transfer the materials under entirely anhydrous conditions were developed previously,[6] with some improvements, and will be described elsewhere.[14,17]

Rate Measurements.—Standard solutions of the complex, $C_6H_5COCl:AlCl_3$, were prepared by adding aluminum chloride to a mixture of benzoyl chloride in ethylene chloride, and this mixture was stirred (using a magnetic stirrer) until the aluminum chloride dissolved. Data are reported only for experiments in which colorless standard solutions were used and which remained colorless for at least 4–5 days. Portions of this solution were diluted as necessary with ethylene chloride, and the reactions were started by adding the hydrocarbon to the diluted solution. The reaction mixtures for toluene and *p*-xylene were colorless. Upon addition of naphthalene to the diluted standard solution, the mixture turned orange and gradually darkened upon standing. The standard solutions and reaction mixtures were protected at all times by a blanket of dry nitrogen gas. The reaction vessels were placed in a stirred water-bath which was controlled to ±0.01°.

In the analytical procedure, the reactions were quenched by shaking with ice-water. The organic compounds were extracted with chloroform and 80% pyridine–water mixture was added to the combined extracts. After allowing to stand, a large amount of ethanol was added, and the benzoic acid and pyridine hydrochloride were titrated with standard base. The procedure was developed previously[6] and the details will be reported elsewhere.[17]

(17) Forthcoming papers by H. C. Brown and F. R. Jensen.

BERKELEY 4, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

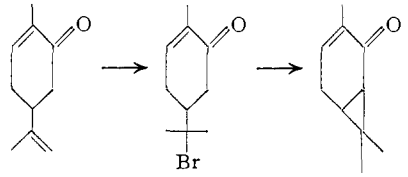
Mechanism of the Carvone Hydrobromide → Eucarvone Transformation

BY EUGENE E. VAN TAMELEN, JOHN MCNARY AND FRANK A. LORNITZO

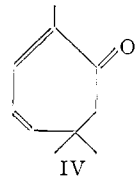
RECEIVED SEPTEMBER 24, 1956

A detailed mechanism for reactions of the carvone hydrobromide → eucarvone type is supported by various pieces of evidence, including the isolation of bicyclo[4.1.0]-3-hepten-2-one intermediates.

In 1894, Baeyer[1] described the properties of the elimination product, later called eucarvone, which results when carvone hydrobromide is treated with alkali. Following the establishment of the correct structure (I) for carvone, Baeyer proposed,[2] by analogy with the dihydrocarvone hydrobromide → carone transformation, that eucarvone possessed the structure III ("carenone"). It remained, however, for Wallach[3] to gather evidence which led to assignment of the correct structure (IV).



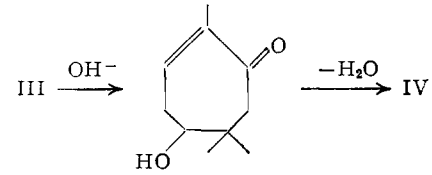
I II III



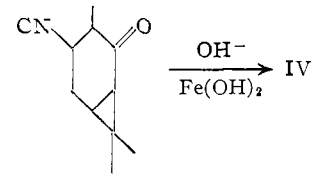
IV

It is natural that detection of this novel change would engender speculation on the nature of the reaction course. Wallach[3] suggested that carvone hydrobromide (II) does in fact ring-close to carenone, but that the primary product is unstable under the conditions of the reaction, suffering ring opening by base to the α,β-unsaturated-δ-hydroxyketone V, which dehydrates to IV. Clarke and Lapworth[4] prepared cyanocarone (VI) and showed that it was converted, on treatment with alkali in the presence of ferrous hydroxide, to eucarvone.

(1) A. Baeyer, *Ber.*, **27**, 810 (1894).
(2) A. Baeyer, *ibid.*, **31**, 2067 (1898).
(3) O. Wallach, *Ann.*, **305**, 242, 274 (1899); **339**, 94 (1905).
(4) R. W. L. Clarke and A. Lapworth, *J. Chem. Soc.*, **97**, 15 (1910).



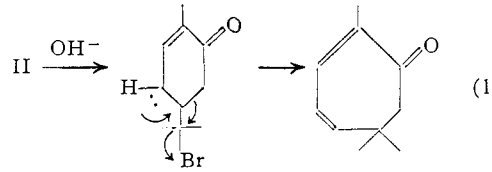
V



VI

The reasonable assumption was made that the reagent pair effected initial elimination to carenone, which subsequently rearranged to eucarvone; this behavior was construed as support for the Wallach mechanism, in particular the instability of carenone.

