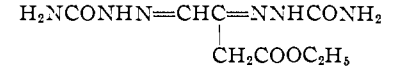
carbazone derivative of the dioxo ester, formed as a result of acid cleavage of the acetal group terminal to the ester molecule, namely,



Anal. Calcd. for $C_8H_{14}N_6O_4$: C, 37.18; H, 5.46; N, 32.62. Found: C, 37.35; H, 5.42; N, 32.75.

The dimethoxyacetoacetate was alkylated with sodium ethylate and butyl bromide to produce **ethyl α-butyl-γ,γ-dimethoxyacetoacetate**, b.p. 128.5–129.5° (4–5 mm.), $n^{20}D$ 1.4342, d^{20}_{20} 1.019, Σ MR_{keto} 62.57, Σ MR_{enol} 63.61, MR calcd. 62.90

Anal. Calcd. for $C_{12}H_{22}O_6$: C, 58.48; H, 8.97. Found: C, 58.25; H, 8.81.

Preparation of 1,1-Dimethoxy-2-heptanone.—The dimethoxy ester was hydrolyzed, by heating in diluted methyl alcohol, by means of potassium hydroxide solution to yield (70%) 1,1-dimethoxy-2-heptanone, b.p. 98–100° (4–5 mm.), $n^{20}D$ 1.4218, d^{20}_{20} 0.939, Σ MR 47.07, MR calcd. 47.10.

This ketone reacted with semicarbazide hydrochloride to form a white crystalline derivative which melted with decomposition at 241.2°. It reacted with 2,4-dinitrophenylhydrazine to yield a fluffy, bright orange powder melting at 185–186°. The ketone reacted with potassium cyanide and ammonium carbonate to yield **5-amyl-5-(dimethoxymethyl)-hydantoin**, melting at 94–95°.

Anal. Calcd. for $C_{11}H_{20}N_2O_4$: N, 11.46. Found: N, 11.38.

Condensation of Isatin with 1,1-Dimethoxy-2-heptanone.—Nine grams (0.051 mole) of the ketone, 5.4 g. (0.036 mole) of isatin, 25 ml. of the 34% potassium hydroxide solution, 45 ml. of water and 25 ml. of ethyl alcohol were stirred and refluxed for 72 hours. In the usual way there was obtained 8 g. (70% yield) of crude product. After recrystallization from benzene–Skellysolve A, **3-butyl-2-dimethoxymethylcinchoninic acid** melted at 155–156°.

Anal. Calcd. for $C_{17}H_{21}NO_2$: neut. equiv., 303.3; N, 4.62. Found: neut. equiv., 296; N, 4.85.

Preparation of 3-Butyl-2-formylcinchoninic Acid.—Three-fourths gram of the dimethoxy acid was dissolved in 75 ml. of 0.4 *N* sulfuric acid and heated on a steam-bath for 5 hours; small quantities of water were added from time to time to keep the volume nearly constant. From the cooled solution was obtained about 0.6 g. (94% yield) of crude product. Recrystallization from hot ethyl alcohol yielded small white crystals which melted with decomposition at 207°. The product reacted with Schiff reagent, and developed a raspberry red coloration in 2 *N* potassium hydroxide solution.

Anal. Calcd. for $C_{15}H_{15}NO_3$: neut. equiv., 257; N, 5.44. Found: neut. equiv., 266.5; N, 5.55.

Attempted Clemmensen Reduction of 3-Butyl-2-formylcinchoninic Acid.—The formyl acid was refluxed in diluted alcoholic solution with concentrated hydrochloric acid and amalgamated zinc. The reaction product behaved like an ethyl ester, therefore, it was redissolved in ethyl alcohol containing sodium hydroxide and refluxed. Upon neutralization, a tan precipitate was recovered. After recrystallization from diluted alcohol, the solid material darkened and melted at 261–264°.

Anal. Calcd. for $C_{15}H_{17}NO_2$: N, 5.95. Found: N, 5.75.

The melting point behavior of a mixture of some of this material with some **3-butyl-2-methylcinchoninic acid**, formed from interaction of isatin and hexyl methyl ketone (m.p. 261–263°), was practically the same as that of either component.

