142° (47%), and trichloromethylmercuric chloride (20% yield). The latter could not be separated from the phenylmercuric halides, and the yield is based on the bromotrichloromethane formed in the bromine cleavage of the RHgX mixture.

Such transfer reactions are not confined to phenyl(bromodichloromethyl)mercury + mercury chloride systems. We found a similar reaction to occur when phenylmercuric chloride and phenyl(bromochloromethyl)mercury[9] were heated in chlorobenzene at reflux for 34 hr. At the end of this time a mixture of $C_6H_5HgCHCl_2$ and $C_6H_5HgCHClBr$ was present (qualitative identification by infrared and nmr: *cf.* ref 9). Bromination of this mixture showed that the former had been formed in 76% yield.

These reactions appear to occur rapidly only at temperatures at which rapid CX_2 transfer from $C_6H_5HgCX_2Br$ to olefins occurs, and thus it is most likely that we are dealing here with bona fide CCl_2 transfer from $C_6H_5HgCCl_2Br$ to ArHgCl and $HgCl_2$. This reaction very likely involves transfer of free or complexed CCl_2 to substrate. If the latter is the case, a three-center transition state (I) may be considered. However, a direct,

$$C_6H_5HgCCl_2Br \rightleftharpoons C_6H_5HgBr{\rightarrow}CCl_2 \xrightleftharpoons{C_6H_5HgCl}$$

$$C_6H_5Hg{-}Br\cdots\overset{Cl\ \ Cl}{\underset{\ddot{}}{C}}\cdots Cl{-}HgC_6H_5 \xrightleftharpoons{-C_6H_5HgBr}$$

I

$$C_6H_5HgCl{\rightarrow}CCl_2 \rightleftharpoons C_6H_5HgCCl_3$$

bimolecular transfer mechanism, which we consider less likely, cannot be ruled out at this time.

It is the greater thermal stability of trichloromethylmercury compounds as compared with bromodichloromethylmercury compounds[5] which makes the observation of these reactions possible. One would have to use isotopic labeling in order to see an analogous reaction between $C_6H_5HgCCl_2Br$ and C_6H_5HgBr. However, one would expect that added phenylmercuric bromide should decrease the rate of olefin consumption in the olefin + $C_6H_5HgCCl_2Br$ reaction. Experiments have shown this to be the case.[8]

The finding that under proper conditions CX_2 insertion into the mercury–halogen bond does indeed occur would lead one to expect that similar insertion should be possible into other metal–halogen linkages. We are exploring this possibility, especially with heavy metal (Sn, Pb, Sb) halides and organometallic halides, and have thus far been able to prepare R_3SnCX_3 compounds by this procedure.[10]

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(9) D. Seyferth, H. D. Simmons, Jr., and L. J. Todd, *J. Organometal. Chem.*, 2, 282 (1964).
(10) D. Seyferth and F. M. Armbrecht, work in progress.
(11) Alfred P. Sloan Foundation Fellow, 1962–1966.

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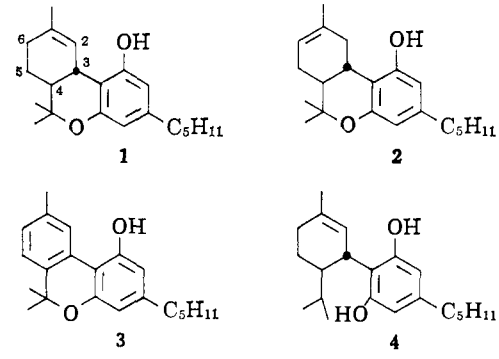
Isolation of *trans*-Δ^6-Tetrahydrocannabinol from Marijuana

Sir:

The structure[1] and the total synthesis[2] of the *dl* modification of a psychotomimetically active constituent, *trans*-Δ^1-tetrahydrocannabinol (**1**), present in hashish, have recently been reported.

We wish to report the isolation of a second psychotomimetically active constituent,[3] *trans*-Δ^6-tetrahydrocannabinol (**2**), from marijuana. Chromatography of a petroleum ether (bp 30–60°) extract of the flowering tops and leaves of a fresh sample of marijuana[4] grown in Maryland on silicic acid yielded on elution with benzene a phenolic fraction. This fraction was shown to contain the *trans*-Δ^1- and -Δ^6-tetrahydrocannabinols, cannabinol (**3**), and cannabidiol (**4**) by thin layer chromatography on silica gel–silver nitrate (5:1). The phenolic fraction was separated into its various components by chromatography on silicic acid–silver nitrate (5:1), using benzene as the eluting solvent. Cannabinol was eluted first followed by the *trans*-Δ^1-tetrahydrocannabinol and then the *trans*-Δ^6-tetrahydrocannabinol. The cannabidiol was eluted from the column with ether. The *trans*-Δ^6-tetrahydrocannabinol (**2**) was also obtained from the phenolic fraction present in a fresh sample of marijuana of Mexican origin. In this case the phenolic fraction was separated into its constituents by partition chromatography.[5] N,N-Dimethylformamide on Celite was used as the stationary phase and cyclohexane saturated with N,N-dimethylformamide as the mobile phase. The *trans*-Δ^1-tetrahydrocannabinol accounted for 90% and the *trans*-Δ^6-tetrahydrocannabinol 10% of the total tetrahydrocannabinol content of the above two samples of marijuana.