These suggestions for the course of the reaction, although reasonable, are not proved by the experimental findings described. The results of Clarke and Lapworth strongly suggest that carenone does readily ring-expand in a basic medium, but they do not *necessitate* its intermediation in the carvone hydrobromide → eucarvone change. By applying simple electronic principles, one can write a *concerted, elimination–rearrangement process* (1) which

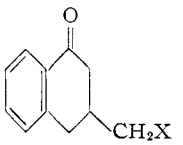


(1)

does not require III and therefore contrasts with the Wallach mechanism or any other ring closure operation. Since there is no appreciable amount

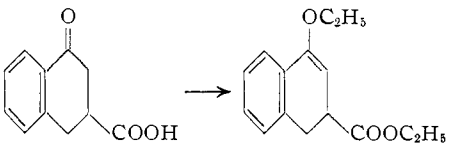
of carenone present in equilibrium with eucarvone,[5] the isolation of carenone as an elimination product of II, would disprove (1) and confirm this feature of the Wallach suggestion. However, despite various efforts,[3,4,6] carenone has so far not been isolated. A large portion of the work described in this contribution deals with efforts in that direction.

Our first encounter with an isolable bicyclo-[4.1.0]-3-hepten-2-one was occasioned by studies carried out in the α-tetralone series. Because of certain mechanistic considerations (*vide infra*), it seemed that an unusually good opportunity for trapping the intermediate would be afforded by inclusion of the double bond in a benzenoid ring; and consequently, we initiated a scheme, patterned after one previously reported from this Laboratory,[7,9] designed to provide a ketone of the type VII.



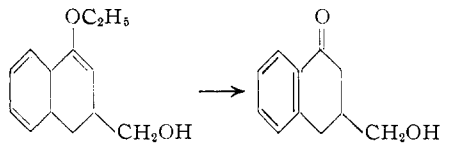
VII

The readily available 3-carboxy-α-tetralone (VIII) was converted first of all to the enol ether ester X



VIII X

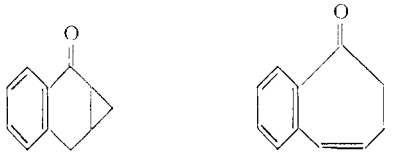
by (a) esterification, which yielded the crystalline (m.p. 40.0–40.5°) ethyl ester IX, followed by (b) enol etherification, effected with ethyl orthoformate and mineral acid catalyst. The unstable enol ether ordinarily was not isolated; the reaction mixture containing it could be reduced directly with lithium aluminum hydride to give, after acid hydrolysis of the intermediary enol ether alcohol XI, 3-hydroxymethyl-α-tetralone (XII) in 59%



XI XII

over-all yield from IX. Tosylation of the liquid keto alcohol by means of *p*-toluenesulfonyl chloride in pyridine furnished the tosylate VII (X = $OSO_2C_6H_4CH_3$-*p*), which was obtained in polymorphic forms: one melting at 96.0–96.5° and the other, 99–100°.

With the desired structural type available, its behavior under basic conditions was studied. On treatment of the tosylate with two moles of sodium hydroxide in ethanol at steam-bath temperatures for about five hours, there was formed in excellent yield a substance (b.p. 123° (1.0 mm.)), the analysis of which indicated formation from VII by loss of *p*-toluenesulfonic acid. In the assumption that the behavior of the sulfonate was normal, the elimination product should be either the cyclopropyl ketone XIII or the ring-expanded benzcyclo-



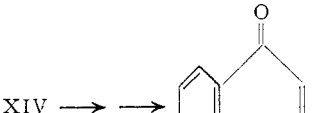
XIII XIV

heptenone XIV; taking into account the severity of the reaction conditions as well as the demands of the Wallach mechanism, the latter structure might be the anticipated one. However, *the elimination product from VII is the cyclopropyl ketone XIII*, as the following observations show. The ultraviolet spectrum of the substance resembled very closely that of α-tetralone and the ketol XII (Table I); in XIV, the double bond present would be expected to modify markedly the chromophoric properties of the simple tetralone system. Furthermore, drastic base treatment of the initial elimination product yielded an *isomeric ketone*, which must be formulated as the benzcycloheptenone XIV. The rearrangement was found to be surprisingly sluggish. Further treatment of the tricyclic ketone with alcoholic alkali or methoxide in methanol had no effect; however, on being heated for 2.5 hours with an excess of potassium *t*-butoxide in boiling *t*-butyl alcohol, it was transformed in good yield into the isomer. The ketone XIV, too, was a liquid (b.p. 80–83° (0.22 mm.)), which absorbed at higher wave lengths in the ultraviolet than its precursor (Table I).