Ultraviolet Absorption Spectra of Substituted Cinchoninic Acid.—The absorption data were obtained for dilute aqueous solutions of the acids through use of a Beckman quartz spectrophotometer, model DU. It was noted that substitution of alkyl groups into the 2-, 3- or 2,3-positions of cinchoninic acid does not significantly change the maximum or minimum points of absorption. On the contrary, the 2-formylcinchoninic acids were observed to exhibit a change, evidently due to a lengthening of the conjugation of unsaturation in such compounds.

X-Ray Diffraction Patterns for Substituted Cinchoninic Acids.—The X-ray diffraction patterns[25] were obtained for the K_α radiation (1.5405 Å.) of copper obtained in a Hayes X-ray diffraction unit operating at 30 kv. and 15 ma. A Spectron recording spectrometer was used for tracing the X-ray intensity in the range of rotation of the mounted sample from 2° to about 50°. The intensity apices of the curves were easily measured in terms of degrees of angle of diffraction. Conversion of these angular values to linear measurements of the distances, d, between the unit cell interfaces of the crystalline compound studied was made by the use of a table.[26]

(25) Appreciation is hereby expressed to Dr. S. H. Simonsen, of the Dept. of Chemistry, The University of Texas, for his aid in securing these X-ray diffraction data.

(26) Tables for Conversion of X-Ray Diffraction Angles to Interplanar Spacing, Applied Mathematics Series 10, National Bureau of Standards, U. S. Department of Commerce, Washington, D. C.

AUSTIN, TEXAS

[CONTRIBUTION FROM THE INSTITUTE FOR INFECTIOUS DISEASES, THE UNIVERSITY OF TOKYO AND NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Studies on Azulenes. I. 2- and 3-Substituted S-Guaiazulene

BY TYUNOSIN UKITA, HIROSHI WATANABE AND MAKOTO MIYAZAKI

RECEIVED DECEMBER 28, 1953

The tertiary alcohol obtained from the reaction of α-kessyl ketone with isopropylmagnesium iodide on dehydrogenation gave 2-isopropyl-S-guaiazulene as the product. In addition S-guaiazulene (1,4-dimethyl-7-isopropylazulene) was obtained. On acetylation S-guaiazulene yielded 3-acetyl-S-guaiazulene and the latter compound was converted to 3-isopropenyl-S-guaiazulene. Catalytic hydrogenation of this substance gave two rearrangement products, 2-isopropenyl- and 2-isopropyl-S-guaiazulene. S-Guaiazulene was also obtained in this case.

Considerable interest has recently been shown in the azulenes. They are more stable than most polyenes and possess properties similar to aromatic compounds.

Because of the interesting chemistry of the azulenes and their known anti-inflammatory action,[1] we undertook a study of a series of these substances.

Recently Herz[2] attempted to prepare 1-isopropyl-4,8-dimethylazulene from 1-isopropyl-4,7-dimethylindan by the ring expansion reaction with diazoacetic ester. However he found that in the dehydrogenation step rearrangement of the isopropyl group occurred to give 2-isopropyl-4,8-dimethylazulene (vetiveazulene). However, 1,4,8-trimethylazulene and 1,3,4,8-tetramethylazulene[3] can be prepared by this procedure without migration of the methyl group. Furthermore Wagner–Jauregg[4]

(1) C. Pommer, *J. Exptl. Path. Pharmacol.*, **199**, 74 (1942).

(2) W. Herz, THIS JOURNAL, **74**, 1350 (1952); **75**, 73 (1953).

(3) Pl. A. Plattner, A. Fürst and H. Schmidt, *Helv. Chim. Acta*, **28**, 1647 (1945).

(4) T. Wagner-Jauregg, H. Arnold and F. Hüter, *Ber.*, **75**, 1293 (1942).

prepared 1-isopropyl-4,7-dimethylazulene and 1-isopropyl-4,6-dimethylazulene and found that in neither case had the isopropyl group undergone rearrangement.

Evidently the migration of the isopropyl group during the dehydrogenation reported by Herz is not a general reaction, although in the present study two additional examples of the rearrangement of an isopropyl group have been observed.

