acid from electronic effects such as (i) competitive formation of a sulfonium ion adjacent to C_1, or (ii)[18] diminution of hyperconjugative stabilization (a result of the substitution of sulfur for hydrogen at C_7). Either effect would destabilize an incipient carbonium ion at C_1.

As a demonstration of the flexibility afforded cannabinoid synthesis by the dithiane masking group,[19] compound **9** (0.10 mmol) was treated with mercuric oxide (0.21 mmol) and boron trifluoride etherate (0.50 mmol) in 15% aqueous THF[20] to form Δ^1-aldehyde **14** (65%, identified as its acetate).[21] Oxidation of this acetate to the corresponding acid has been reported.[21] Reduction of **14** with $LiAlH_4$ proceeded smoothly and furnished the allylic alcohol **15** (66%), the optically active form of which[22] is a major metabolite of Δ^1-THC in man.

The implications of the ability to inhibit the isomerization of normally labile double bonds to general synthesis are being investigated further.

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(5) *cis*-**4**: NMR (CCl_4) δ 4.93 (d, 1, $J_{2,3}$ = 6 Hz, C_3 H), 3.87 (dd, 1, $J_{1,2}$ = 3, $J_{2,3}$ = 6 Hz, C_2 H). *trans*-**5**: NMR (CCl_4) δ 4.67 (m, 1, $J_{2,3}$ = 2 Hz, C_3 H), 3.95 (m, 1, $J_{1,2}$ = 6 Hz, C_2 H). The mixture had satisfactory C, H analysis.
(6) Ketone **6**: IR (CCl_4) 3460 (OH), 1670 (C=O) cm^{-1}; NMR (CCl_4) δ 7.18 (dt, 1, J_d = 10, J_t = 2 Hz, C_3 H), 5.98 (dd, 1, J = 10, 3 Hz, C_2 H), 3.13 (s, 1, OH, exchangeable), 2.6–1.3 (m, 5), 1.25, 1.15 (2s, 6, $-C(CH_3)_2$). For related compounds displaying similar transannular coupling, see W. G. Dauben, G. W. Shaffer, and N. D. Vietmeyer, *J. Org. Chem.*, **33**, 4060 (1968).
(7) Pure samples of **4** and **5** gave ketone **6** under these conditions, albeit at different rates.
(8) A second compound isolated (11%) was tentatively identified as 4-(1-hydroxy-1-methylethyl)-3-methoxycyclohexanone: NMR (CCl_4) δ 3.33 (s, 3, OCH_3), 4.16 (m, 1, C_3 H); IR (neat) 1720 (C=O) cm^{-1}.
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(11) (a) First isomer eluted: NMR ($CDCl_3$) δ 6.06, 5.98 (AB, 2, J = 11 Hz, olefinics), 4.30 (s, 1, SCHS), 2.93 (m, 4, methylene protons α to sulfur), 2.38 (s, 1, OH, exchangeable), 2.33–1.67 (m, 5), 1.25, 1.22 (2s, 6, $-C(CH_3)_2$); mol wt (high resolution mass spectrometry) 274.10456 (calcd for $C_{13}H_{22}O_2S_2$, 274.10613). (b) Identical results were observed with the second isomer eluted (9%): NMR ($CDCl_3$) δ 6.10, 5.93 (AB, 2, J = 11 Hz, olefinics), 4.25 (s, 1, SCHS), 2.93 (m, 4, methylene protons α to sulfur), 2.33–1.67 (m, 5), 1.25, 1.18 (2s, 6, $-C(CH_3)_2$).
(12) Compound **9**: NMR (CCl_4) δ 6.97 (br, 1, olefinic), 6.11, 6.03 (2, aromatics), 4.53 (s, 1, C_7 H), 3.22 (br, 1, C_3 H), 2.77 (m, 4, methylene protons α to sulfur), 2.37 (m, C_1'' H_2), 1.37, 1.03 (2s, 6, C_8 $(CH_3)_2$), 0.88 (t, 3, C_5'' H_3). **10**: NMR (CCl_4) δ 6.23 (br, 1, olefinic), 6.22, 6.02 (2, aromatics), 4.38 (s, 1, C_7 H), 3.12 (br, 1, C_3 H), 2.77 (m, 4, methylene protons α to sulfur), 2.37 (m, C_1'' H_2), 1.33, 1.00 (2s, 6, C_8 $(CH_3)_2$), 0.90 (t, 3, C_5'' H_3).
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(14) Compound **9** suffers partial decomposition after 1 h, which can be forestalled by acetylating the phenolic hydroxyl group.
(15) Prepared from **12**[16] with 1,3-propanedithiol and boron trifluoride etherate followed by ester hydrolysis.
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A Failure of the Reactivity–Selectivity Principle for the Quaternization of Pyridines

Sir:

Figure 1 shows linear free-energy relationships between logarithms of second-order rate constants for the nucleophilic attack of a series of 3- and 4-substituted pyridines on four alkylating agents of widely varied reactivity. The results are of interest because the unit slope of each line shows that *there is no variation in selectivity* among the nucleophiles in response to the the changing reactivity of the alkylating agent. The behavior is exactly equivalent to that observed by Ritchie and his students[1-10] for the reactivity of a series of resonance-stabilized carbonium ions with (mostly anionic) nucleophiles in water. Ritchie found that his kinetic data followed the one-parameter equation $\log k/\log k_0 = N+$ where $N+$ is characteristic of the nucleophile and is insensitive to variation of the attacking electrophile over a wide range of carbonium stability.

Pross,[11] Giese,[12] and Johnson[13] have reviewed the present status of the reactivity-selectivity principle (RSP) and the

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