TABLE I

Compound	λ_{max}, mμ	log ε
α-Tetralone	248	4.09
	293	3.25
XII	248	4.07
	295	3.27
XIII	244	4.15
	287	3.29
XIV	231, 236	4.48, 4.44,
	267, 320	3.70, 3.43

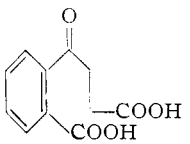
Because of the drastic conditions employed in the ring expansion, it is necessary to consider a structure, XV, which could well result by consecutive, base-catalyzed shifts of the olefinic bond. Structure XIV was favored, however, because of



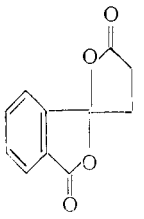
XV

its ultraviolet spectrum; and the choice was confirmed by ozonization, which produced β-(2-carboxybenzoyl)-propionic acid (XVI), along with some of the corresponding dilactone XVII. Although we have acquired no direct evidence that the rearrangement product from XIII does not con-

(5) E. J. Corey, H. J. Burke and W. A. Remers, THIS JOURNAL, **78**, 180 (1956).
(6) E. J. Corey and H. J. Burke, *ibid.*, **78**, 174 (1956).
(7) *Cf.* S. A. Julia, *Compt. rend.*, **241**, 882 (1955).



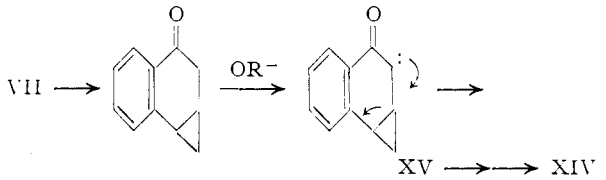
XVI



XVII

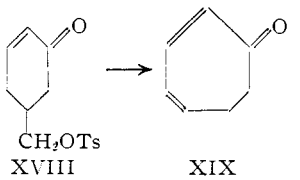
tain at least some of the cross-conjugated ketone, it is pertinent to note that the refractive indices of six out of seven distillation fractions did not vary by more than 0.0013 unit and that no β-(2-carboxyphenyl)-propionic acid, the expected oxidation product of XV, apparently was formed along with XVI and XVII.

Thus little difficulty was encountered in proving that *the change VII → XIV is intermediated by a carenone.* Now it is true that the case described does not constitute a fair test for the generality of the carenone mechanism; the ring closure step to the cyclopropyl ketone XIV is much favored over a concerted mechanism corresponding to (1), since anion formation undoubtedly is more readily accomplished in this case at the 2- than at the 4-carbon of the tosylate VII. For the same reason, a sequence featuring ring closure to the *isomeric* cyclopropyl ketone, although not definitely ruled, out,



is unlikely. Thus it is still possible that, whereas the change VII → XIV proceeds by way of a cyclopropyl ketone, the carvone hydrobromide → eucarvone reaction is concerted.

A few years ago there was reported from this Laboratory the transformation of 5-hydroxymethyl-2-cyclohexenone tosylate (XVIII) to 2,4-cycloheptadienone (XIX),[8] a tropone and tropolone precursor.[9] This operation was patterned

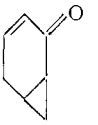


XVIII XIX

after the carvone hydrobromide → eucarvone reaction, and it seemed that it would serve equally well as a mechanism model. The tosylate in this system leads much more readily than the one in the α-tetralone series, to ring-expanded product, in that elimination–rearrangement was easily accomplished by utilizing a slight excess of dilute alkali at room temperature.[9] Trapping norcarenone (XX), if present, appeared a delicate operation, therefore. We finally found that if less than an equivalent of dilute alkali was added at 0° to an ethanolic solution of the tosylate XVIII, at such a

(8) E. E. van Tamelen and G. T. Hildahl, THIS JOURNAL, **75**, 5451 (1953).

(9) E. E. van Tamelen and G. T. Hildahl, *ibid.*, **78**, 4405 (1956).

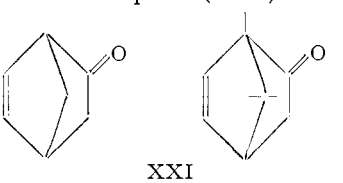


XX

rate that the *p*H was maintained at 7.6–7.8, *a liquid product, C_7H_8O, possessing the expected characteristics of norcarenone, could be isolated.* The ultraviolet spectrum displayed a low intensity band (ε 620) at 292 mμ, indicating about 10% of 2,4-cycloheptadienone, and a more intense band (ε 8710) at 218 mμ, ascribable to norcarenone. The infrared spectrum revealed broad carbonyl absorption at about 6.05 μ. Mild treatment of the new ketone with dilute alkali effected, as expected, smooth conversion to 2,4-cycloheptadienone.