Some time ago, Ukita following up the work of Kanaoka[5] investigated the structures of kessoglycol[6] and α-kessyl alcohol,[7] components of the root of *Valeriana officinalis L.* var. *Latifolia* Miq. He established the structure, 3,6-dihydroxy-7,10-epoxy - 1,4 - dimethyl - 7 - isopropylbicyclo(0,3,5) decane, for kessoglycol and since kessoglycol could be converted to kessyl alcohol by reduction of the 6-hydroxy group, the structure of α-kessyl alcohol was established as 3-hydroxy-7,10-epoxy-1,4-dimethyl-7-isopropylbicyclo(0,3,5)decane (II). The position of the hydroxyl group in II has been discussed by Treibs.[8,9]

α-Kessyl ketone (III), obtained by oxidation of α-kessyl alcohol, was treated with methyl- and isopropylmagnesium iodide, and the products were converted to azulenes by dehydrogenation over a palladium–carbon catalyst. The properties of the methyl derivative VIIa were found to be identical with those of the substance obtained by Treibs[8] by the same reaction; the visible absorption spectrum of VIIa shows a shift in the absorption maxima of this compound toward longer wave lengths in relation to I (Table I). Since Plattner's[10] work on the spectra of azulenes indicates that substitution of alkyl groups in even-numbered positions causes a shift toward shorter wave lengths and substitution of odd-numbered positions a shift toward longer wave lengths, it is concluded that the new methyl group of VIIa is located in an odd-numbered position of S-guaiazulene; the product VIIa is thus 3-methyl-S-guaiazulene.

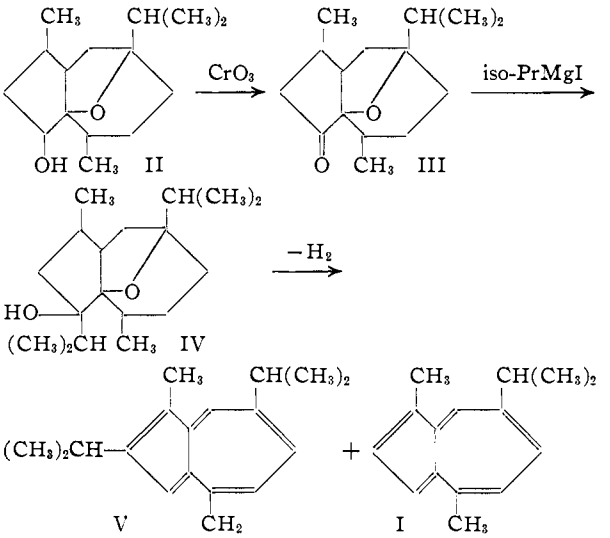
TABLE I

WAVE LENGTHS AT MAXIMUM ABSORPTIONS IN VISIBLE SPECTRA[a]

	ε	λ, mμ
S-Guaiazulene (I)	435	604
2-Isopropyl-S-guaiazulene (V)	405	588
2-Isopropyl-S-guaiazulene (IX)	395	588
2-Isopropenyl-S-guaiazulene (VIII)	420	582
3-Isopropenyl-2-guaiazulene (VII)	405	620
3-Methyl-S-guaiazulene (VIIa)	395	632
3-Acetyl-S-guaiazulene (VI)[b]	460	578

[a] The spectra were taken for petroleum ether solutions. [b] The absorption maxima of this compound cannot be compared with those of the alkyl derivatives.

In the case of the isopropyl derivative, however, dehydrogenation of the alcohol IV yielded I and a second azulene V. The latter gave a TNB complex, m.p. 155–157°, with analytical values corresponding to the TNB complex of an isopropyl-S-guaiazulene ($C_{18}H_{24}\cdot C_6H_3O_6N_3$). The maximum absorption in visible spectrum of V (Table I) shows a shift toward shorter wave lengths, indicating that the new isopropyl group is located at an even-numbered position. V, therefore, must be 2-isopropyl-S-guaiazulene. It appears therefore that in this reaction a migration of the isopropyl group has occurred similar to that reported by Herz.[2]



The migration of the isopropyl group attached to the 3-position of S-guaiazulene also was observed in another series of reactions starting from S-guaiazulene (I).