1 **2** **3** **4**

It was demonstrated that **2** was not an artifact formed during the workup of the marijuana extract by two different experiments. Chromatography of a pure sample of **1** by either of the two methods described did not result in the formation of any of **2**. The tetrahydrocannabinol (**2**) was not formed during the extraction of the marijuana with petroleum ether, since the petroleum ether extracts of a 2-year-old sample of marijuana of

(1) Y. Gaoni and R. Mechoulam, *J. Am. Chem. Soc.*, **86**, 1646 (1964).
(2) Y. Gaoni and R. Mechoulam, *ibid.*, **87**, 3273 (1965).
(3) R. Adams, C. K. Cain, W. D. McPhee, and R. B. Wearn, *ibid.*, **63**, 2209 (1941). These workers obtained **2** by a partial synthesis from cannabidiol (**4**) and demonstrated the physiological activity of **2** by clinical experiments on humans.
(4) We wish to thank Dr. M. Lerner of the U. S. Customs Laboratories, Baltimore, Md., for supplying the marijuana used in this investigation.
(5) R. S. DeRopp, *J. Am. Pharm. Assoc.*, **49**, 756 (1960).

Spanish origin and a 3-year-old sample of Mexican origin showed only the presence of **1** by thin layer chromatography.

The *trans*-Δ^6-tetrahydrocannabinol (**2**), $[\alpha]^{27}D$ $-260°$ (*c* 0.700, absolute EtOH), λ_{max}^{EtOH} 283 (ϵ 1390), 276 (ϵ 1330), and 209 mμ (ϵ 41000) (*Anal.* Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.9; H, 9.8), had the same optical rotation as a tetrahydrocannabinol Adams, *et al.*,[3] obtained from the treatment of cannabidiol with *p*-toluenesulfonic acid in refluxing benzene. Treatment of cannabidol with *p*-toluenesulfonic acid under the conditions described by Adams yielded a product identical in all respects (infrared, ultraviolet, nmr, and optical rotation) with the natural product **2**. This material was also identical in all respects except optical rotation with the totally synthetic *dl-trans*-Δ^6-tetrahydrocannabinol prepared by Taylor, *et al.*[6] Adams[3] assigned a Δ^6 position for the double bond in **2**, but did not make any stereochemical assignments at C-3 and C-4.

The stereochemistry at C-3 and C-4 in **1** and **2** was shown to be identical. Hydrogenation of **2** in the presence of a platinium catalyst yielded a colorless resin, $[\alpha]^{27}D$ $-109°$ (*c* 0.502, absolute EtOH), which had an infrared spectrum that was identical with the infrared spectrum of the colorless resin, $[\alpha]^{27}D$ $-108°$ (*c* 0.507, absolute EtOH) (*Anal.* Calcd for $C_{21}H_{32}O_2$: C, 79.68; H, 10.19. Found: C, 79.5; H, 10.5), obtained by the catalytic hydrogenation of **1**. This result established that **1** and **2** had the same stereochemistry at C-3 and C-4, but different positions of the double bond. Treatment of **1** with a catalytic amount of *p*-toluenesulfonic acid in toluene for 10 hr at 100° resulted in over 90% conversion to **2**. This also indicated that **1** and **2** differed only in the position of the alicyclic double bond.

(6) E. C. Taylor, K. Lenard, and Y. Shvo, *J. Am. Chem. Soc.*, **88**, 367 (1966).

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Reductive Acylation of Ketones[1]

Sir:

We wish to report some one-step transformations of the type

$$RCOR' \longrightarrow RR'CHOCOR''$$

brought about in high yield under neutral, mild, and convenient conditions.

Although ketone-to-ester conversions involving reduction of the ketone followed by acid- or base-catalyzed esterification in a separate step have been extensively investigated, very few reports have appeared in the literature describing the occurrence of such conversions under free-radical conditions.[2] In all of these cases, however, per cent conversions to the desired product were not high and the R''CO– group was, by the nature of the reaction, derived from the starting carbonyl compound.