Fortified by our experience in the model cases, we addressed ourselves to the problem of arresting the carvone hydrobromide → eucarvone reaction at the carenone stage. Initial investigations showed that this system was even more sensitive than the previous one. As expected, exposure of carvone hydrobromide to too high a *p*H (> *ca.* 9–10) largely resulted in eucarvone formation, whereas at *p*H 7 or below, elimination to carvone seriously intervened. Although in no case could these undesired reactions be completely separated from the simple ring closure step, operating under the conditions described above for the norcarenone case enabled us to isolate a liquid fraction (containing essentially no eucarvone but almost certainly contaminated by isomers, especially carvone) which gave a correct analysis for $C_{10}H_{14}O$ and, on further treatment with base, generated eucarvone. *These observations prove the presence of a eucarvone precursor, which, with little doubt, is carenone (III).* We therefore consider the concerted mechanism (1) excluded for all cases studied.

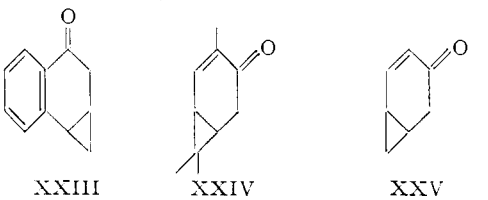
Before leaving the matter of ring closures, we consider briefly other elimination pathways open to the substances II, VII and XVIII. First, bearing in mind that α-alkylation of α,β-unsaturated ketones accompanied by double bond migration is a normal phenomenon, ring closure to dehydrocamphor and norcamphor (XXI) is conceivable.



XXI

It is clear, however, that this structural type would be formed *irreversibly* and that the major reaction cannot, therefore, proceed by this route. Initial formation of carbonium ion, or elimination to dienone, is, for equally apparent reasons, improbable.

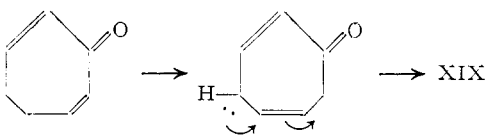
The most plausible alternate is ring closure to the isomeric cyclopropyl ketones XXIII → XXV but



XXIII XXIV XXV

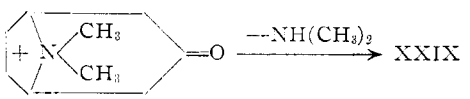
again several arguments may be advanced to controvert the proposal. With reference to the tetralone case, we have already expressed reasons for preferential formation of structure XIII. Also, formulation XXIV for carenone is obviously unable to account for the conversion to eucarvone.

We cannot so easily dispose, however, of the alternate XXV for the simplest case.[10] Assignment of structure XX in preference to XXV rests in part on analogy with the carenone formulation. Beyond that, one might expect, on the basis of XXV, a peak at somewhat higher wave lengths than that calculated (227 mμ) for an unsubstituted 2-cyclohexenone, in that the cyclopropane ring extends the conjugation.[11] In fact, the reverse is true—a substantial (Δ = 9 mμ) hypsochromic shift was found. Finally, on the basis of XXV, ring expansion to the cross-conjugated cycloheptadienone XXIX would be anticipated (*vide infra*); a



XXIX

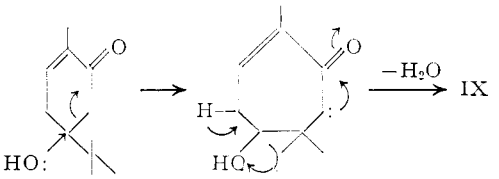
series of base-catalyzed 1,3-shifts are then necessary to attain the observed final structure XIX. Now the *primary product*[12] of base-promoted tropinone methiodide decomposition is undoubtedly the ketone XXIX, which ordinarily appears to isomerize partially, under the conditions of the reaction, to



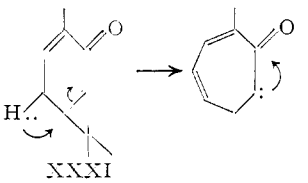
the 2,4- and the 3,5-isomers. We have been able to obtain, by operating under closely-defined conditions,[13] a tropinone methiodide elimination product, C_7H_8O, which, substantially free from the 2,4-isomer, appears to be largely XXIX. This material fails to give 2,4-cycloheptadienone under the mild basic conditions which serve to convert norcarenone to the product in high yield. This result strongly suggests that the cross-conjugated ketone XXIX cannot be an intermediate in the over-all change VII → XIX and therefore that formula XXV does not represent the structure of the intermediate, elimination product.[14]

Having established the fact and the nature of the ring-closure, we proceed to the second phase of the discussion, that dealing with the ring-opening reaction of the cyclopropyl ketone to yield observed product.