Condensation of I with acetyl chloride or acetic anhydride gave monoacetyl-S-guaiazulene (VI), which formed a trinitrobenzene complex. This substance is assigned the structure 3-acetyl-S-guaiazulene on the basis of the known behavior of azulenes in reactions of this type.

Brown[11] predicted electrophilic substitution in the 1- and 3-positions from quantum mechanical calculations of polarization energy and π-electron densities. Anderson[12] found substitution to occur in the 1-position when the methyl derivative of azulene was prepared; he also prepared diacetyl- and mononitroazulenes.

More recently, Anderson and co-workers[13,14] reported a comprehensive study of electrophilic substitution of the azulene nucleus and proved that acetylation of azulene occurs at the 1-position.

According to Brown's theory, acetylation of I by the Friedel–Crafts reaction should yield 3-acetyl-S-guaiazulene (VI).

Treatment of VI with methylmagnesium iodide gave a tertiary alcohol which underwent dehydration during chromatographic purification with alumina to form blue isopropenyl-S-guaiazulene (VII). Catalytic reduction of VII with palladium–carbon catalyst was stopped when 1 mole of hydrogen had been absorbed and the product chromatographed

(5) K. Kanaoka, *et al.*, *J. Pharm. Soc., Japan*, **61**, 6, 8, 9, 123 (1941).
(6) T. Ukita, *ibid.*, **64**, 285 (1944); *C. A.*, **45**, 2912 (1951).
(7) T. Ukita, *J. Pharm. Soc., Japan*, **65**, 458 (1948); *C. A.*, **45**, 5683 (1951).
(8) W. Treibs, *Ann.*, **570**, 165 (1950).
(9) W. Treibs, *ibid.*, **576**, 120 (1952).
(10) M. Gordon, *Chem. Revs.*, **50**, 127 (1952).
(11) R. D. Brown, *Trans. Faraday Soc.*, **44**, 948 (1948).
(12) A. G. Anderson, Jr., and J. A. Nelson, THIS JOURNAL, **72**, 3824 (1950).
(13) A. G. Anderson, Jr., and J. J. Tazuma, *ibid.*, **75**, 4979 (1953).
(14) A. G. Anderson, Jr., Jerry A. Nelson and James J. Tazuma, *ibid.*, **75**, 4980 (1953).

over alumina. Each fraction was recrystallized as the TNB complex and the mixture separated into unreacted VII, S-guaiazulene, VIII, IX and some resinous material. The analytical values indicate that the TNB complex of VIII corresponds to isopropenyl-S-guaiazulene ($C_{18}H_{22}\cdot C_6H_3O_6N_3$), and the TNB complex of IX to an isopropyl-S-guaiazulene ($C_{18}H_{24}\cdot C_6H_3O_6N_3$). On admixture of any two of the TNB complexes a remarkable depression of the melting point was observed.

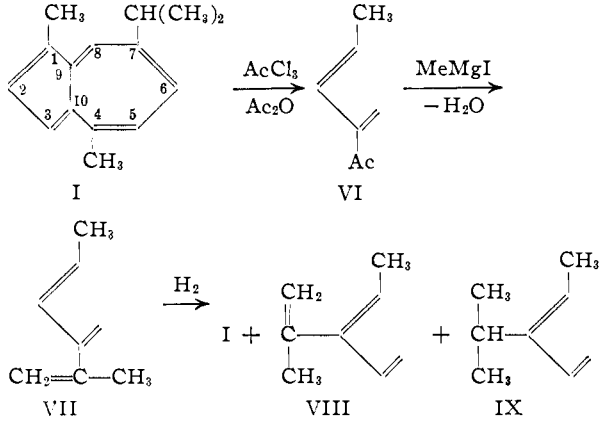
The visible absorption spectra of I, VI, VII, VIII and IX show that the new alkyl group of the compound VII is located in an odd-numbered position and those of VIII and IX in even-numbered position of S-guaiazulene (Table I).

On the assumption that I was acetylated in the 3-position, VII should be 3-isopropenyl-S-guaiazulene, since the migration of new substituents could not have occurred.

