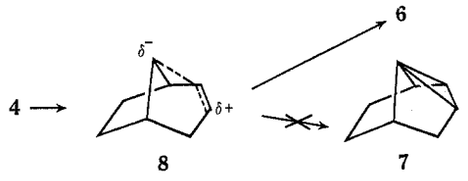
ilized carbene would be of the unsymmetrical homoallylic type indicated in **8**, as has been suggested for the



related carbonium ion.[11] Although the nonclassical carbene rationalization is an attractive one for explaining the chemistry of **2**, present results do not allow a decision between it and alternative mechanisms. We plan to pursue experiments which will help to distinguish between possible mechanisms.

Experimental Section[12]

Bicyclo[3.2.1]oct-2-en-8-one was prepared by the method of Foote and Woodward,[13] except that dioxane was used in place of methanol for cleavage of the ethylene ketal. This gave the ketone with only a trace of the ketal (by gc), boiling at 74–75° (8 mm) [lit. bp 130° (25 mm),[13] 69–70° (5 mm)[11]].

Bicyclo[3.2.1]octan-8-one was prepared from the bicyclo[3.2.1]oct-2-en-8-one described above by hydrogenation over platinum oxide in methanol.[13] This produced a mixture containing 40% ketone and 60% of a higher boiling material presumed to be the corresponding dimethyl ketal. Treatment of the mixture under the cleavage conditions mentioned above gave the ketone in 73% yield after sublimation (90°, aspirator pressure) as a white, waxy solid melting at 141–144.8° (st, lit.[13] mp 140–141°).

Bicyclo[3.2.1]octan-8-one Tosylhydrazone (3).—Bicyclo[3.2.1]octan-8-one (1.24 g, 0.01 mol) in 5 ml of methanol was added all at once to a gently refluxing solution of 1.96 g (0.0105 mol) of *p*-toluenesulfonylhydrazine[14] in 10 ml of methanol. More methanol (5 ml) was added and the solution was allowed to reflux for 20 min. An equal volume of hot water was added and the tosylhydrazone was allowed to crystallize. Collection of the solid and recrystallization from methanol–water gave 2.64 g (90% yield) of white, crystalline **3** melting at 182.5–184° dec.

Anal. Calcd for $C_{15}H_{20}N_2O_2S$: C, 61.62; H, 6.90. Found: C, 61.48; H, 6.86.

Bicyclo[3.2.1]oct-2-en-8-one Tosylhydrazone (4).—Bicyclo[3.2.1]oct-2-en-8-one was converted to the crystalline tosylhydrazone in 98% yield by the same procedure as described above for **3**, mp 182.5–183.5° dec.

Anal. Calcd for $C_{15}H_{18}N_2O_2S$: C, 62.04; H, 6.25. Found: C, 62.28; H, 6.13.

Decomposition of Tosylhydrazone 3.—**3** (294 mg, 1 mmol) and 112 mg (2 mmol) of sodium methoxide were slurried in 5 ml of dry diglyme in a single-necked flask fitted with a condenser, and the mixture was heated at 145–150° with magnetic stirring for 1 hr. Rapid evolution of nitrogen was over in about 10 min. The reaction mixture was allowed to cool, and then poured into 50 ml of water. The aqueous solution was extracted with five 10-ml portions of pentane and the combined pentane extracts were washed with eight 10-ml portions of water and dried ($MgSO_4$). The pentane solution was concentrated by distillation (glass helicies column) to about 1 ml and analyzed by gas chromatography on a 150 ft × 0.01 in. stainless steel capillary column coated with tris-β-cyanoethoxypropane (TCEP) and operated at 58° and 25 psi nitrogen pressure. The analysis showed peaks at 5.4, 6.4, and 9.2 min in the respective relative amounts of 1.5, 98, and *ca.* 0.5%. A duplicate experiment using 4 equiv of base gave the same product composition within experimental error. The major product has the same gc retention time and ir and nmr spectra as an authentic sample of tricyclo[3.3.0.$0^{2,8}$]octane (**5**) prepared by the method of Schwarz, *et al.*[5]

(11) N. A. LeBel and L. A. Spurlock, *Tetrahedron*, **20**, 215 (1964).