Table I. Summary of Results

Reactants (mmole)	Reaction conditions[a]	Product[b]
In 0.148 g of C_6H_6	0.5 hr	
CH_3COCl (0.396)		$OCOCH_3$
$C_6H_5COCH_3$ (0.410)		|
$(C_6H_5)_3SnH$ (0.528)[d]		$C_6H_5CHCH_3$
In 0.187 g of C_6H_6	2 hr	
CH_3CH_2COCl (0.492)		$OCOCH_2CH_3$
$C_6H_5COCH_3$ (0.491)		|
$(C_6H_5)_3SnH$ (0.500)		$C_6H_5CHCH_3$
In 0.153 g of C_6H_6	15 hr	
CH_3COCl (0.436)		$OCOCH_3$
$C_6H_5COCH_2CH_3$ (0.432)		|
$(C_6H_5)_3SnH$ (0.703)[d]		$C_6H_5CHCH_2CH_3$
In 0.230 g of C_6H_6	40 hr	
CH_3COCl (0.654)[c,d]		$OCOCH_3$
$C_6H_5COCH(CH_3)_2$ (0.445)		|
$(C_6H_5)_3SnH$ (0.657)		$C_6H_5CHCH(CH_3)_2$
In 0.196 g of C_6H_6	0.5 hr[a]	
C_6H_5COCl (0.619)[c]	122°	$OCOC_6H_5$
$C_6H_5COCH_3$ (0.383)		|
$(C_6H_5)_3SnH$ (0.625)		$C_6H_5CHCH_3$

[a] It was not determined whether a shorter reaction time would be adequate. [b] In all cases the ketone was quantitatively converted to the single product indicated, as judged by nmr spectroscopy and gas chromatographic analysis. [c] Use of equimolar amounts of reagents resulted in only 70% conversion. [d] It was not determined whether this large an excess was necessary for "quantitative" conversion. [e] Ambient temperature unless indicated otherwise.

In order to determine the feasibility of a free-radical approach to effecting this conversion, it was desired to have the acyl radical which was to be added to the ketone generated in a clean reaction (no other radicals formed) at a reasonably low temperature. The method of generation used, which appears to meet these criteria, is the reaction of an organic halide with an organotin hydride, conditions which are known to bring about reduction of the halide, presumably by a free-radical mechanism.[8]

It was thought that the following reactions would occur.[9]

$$R''COCl + (C_6H_5)_3Sn\cdot \longrightarrow R''\dot{C}O + (C_6H_5)_3SnCl \quad (1)$$

$$R''\dot{C}O + RCOR' \longrightarrow RR'\dot{C}OCOR'' \quad (2)$$

$$RR'\dot{C}OCOR'' + (C_6H_5)_3SnH \longrightarrow RR'CHOCOR'' + (C_6H_5)_3Sn\cdot, \text{ etc.} \quad (3)$$

(1) This work was supported by American Cancer Society Institutional Grant 41-F.

(2) Rust, Seubold, and Vaughan[3] treated benzaldehyde with *t*-butyl peroxide for 30 hr at 130° and obtained 35% conversion to *sym*-diphenylethylene glycol dibenzoate; Beckwith and Evans[4] carried out the same reaction for 72 hr at 132° and obtained 31% conversion. Huang and Lee[5] treated *o*-tolualdehyde with *t*-butyl peroxide for 32 hr at 125° and obtained 5% conversion to α,α'-di(α-methylbenzoyloxy)-2,2'-dimethylbibenzyl. Urry, Trecker, and Hartzler[6] treated 2-phenyl-1,2-dimethylbutanal with *t*-butyl peroxide for 20 hr at 140° and obtained 38% conversion to α,α,β-trimethyl-β-phenethyl β'-phenyl,α',β'-dimethylbutyrate. Kupchik and Kiesel[7] treated benzoyl chloride with triphenyltin hydride and obtained 87% conversion to benzyl benzoate; they also treated *p*-methylbenzoyl chloride similarly and obtained 79% conversion to *p*-tolyl *p*-toluate.

(3) F. F. Rust, F. H Seubold, and W. R. Vaughan, *J. Am. Chem. Soc.*, **70**, 3258 (1948).

(4) A. L. J. Beckwith and G. W. Evans, *J. Chem. Soc.*, 130 (1962).

(5) R. L. Huang and H. H. Lee, *ibid.*, 2500 (1964).

(6) W. H. Urry, D. J. Trecker, and H. D. Hartzler, *J. Org. Chem.*, **29**, 1663 (1964).

(7) E. J. Kupchik and R. J. Kiesel, *ibid.*, **29**, 3690 (1964).

(8) D. H. Lorenz, P. Shapiro, A. Stern, and E. I. Becker, *ibid.*, **28**, 2332 (1963); E. P. Kupchik and R. J. Kiesel, *ibid.*, **29**, 764, 3690 (1964); L. W. Menapace and H. G. Kuivila, *J. Am. Chem. Soc.*, **86**, 3047 (1964).

(9) Although the reactions in Table I appear to be most easily visualizable in these terms, no evidence in favor of this scheme can be offered in addition to that already given.