According to Plattner's work,[10] cited above, the absorption maxima attributable to differences in the alkyl group substituted on the same position of the azulene nucleus are not large and the absorption maxima of isopropyl and isopropenyl derivatives are practically identical.

From the results of visible absorption spectra, compounds VIII and IX are probably 2-isopropenyl and 2-isopropyl-S-guaiazulene, respectively, formed by the migration of the isopropenyl group from the 3- to the 2-position during the catalytic hydrogenation of VII.

Admixture of the TNB complex of IX with that of V gave no depression of the melting point (150–154°), thus IX was concluded to be 2-isopropyl-S-guaiazulene and VIII is 2-isopropenyl-S-guaiazulene.



This is the first example of migration of a substituent attached to the azulene nucleus occurring under such mild conditions.

Previous reports concerning the behavior of alkyl groups attached to the 1-position of the azulene nucleus during the dehydrogenation[2-4] are in agreement with our conclusion that an isopropyl group introduced into the 3-position of S-guaiazulene, a compound which has another group in the 4-position, has a tendency to undergo rearrangement very easily.

An attempt is now being made to prepare 2-isopropyl-S-guaiazulene by a method which would exclude the possibility of rearrangement.

Acknowledgment.—This work was partially supported by the Scientific Research Fund of the Ministry of Education. The authors are grateful to Misses Reiko Ohta and Eiko Kondo and Mr. Bunhei Kurihara for the elemental analyses.

Experimental

Grignard Reaction and Dehydrogenation of α-Kessyl Ketone. 3-Methyl-S-guaiazulene (VIIa).—An ether solution containing 2.5 g. of α-kessyl ketone was added dropwise to a mixture of 0.65 g. of magnesium and 3.5 g. of methyl iodide in 20 ml. of absolute ether; the mixture was stirred at room temperature for 24 hours. After the decomposition of the reaction product with an aqueous solution of ammonium chloride, the ether layer was separated, washed with water, and dried. Removal of the ether left an oily substance; the unreacted ketone was removed with Girard P reagent. The alcohol formed was separated as the phenylurethan which was recrystallized from petroleum–benzene to give fluffy crystals, 1.6 g., m.p. 146°.

Anal. Calcd. for $C_{23}H_{33}O_3N$: C, 74.14; H, 9.21; N, 3.76. Found: C, 74.08; H, 9.03; N, 3.70.

A mixture of 1.0 g. of the phenylurethan, 1.0 g. of potassium hydroxide and 3 ml. of alcohol was boiled for 12 hours; the alcohol was removed by distillation, and the residue taken up in petroleum ether. Evaporation of petroleum ether yielded an oil, 0.6 g., b.p. 135–147° (6 mm.).

Anal. Calcd. for $C_{16}H_{28}O_2$: C, 76.12; H, 11.19. Found: C, 76.35; H, 10.89.

A solution of 50 mg. of the tertiary alcohol thus obtained in 1.2 ml. of benzene was passed slowly over a 3% palladium–carbon–asbestos catalyst at 270–280° in a nitrogen stream. A petroleum ether solution of the methyl-S-guaiazulene formed was chromatographed; trinitrobenzene complex, m.p. 139–140°.

Anal. Calcd. for $C_{16}H_{20}\cdot C_6H_3O_6N_3$: C, 62.11; H, 5.45. Found: C, 62.38; H, 4.99.

2-Isopropyl-S-guaiazulene (V).—The procedure described above was carried out with 5.8 g. of α-kessyl ketone, 12 g. of isopropyl iodide and 1.5 g. of magnesium. After decomposition of the reaction product, the ketone was removed with Girard reagent, and 5.0 g. of tertiary alcohol IV was obtained. Since IV is decomposed even by distillation under reduced pressure it was used directly for the dehydrogenation. The azulene formed was chromatographed twice. Repeated fractional recrystallization of its trinitrobenzene complex gave 10 mg. of crystals, m.p. 155–157°.

Anal. Calcd. for $C_{18}H_{24}\cdot C_6H_3O_6N_3$: C, 63.56; H, 6.01; N, 9.27. Found: C, 63.38; H, 5.85; N, 9.50.

Approximately 30 mg. of the trinitrobenzene complex, m.p. 147–149°, of I was obtained at the same time.