(12) Melting points and boiling points are uncorrected. Nmr spectra were recorded on a Varian Associates A-60 spectrometer, using tetramethylsilane as an internal standard.

(13) C. S. Foote and R. B. Woodward, *Tetrahedron*, **20**, 687 (1964).

(14) L. Friedman, R. L. Little, and W. R. Reichle, *Org. Syn.*, **40**, 93 (1960).

In a larger scale experiment[15] 3.62 g (0.0124 mol) of **3** was decomposed in 25 ml of diglyme with 2.98 g (0.0552 mol) of sodium methoxide. The crude product (1.20 g, 90% yield) was distilled at 131–136° (647 mm) [lit.[5] bp 68–72° (45 mm)] to give 0.916 g of a colorless oil (69% overall yield). The tricyclooctane was 95% pure by gc analysis.

Decomposition of Tosylhydrazone 4.—Decomposition of **4** and analysis of the products were carried out as described above for **3**. With 2 equiv of base, gc analysis showed peaks at 6.3 and 9.1 min in the relative amounts of 2 and 98%, respectively. With 4 equiv of base 4% of the minor component was observed. The major product is a colorless liquid which appears to polymerize readily. Pure compound was isolated by preparative gas chromatography on a 6 ft × 0.25 in. column packed with 10% FFAP[16] on Chromosorb W, operating temperature 72°, helium flow 50 ml/min. Spectral data for the compound are listed in the text above and are consistent with bicyclo[3.3.0]octa-1,7-diene (**6**) as the structure.

Hydrogenation of the decomposition product over platinum oxide in pentane gave a colorless liquid which was shown to be identical with a sample of bicyclo[3.3.0]octane by a comparison of their gc retention times and nmr spectra. The nmr spectrum (CCl_4) consists of a broad singlet at δ 2.48 (2 H, bridge) and a highly symmetrical complex multiplet centered at δ 1.5 (12 H). The authentic sample of bicyclo[3.3.0]octane was prepared by the thermal decomposition of bicyclo[3.3.0]octan-2-one[17] semicarbazone, mp 183–184° dec (lit.[18] mp 180° dec), with potassium hydroxide as described by Cook and Linstead.[18] The hydrogenation product was also compared with a sample of bicyclo[4.2.0]octane prepared by hydrogenation over platinum oxide in pentane of the photolysis product of 1,3-cyclooctadiene.[19] The two had different gc retention times on the 150-ft capillary column at 58° and different nmr spectra. The nmr spectrum (neat) of bicyclo[4.2.0]octane consists of a broad singlet at δ 2.28 (2 H, bridge), a complex multiplet centered at δ 1.78 (4 H, C_7, C_8), and a singlet at δ 1.48 (8 H, C_2, C_3, C_4, C_5).

Registry No.—**1**, 34952-71-1; **2**, 34952-72-2; **3**, 34956-57-5; **4**, 34956-58-6; **5**, 2401-89-0; **6**, 34956-60-0.

Acknowledgment.—We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Graduate School of the University of Nevada, Reno, for support of this research.

(15) Data of Dean Evans, University of Nevada.

(16) FFAP is a modified Carbowax 20M stationary phase available from Varian Aerograph, Walnut Creek, Calif.

(17) A. C. Cope and W. R. Schmitz, *J. Amer. Chem. Soc.*, **72**, 3056 (1950).

(18) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 946 (1934).

(19) (a) R. S. H. Liu, *J. Amer. Chem. Soc.*, **89**, 112 (1967); (b) W. J. Nebe and G. J. Fonken, *ibid.*, **91**, 1249 (1969).

The Dienone–Phenol Rearrangement. The So-Called Medium Effect[1]

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Among the acid-catalyzed rearrangements of dienones to phenols[3–6] are found examples in which the course of

(1) Supported by a grant from the Robert A. Welch Foundation.

