explained by an intramolecular hydrogen bonding in this acid competing with its intermolecular association.

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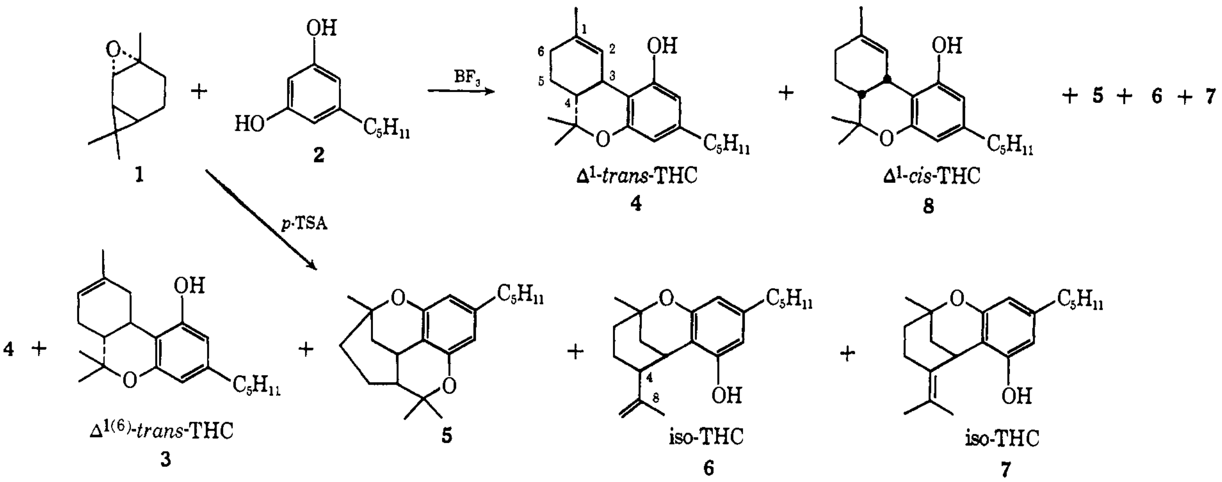
Hashish. A Stereospecific Synthesis of (−)-Δ^1- and (−)-$\Delta^{1(6)}$-Tetrahydrocannabinols[1]

Sir:

Two stereospecific syntheses of (−)-$\Delta^{1(6)}$-tetrahydrocannabinol (THC, **3**) have been reported which utilize the condensation of olivetol with either (−)-verbenol[2] or (+)-*cis*- or *trans*-*p*-mentha-2,8-dien-1-ol[3] in the presence of acids. In both cases the synthesis of (−)-Δ^1-THC (**4**) was achieved by addition and then elimination of hydrogen chloride to form **3**.

Scheme I



We wish to report an entry into cannabinoids *via* carane derivatives that provides a one-step stereospecific synthesis, leading to (−)-$\Delta^{1(6)}$-THC, and hence to (−)-Δ^1-THC. Furthermore, a slight change in the experimental conditions also provides the first one-step synthesis of Δ^1-THC (**4**) of high optical activity.

We have found that by allowing (+)-*trans*-2-carene oxide[4,5] (**1**) to react with an equimolar quantity of olivetol (**2**) in the presence of *p*-toluenesulfonic acid (0.05 mol/mol of olivetol) in benzene, a complex mixture of products was obtained. This mixture contained (glc)[6] 23% $\Delta^{1(6)}$-THC, 7% Δ^1-THC, 13% citrylidenecannabis (**5**) and Δ^8-iso-THC (**6**), 11% $\Delta^{4(8)}$-iso-THC (**7**), and 34% unreacted olivetol.[7] Careful chromatography of this mixture on silica gel and elution with 60:40 hexane–benzene, followed by chromatography on Florisil and elution with 2:98 ether–petroleum ether (bp 30–40°), gave (−)-$\Delta^{1(6)}$-THC (infrared nmr, glc, and tlc identical with those of authentic material; $[\alpha]_D$ −245° ($CHCl_3$), indicating an optical purity of *ca.* 95%).[8] Since (−)-$\Delta^{1(6)}$-THC has already been converted to (−)-Δ^1-THC,[2,3] this route constitutes yet another stereospecific synthesis of (−)-**4**.