3-Acetyl-S-guaiazulene (VI).—A mixture of 50 ml. of carbon disulfide, 8.1 g. of aluminum chloride and 4.8 g. of acetyl chloride (3.1 g. of acetic anhydride) was stirred and boiled gently; 6.0 g. of I dissolved in 20 ml. of carbon disulfide was added dropwise. The mixture was stirred until the reaction was complete (3 days). The solvent was removed by distillation, ice-water added to the residue, and the mixture shaken with petroleum ether. After drying, the petroleum solution was poured through an alumina column. Unreacted I appeared in the eluate and the desired acetyl-S-guaiazulene was obtained only after elution with benzene. Recrystallization from alcohol yielded violet scaly crystals, m.p. 85–85.5°, yield 18%.

Anal. Calcd. for $C_{17}H_{20}O$: C, 85.00; H, 8.33. Found: C, 85.32; H, 8.51.

Trinitrobenzene complex, m.p. 120–121°.

Anal. Calcd. for $C_{17}H_{20}O\cdot C_6H_3O_6N_3$: C, 60.93; H, 5.08; N, 9.27. Found: C, 61.20; H, 5.37; N, 9.53.

3-Isopropenyl-S-guaiazulene (VII).—Methylmagnesium iodide was obtained by gently boiling 0.62 g. of magnesium and 3.6 g. of methyl iodide in absolute ether; while the vessel was immersed in ice-water, 0.6 g. of acetyl-S-guaiazulene (VI) dissolved in a small amount of absolute ether was added dropwise. After 5 hours, the complex was decomposed with 10% ammonium chloride solution, the ether layer was separated, washed with water and dried. After evaporation of the ether, the residue was taken up in pe-

troleum ether and passed through an alumina column. Part of the tertiary alcohol formed during the reaction underwent partial dehydration and flowed out, while the rest which was adsorbed on the alumina was dehydrated there, and subsequently eluted by petroleum ether. Removal of petroleum ether gave a blue oil in 45% yield, the trinitrobenzene complex of which was recrystallized from alcohol, m.p. 85–86°.

Anal. Calcd. for $C_{18}H_{22}\cdot C_6H_3O_6N_3$: C, 63.85; H, 5.58; N, 9.31. Found: C, 63.72; H, 5.40; N, 9.08.

Reduction of VII.—An alcoholic solution of 0.3 g. of VII was shaken with 0.3 g. of 10% palladium–carbon in a hydrogen stream. After 6 hours 1 mole of hydrogen had been absorbed and the reduction was stopped. The solvent was removed by distillation *in vacuo*, and the residue was dissolved in petroleum ether and chromatographed through an alumina column. The azulene fraction was separated from the effluent and recrystallized as the trinitrobenzene complex. The azulenes in the order in which they were obtained were: (a) unreacted 3-isopropenyl-S-guaiazulene (VII), TNB complex, m.p. 85–86°. (b) 2-Isopropenyl-S-guaiazulene (VIII), TNB complex, m.p. 74–75°. *Anal.* Calcd. for $C_{18}H_{22}\cdot C_6H_3O_6N_3$: C, 63.84; H, 5.58; N, 9.31. Found: C, 63.65; H, 5.32; N, 9.12. (c) I mixed with 2-isopropyl-S-guaiazulene (IX), TNB complex, m.p. 150–153°. *Anal.* Calcd. for $C_{18}H_{24}\cdot C_6H_3O_6N_3$: C, 63.56; H, 6.01; N, 9.27. Found: C, 62.94; H, 5.60; N, 9.02.

I and IX were separated by chromatography and repeated fractional crystallization. The yields of the TNB complexes of VII, VIII and IX were a few mg. each; that of the TNB complex of I was about 30 mg., m.p. 148–149°.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF UTAH]

Seven-membered Ring Compounds. VIII.[1] The Cyclization of Benzosuberane-5,6-diacetic Acid

BY W. J. HORTON, H. W. JOHNSON[2] AND J. L. ZOLLINGER[2]

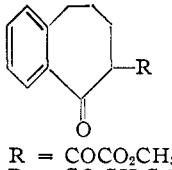
RECEIVED APRIL 1, 1954

Benzosuberone-6-acetic acid has been prepared by two methods, one of which required but three steps from allylbenzene. The cyclization of a mixture of *cis*- and *trans*-benzosuberane-5,6-diacetic acids gave isomeric ketones which were separated by fractional crystallization.