(2) Postdoctoral Fellow, 1969–1971.

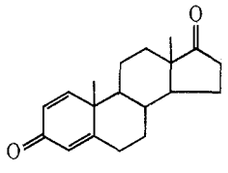
(3) N. L. Wendler in "Molecular Rearrangements," Part 2, P. de Mayo, Ed., Interscience, New York, N. Y., 1964, pp 1028–1034.

(4) A. J. Waring in "Alicyclic Chemistry," Vol. 1, H. Hart and G. J. Karabatsos, Ed., Academic Press, New York, N. Y., 1966, pp 207–215.

(5) H. J. Shine, "Aromatic Rearrangements," Elsevier, Amsterdam, 1967, pp 55–66.

(6) B. Miller in "Mechanisms of Molecular Migrations," Vol. 1, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1968, pp 275–285.

rearrangement is affected by the medium. The rearrangement of 1,4-androstadiene-3,17-dione (**1**) in acetic anhydride–zinc chloride at room temperature gave 1-acetoxy-4-methyl-3-deoxyestrone (**2a**) in 70–92% yield.[7] In contrast, **1** in 48% hydrobromic acid at room temperature gave 55% of 1-methylestrone (**3b**) and only



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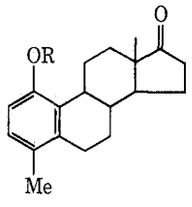
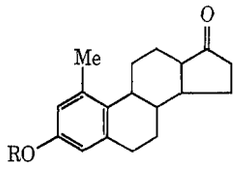
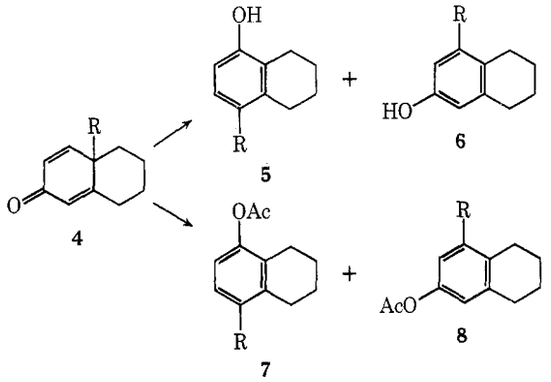


2a, R = Ac
b, R = H
c, R = F_3CCO



3a, R = Ac
b, R = H
c, R = F_3CCO

11% of 1-hydroxy-4-methyl-3-deoxyestrone (**2b**).[8] Similar results were obtained with **1** and concentrated hydrochloric acid at room temperature (48% of **3b**, 25% of **2b**), and by boiling **1** in a mixture of acetic and hydrochloric acids (35% of **3b**, 10% of **2b**). Furthermore, **1** in trifluoroacetic anhydride at room temperature gave 80% of **2c** and 10% of **3c** (determined after hydrolysis of the esters).[9] Simpler examples are known in the hexahydronaphthalenes. Rearrangement of 10-methyl-2-keto-$\Delta^{1,9:3,4}$-hexahydronaphthalene (**4a**) in concentrated hydrochloric acid at 100° gave 62% of 4-methyl-*ar*-2-tetralol (**6a**) and only 10% of 4-methyl-*ar*-1-tetralol (**5a**).[8] Rearrangement of **4a** in



4 **5** **6** **7** **8**

a, R = Me; b, R = Et; c, R = Pr; d, R = Bu

acetic anhydride–sulfuric acid at room temperature gave 80% of **7a** and 20% of **8a**, while rearrangement in 30–50% aqueous mineral acid gave 80% of **6a** and 20% of **5a**.[10]

These results have given rise to the belief that the medium influences the direction of migration in dienone–phenol rearrangements.[4,5] The reasons behind this influence are not known, although it has been noted that steric and electronic effects are probably responsible.[8]