However, it was found that in the above condensation reaction, if the molar ratio of **1** was increased (1.6 mol/mol of olivetol), the major products formed were Δ^1-*trans*-THC (28%) and Δ^1-*cis*-THC (**8**) together with other products, but no $\Delta^{1(6)}$-THC was formed (Scheme I). Similar results were obtained by the addition of 1% boron trifluoride etherate in methylene chloride to an equimolar ratio of **1** and **2** in methylene chloride at room temperature. The mixture of products thus obtained was chromatographed on Florisil and eluted with 2:98 ether-petroleum ether (30–40°). A fraction, $[\alpha]_D$ −59° ($CHCl_3$), contained **4** and **8** (60:40 ratio), as shown by gas chromatographic[6] and nmr analyses[9] and by conversion to $\Delta^{1(6)}$-THC and iso-THCs on treatment with *p*-toluenesulfonic acid in refluxing benzene.[1,6,10] This fraction was separated by preparative vpc (column 3.8% SE 30 on Diatoport S; gas, helium; oven temperature, 240°) to give (−)-Δ^1-THC[6] with an optical purity of >80% by comparison with the ORD curve of an authentic sample.[11] This therefore provides the first one-step synthesis of optically active Δ^1-THC.

It is interesting to note that no cannabidiol[3] was formed in any of these reactions and that the ratio of trans to cis products was *ca.* 1.2 with *p*-toluenesul-

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(1) Hashish. V. For part IV see R. K. Razdan and B. Zitko, *Tetrahedron Lett.*, 4947 (1969).

(2) R. Mechoulam, P. Braun, and Y. Gaoni, *J. Amer. Chem. Soc.*, **89**, 4552 (1967).

(3) T. Petrzilka, W. Haefliger, and C. Sikemeier, *Helv. Chim. Acta*, **52**, 1102 (1969).

(4) Supplied by Glidden and Co., $[\alpha]_D$ −45.0° (neat), n^{20}_D 1.4642, bp 75° (5 mm). It contains Δ^3-carene oxide as impurity (estimated as 15% by glc and nmr). It was synthesized from Δ^3-carene.

(5) B. A. Arbuzov and A. R. Vil'chinskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 954 (1967); *cf. Chem. Abstr.*, **68**, 22063 (1968). For a reaction of *trans*-4-carene oxide in the presence of acids see von G. Ohloff and W. Giersch, *Helv. Chim. Acta*, **51**, 1328 (1968).

(6) The compounds were identified on the basis of relative retention times of authentic samples and by addition of authentic samples to the reaction mixture with subsequent glc.

(7) The yield of $\Delta^{1(6)}$-THC is 54% of theory, on the basis of olivetol reacted.

(8) The material after silica gel chromatography was identical with **3** except it had $[\alpha]_D$ −212° ($CHCl_3$). We attribute this difficulty in obtaining optically pure **3** to our carene oxide, which was not prepared from the natural Δ^2-carene.[4] Further experiments utilizing the natural Δ^2-carene are planned to confirm this point.

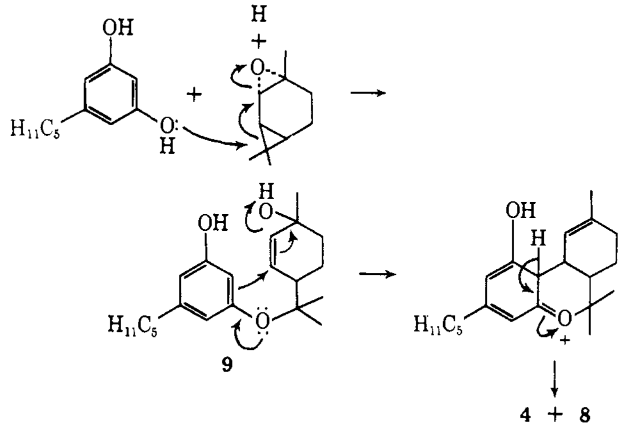
(9) The nmr showed a clear separation of signals at δ ($CDCl_3$) 1.08 (s, one of the geminal methyls) and 3.18 (br, d, C-3 proton), which correspond to Δ^1-*trans*-THC, and similarly 1.26 (s) and 3.56 (br) corresponding to Δ^1-*cis*-THC. See K. E. Fahrenholtz, M. Lurie, and R. W. Kierstead, *J. Amer. Chem. Soc.*, **89**, 5934 (1967).

(10) Some **5** and **8** were also formed as expected.[1]

(11) Both ORD curves were found to be parallel in the 280–600-mμ region; $[\alpha]_D$ −131 ± 2° (cyclohexane); an authentic sample of (−)-**4** had $[\alpha]_D$ −148 ± 2°.

fonic acid, whereas it was *ca.* 0.6 (*i.e.*, increase of cis products) with the use of boron trifluoride etherate. We interpret these results as suggesting that *trans*- and *cis*-Δ^1-TNCs are first formed (Scheme II) and are then converted into their transformation products **3** and **5** → **7**, respectively. This is in complete agreement with the known acid-catalyzed transformations in cannabinoids.[1,12] Furthermore, the results suggest that the reaction has a more concerted character when a nonprotonic acid catalyst like BF_3 is used, whereas acid catalysts like *p*-TSA, which give a more carbonium ion character to the allylic system in the intermediate **9**, give the trans products, which are more thermodynamically and kinetically stable.[1,2]

Scheme II



Further work along these lines is in progress and will be the subject of future communications.