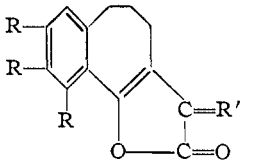
An approach to colchicine[3] involving final closure of the C ring became unpromising when it was found that reactions involving the keto group of methyl 2,3,4-trimethoxybenzosuberone-6-acetate were unsuccessful. This approach has been further explored in a model compound as an introduction to the synthesis of analogs of colchicine which lack a methoxyl group in the 4-position.

The final compounds obtained herein, *cis*- and *trans*-2-keto-1,2,3,3a,4,5,6,10b-octahydrobenz[e]-azulene (XI) are related to the 6-keto compound[4] and to 3-keto-1,2,3,4,5,6-hexahydrobenz[e]azulene.[5] The general plan which we have used to obtain a third ring is similar to one which appeared during the progress of this work[6] and which did not report ring closure.

In a previous paper[7] the pyrolysis of methyl benzosuberone-6-glyoxylate (I) was successful only if methanol was repeatedly added to reopen the ring of the enol lactone II which presumably formed during the pyrolysis and was known to decompose when heated. This pyrolysis has now been conducted more easily and in excellent yield in benzyl alcohol at 185°. In support of the above proposed mechanism, the lactone II or the methyl glyoxylate I was used and the benzyl ester III was produced in both cases.



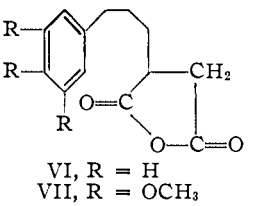
I, R = $COCO_2CH_3$
III, R = $CO_2CH_2C_6H_5$
IV, R = CO_2CH_3
V, R = CH_2CO_2H



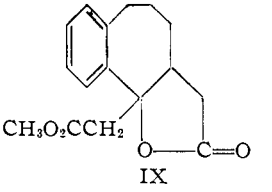
II, R = H; R′ = O
VIII, R = OCH_3; R′ = H_2

The alkylation of either III or IV with methyl bromoacetate followed by hydrolysis gave benzosuberone-6-acetic acid (V).

A second preparation of V arose from the investigation which demonstrated that γ-3,4,5-trimethoxyphenylpropylsuccinic anhydride (VII) cyclized in polyphosphoric acid to VIII.[3] By hydrogenation of γ-phenylallylsuccinic anhydride[8] the required material VI was obtained and although it failed to react in polyphosphoric acid it cyclized when aluminum chloride was used producing V in 75% yield.



VI, R = H
VII, R = OCH_3



IX

The methyl ester of V in the Reformatsky reaction with methyl bromoacetate gave the lactone IX.[9] Hydrogenolysis of this lactone and saponification gave benzosuberane-5,6-diacetic acid (X).

It seems likely that the geometrical isomers of IX were obtained in the Reformatsky reaction and that the form present in smaller amount was

(1) Paper VII, THIS JOURNAL, **76**, 1909 (1954).

(2) From the Doctoral Research of H. W. Johnson and J. L. Zollinger.

(3) P. D. Gardner and W. J. Horton, THIS JOURNAL, **75**, 4976 (1953).

(4) J. R. Nunn and W. S. Rapson, *J. Chem. Soc.*, 1051 (1949).

(5) J. W. Cook, R. Philip and A. R. Somerville, *ibid.*, 164 (1948).

(6) A. G. Anderson, Jr., and H. F. Greef, THIS JOURNAL, **74**, 5203 (1952).

(7) W. J. Horton, C. E. Hummel and H. W. Johnson, *ibid.*, **75**, 944 (1953).

(8) C. S. Rondesvedt, Jr., *Org. Syntheses*, **31**, 85 (1951).

(9) Lactone formation in the Reformatsky reaction has been reported. W. E. Bachmann and G. D. Johnson, THIS JOURNAL, **71**, 3463 (1949).