We have now found that the so-called solvent or medium effect appears to apply only to dienone **4a** and not the higher homologs **4b–d**. That is, the medium effect is not a general phenomenon, and, insofar as compounds **4** are concerned, the difference in types of rearrangement must be sought not in the nature of the medium but in the nature of the migrating groups. The first indication of this situation was provided in fact by Bell, who found that rearrangement of **4b** in acetic anhydride–sulfuric acid gave only **8b**, and not the anticipated **7b**.[11] We have carried out rearrangements of **4a–d** in acetic anhydride–sulfuric acid and in aqueous sulfuric acid. Results are given in Table I. The results with **4a** agree with those of Hopf and Dreiding,[10] while the result with **4b** in acetic anhydride–sulfuric acid confirms Bell's work in that **8b** predominates, although we have found the other isomer **7b** to be formed too.

TABLE I

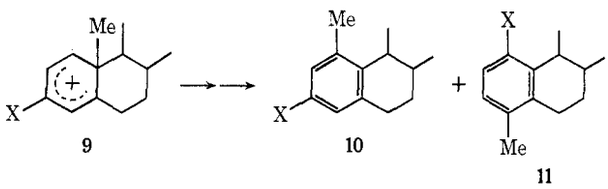
PRODUCTS[a] OF REARRANGEMENT OF **4a–d** IN ACETIC ANHYDRIDE–SULFURIC ACID AND IN AQUEOUS SULFURIC ACID

	—20.6 *N* H_2SO_4[b]—		—Ac_2O–H_2SO_4[c]—	
Compd	**5**, %	**6**, %	**7**, %	**8**, %
4a	14	86	84	16
4b	23	77	10	90
4c	2	98	7	93
4d	8	92	1	99

[a] Normalized to 100%. For total yields, see Experimental Section. [b] At 51.5°. [c] At room temperature.

The data in Table I show that **6** predominates in all of the tetralols and that **8** predominates in all of the acetates except the two in which R = Me. Obviously it is not only the medium which affects product distribution but also the nature of the angular group R.

Wolff and Dannenberg[12] have recently surveyed rearrangements to steroidal products which originate from the ion **9** (X = OH, OEt, Br, Cl, Me, *t*-Bu, C_6H_5, OAc, O_2CCF_3, H), and have concluded that the division in pathways to **10** and **11** is influenced by the resonance



9 **10** **11**

effect of the substituent X in **9**. The value of $\Delta\sigma$ ($\sigma_p - \sigma_m$) is used as a measure of the effect for each substituent, and it is found that the **11**-type product is obtained when $\Delta\sigma$ is larger than −0.21. The $\Delta\sigma$ values quoted for OH (−0.49) and OAc (−0.08) illustrate Wolff and Dannenberg's relationship insofar as it would concern compounds which appear in our own work (**5a–8a**). The relationship is not valid, however, for rearrangements of our **4b–d** and it is evident that the resonance effect of substituent X in **9** can be only

(7) A. S. Dreiding and A. Voltman, *J. Amer. Chem. Soc.*, **76**, 537 (1954).
(8) A. S. Dreiding, W. J. Pummer, and A. J. Tomasewski, *ibid.*, **75**, 3159 (1953).
(9) E. Hecker and E. Meyer, *Chem. Ber.*, **97**, 1926 (1964).
(10) H. W. Hopf and A. S. Dreiding, *Angew. Chem., Int. Ed. Engl.*, **4**, 690 (1965).
(11) K. H. Bell, *Tetrahedron Lett.*, 397 (1967).
(12) T. Wolff and H. Dannenberg, *Tetrahedron*, **27**, 3417 (1971).

a small part of the several factors which control product formation.

It is evident from the results in Table I that the migratory aptitude of the angular alkyl group plays a dominant role. There still remain to be unravelled, however, those factors which control rearrangement of the angular methyl compound, **4a**.

The data in Table I were obtained from rearrangements at room temperature in acetic anhydride–sulfuric acid and at 51.5° in 20.6 *N* sulfuric acid. The effect of temperature on rearrangement of **4a** was measured. The ratio **7a**:**8a** was 85:15 at 100°. Rearrangement of **4a** in concentrated hydrochloric acid at 100° gave **5a** and **6a** in the ratio 15:85. These data show that temperature does not affect the trend in product formation. We assume that this will apply to rearrangements of **4b–d**, too.