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(12) B. Yagen and R. Mechoulam, *Tetrahedron Lett.*, 5353 (1969).
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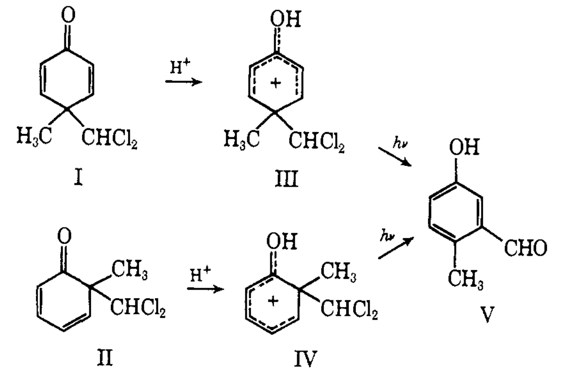
Photochemical Rearrangement of Cyclohexadienyl Cations

Sir:

In the presence of sulfuric acid, 4,4-dimethyl- and 4,4-diphenyl-substituted cyclohexa-2,5-dienones readily undergo the dienone–phenol rearrangement.[1] In contrast, the "abnormal Reimer–Tieman" dienones 4-methyl-4-dichloromethylcyclohexa-2,5-dienone (I) and 6-methyl-6-dichloromethylcyclohexa-2,4-dienone (II) do not rearrange under similar conditions.[2] Furthermore, they can be recovered quantitatively from concentrated sulfuric acid by dilution with water,[3] in spite of the fact that their uv-visible and nmr spectra clearly indicate the formation of the ionic species responsible for the normal rearrangement, the oxygen-protonated, delocalized cyclohexadienyl cations III and IV, respectively.[4,5] Only heating at 60° for 24 hr causes partial 1,2 migration of the methyl group in I and generates, after hydrolysis, 2-methyl-4-hydroxybenzaldehyde.[6]



In the present communication we report the efficient photorearrangement of ions III and IV to the same photoproduct, 2-methyl-5-hydroxybenzaldehyde (V).

Figures 1 and 2 show successive changes in the uv-visible absorption spectra of IV and III following short-duration irradiations[7] with light of 370 and 262 nm, respectively, at ambient temperature. Figure 1a illustrates the gradual disappearance of IV (λ_{max} 370 nm) with simultaneous increase in absorbance at 258 and 298 nm. That these two absorption bands do not belong to the same species is shown by the subsequent changes shown in Figure 1b. Thus the peak at 298 nm continues to increase upon further irradiation whereas that at 258 nm gradually decreases after reaching a maximum. The final product (λ_{max} 298 and 388 nm) seems to be photostable. The absorption spectrum of a solution of IV irradiated to any per cent conversion remained unchanged after standing in the dark for extended times. This testifies that the changes in Figure 1 are photochemical with no interference from thermal reactions. It is quite clear that ion IV is converted photochemically to an intermediate species (λ_{max} 258 nm) which in turn undergoes photolysis to a product absorbing at λ_{max} 298 nm. The three isosbestic points at 248, 272, and 332 nm in Figure 1b indicate that the intermediate → product photoconversion preserves a constant stoichiometry and that the transformation is void of competitive or consecutive slow reactions. On the other hand the isosbestic point at 329 nm in Figure 1a merely indicates a coincidental equality of extinction coefficients at that wavelength for the three species present.

Figure 2 shows changes in the absorption spectrum of III on irradiation at 262 nm. Again the photoreaction is quite clean and the final product exhibits a uv-visible spectrum (λ_{max} 298 and 388 nm) indistinguishable from that obtained from IV.

Preparative-scale photolysis of either III or IV 10^{-2} *M* in 96% H_2SO_4 at 17° was accompanied by HCl liber-

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(1) (a) F. G. Bordwell and K. M. Wellman, *J. Org. Chem.*, **29**, 509 (1964); (b) H. E. Zimmerman and D. I. Schuster, *J. Amer. Chem. Soc.*, **84**, 4527 (1962); (c) A. J. Waring, *Advan. Alicyclic Chem.*, **1**, 207 (1966).

(2) K. v. Anwers and G. Keil, *Ber.*, **35**, 4207 (1902).

(3) H. Budzikiewicz, *Tetrahedron Lett.*, 12 (1960).

(4) E. C. Friedrich, *J. Org. Chem.*, **33**, 413 (1968).

(5) V. P. Vitullo, *ibid.*, **34**, 224 (1969).

(6) T. G. Miller, *ibid.*, **27**, 1549 (1962).

(7) Bausch & Lomb high intensity monochromator with 125-W high-pressure Hg arc.