Experimental Section

Materials.—Commercially available 2-methylcyclohexanone (Aldrich Chemical Co.) and 2-propylcyclohexanone (K and K Laboratories) were used. 2-Ethyl- and 2-butylcyclohexanone were prepared by oxidation[13] of the corresponding cyclohexanol (K and K Laboratories). The four cyclohexanones were fractionally distilled before use in the annelation with 2-butyn-3-one (Farchan Research Laboratories). Annelation was carried out as described by Woodward and Singh,[14] and the products **4** were fractionally distilled, giving [yield, boiling point, ir (cm^{-1}) in $CHCl_3$] **4a**, 10.3%, 93–98° (2 mm), 1650, 1625; **4b**, 6.8%, 99–105° (1 mm), 1670, 1630; **4c**, 5.1%, 102–111° (1 mm), 1665, 1625; **4d**, 2.9%, 107–117° (1 mm), 1660, 1630.

Rearrangements. A. In Acetic Anhydride.—A solution of 500 mg of dienone **4** in 50 ml of acetic anhydride containing 3–4 drops of concentrated sulfuric acid was either allowed to stand 24 hr at room temperature or heated at 100° for 30 min. The solution was diluted with water and extracted with ether, and the ether was pumped off after drying over magnesium sulfate. Portions of the weighed residue were chromatographed quantitatively on a Varian Aerograph Model 700 gas chromatograph using a 10-ft (**4a**) or 20-ft (**4b–d**) 10% Carbowax 60/80 Chromosorb W column at 150°.

Total yields were: from **4a**, 72%; **4b**, 85–90%; **4c**, 79–83%; **4d**, 81–91%. Several runs were made in each case. Unrearranged dienone was obtained with **4b–d** and was separated quantitatively in the chromatograph.

B. In Aqueous Sulfuric Acid.—A solution of 500 mg of **4** in 5 ml of 20.6 *N* sulfuric acid was kept in a bath at 51.5° for 2 days. Quantitative work-up was as in A. Total yields were: from **4a**, 90%; **4b**, 83%; **4c**, 80–93%; **4d**, 75–89%. Small amounts of unrearranged **4c** and **4d** were obtained in some runs and were separated as in A.

C. In Concentrated Hydrochloric Acid.—A solution of 500 mg of **4a** in 5 ml of the acid was either kept at room temperature for 4 days or boiled for 30 min. Work-up and separation were as in A. Total yields were always close to 90%. Two runs at room temperature gave an average of **5a**:**6a** of 15:85. Five runs at reflux gave the same result.

Product Identification.—Products **5a**, mp 86–87°, **6a**, mp 103–105°, **7a**, mp 73–74°, and **8a** (liquid) were identified by comparison with data in the literature. Furthermore, **6a** was acetylated to form **8a**, while **7a** and **8a** were hydrolyzed to **5a** and **6a** by boiling in aqueous 20% KOH. Product **8b** (liquid) was identified by comparison with data in the literature.[11] Hydrolysis of **8b** gave **6b** (liquid) which was shown by pmr to be identical with **6b** obtained from rearrangement of **4b** in 20.6 *N* sulfuric acid. The identities of the two other products from **4b** were assumed to be as shown because they were the only other products obtained in the rearrangements (**5b** in 20.6 *N* sulfuric acid, and **7b** in acetic anhydride). Products **6c**, mp 66.5–68.5°, **6d** (liquid), **8c** (liquid), and **8d** (liquid) were identified by comparison of their pmr and infrared spectra with those of **6a**, **6b**, **8a**, and **8b**. The amounts of products **5c**, **5d**, **7c**, and **7d** were too small to allow identification. Identities were assumed since no other products than these and the major ones (**6**, **8**) were observed in the glc chromatograms.

Pmr of products (aromatic region) follows: **6a** (d, 6.4, 6.3), **6b** (d, 6.3, 6.2), **6c** (d, 6.4, 6.35), **6d** (d, 6.4, 6.35); J = 3 cps in all cases; **8a** (s, 6.6), **8b** (s, 6.65), **8c** (s, 6.5), **8d** (s, 6.65); **5a** (q, 6.85, 6.40, 6.45, 6.35, J = 8, 8, and 14 cps), **7a** (q, 7.05, 6.90, 6.75, 6.60, J = 9 cps).

Registry No.—**4a**, 703-02-6; **4b**, 13984-73-1; **4c**, 34956-90-6; **4d**, 34956-91-7; **5a**, 4242-05-1; **6a**, 3718-79-4; **6b**, 34956-94-0; **6c**, 34956-95-1; **6d**, 34956-96-2; **7a**, 34956-97-3; **8a**, 34956-98-4; **8b**, 34956-99-5; **8c**, 34957-00-1; **8d**, 34957-01-2.

(13) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1956, p 337.

(14) R. B. Woodward and T. Singh, *J. Amer. Chem. Soc.*, **72**, 494 (1950).

An Improved Synthesis of 5-Alkylresorcinols

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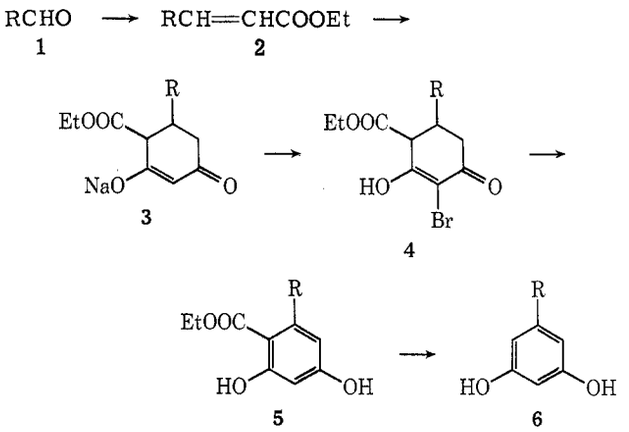
There are at present three general methods for preparing 5-alkylresorcinols;[1-3] however, they are tedious and expensive. I wish to report here an improvement of the last of these methods[3] which should be of convenience to workers requiring 5-alkylresorcinols in pharmaceutical research and, in particular, in the preparation of Cannabis (marijuana) analogs.

The synthetic scheme is outlined as follows.



The aldehyde **1** was converted in high yield to the β-alkylacrylate ester **2** on reaction with the sodium salt of triethyl phosphonoacetate[4] (see Table I). Michael addition of the sodium salt of ethyl acetoacetate to **2** gave **3**. The yield of **3** was dependent on

(1) C. M. Suter and A. W. Weston, *J. Amer. Chem. Soc.*, **61**, 232 (1939). Procedure involves reaction of Grignard reagent with 3,5-dimethoxybenzamide followed by reduction of the ketone product and demethylation. See also applications of their procedure by R. Adams, *et al.*, *ibid.*, **70**, 664 (1948); **71**, 1624 (1949).

(2) J. L. Dever, U. S. Patent 3,278,606 (Monsanto, 1966); *Chem. Abstr.*, **65**, 20062e (1966). Procedure involves conversion of 1,3,5-trichlorobenzene to 1,3-dimethoxy-5-chlorobenzene followed by formation of Grignard reagent, reaction with carbonyl compound, reduction, and demethylation.

(3) (a) R. M. Anker and A. H. Cook, *J. Chem. Soc.*, 311 (1945); (b) F. Korte and H. Sieper, *Justus Liebigs Ann. Chem.*, **630**, 71 (1960); (c) R. Valters and O. Neilands, *Latv. PSR Zinat. Akad. Vestis, Kim. Ser.*, **6**, 710 (1968); *Chem. Abstr.*, **70**, 77495t (1969).

(4) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).