Of the two possibilities which require our attention, one is the Wallach interpretation, which entails, as stated above, ring-opening to yield the δ-hydroxyketone followed by dehydration. This behavior accommodates the observed second order

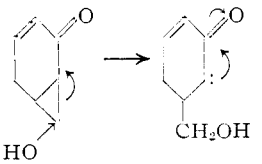


rate, and the ring opening is mechanistically reasonable, implying an SN2 type of attack at the less hindered carbon, with release of a stabilized anion. Alternately, rate-controlled removal of active hydrogen at C-2 may trigger a simple electronic shift XXXI which furnishes the anion of eucarvone. The

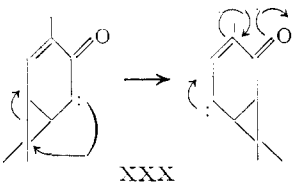


XXXI

very nature of the reaction products from carenone and norcarenone provides the information necessary for deciding between the two possibilities. Were the Wallach mechanism operative in a general sense, one would expect norcarenone to undergo nucleophilic attack at, again, the less hindered carbon, *which in this case is the methylene carbon of the small ring*. The resulting product, 5-hydroxymethyl-2-



cyclohexenone, could hardly be regarded as a 2,4-cycloheptadienone precursor; in fact, this alcohol has already been shown to be relatively stable under alkaline conditions.[9] In addition, the well-

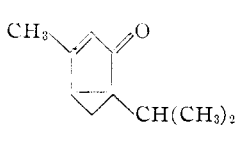


XXX

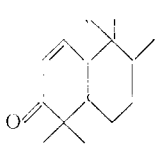
the isomeric ketone III. However, the circuitousness of the reaction course renders it unattractive; and beyond that, one might expect—because of the more stringent stereoelectronic demands of process XXX—ring expansion of XXIV anion, forming XXIX, to represent an easier route and therefore to supervene.

(10) Since our carenone samples are probably contaminated with carvone, the major peak may be displaced from its true position and therefore should not be used as evidence for structural assignment.

(11) For example, umbellulone (i) possesses a peak at 265 mμ, A. E. Gillam and T. F. West, *J. Chem. Soc.*, **98** (1945); R. H. Eastman, THIS JOURNAL, **76**, 4115 (1954). Also, the unsaturated cyclopropyl ketone (ii) derived from cycloartenol (D. S. Irvine, J. A. Henry and F. S. Spring, *J. Chem. Soc.*, 1316 (1955)) has an absorption band at 269 mμ (ε 8700).



(i)



(ii)

(12) J. Meinwald, S. L. Emerman, N. L. Yang and G. Buchi, THIS JOURNAL, **77**, 4401 (1955).

(13) Unpublished results obtained by Miss P. Barth.

(14) None of the evidence acquired can be used to exclude rigidly initial formation of the cyclopropyl ketone XXIV followed by an internal anionic displacement on the single carbon bridge (XXX) to yield

known stability of simpler cyclopropyl ketones to alkali would, by itself, make the Wallach rationalization unlikely.[15] *Thus the reaction course pictured in XXXI must represent the conversion of a carenone to the corresponding cycloheptadienone.* This view is consistent with the great difficulty in bringing about the rearrangement in the benz- series (XIII → XIV), anion formation at the methylene group, which is more weakly activated than the corresponding ones in the purely aliphatic cases, being the serious barrier.

With the ring-expansion feature filled in, this sketch of the carvone hydrobromide → eucarvone mechanism is complete.

Experimental

3-Carbethoxy-α-tetralone (IX).—3-Carboxy-α-tetralone (10.6 g., 0.0603 mole) was dissolved in 17.6 ml. of absolute ethanol and 32.0 ml. of dry benzene. Three drops of concentrated sulfuric acid were added, and the mixture was refluxed for 24 hr., a Cope-separator being used to remove the water liberated. The benzene–ethanol solution was then washed with saturated aqueous bicarbonate solution, followed by saturated salt solution and then dried for a short time over sodium sulfate. The benzene and ethanol were distilled off. A small amount of 95% ethanol (5 ml.) was added and the mixture cooled in a Dry Ice–acetone-bath. The product crystallized out and was collected by vacuum filtration. Cooling the mother liquors afforded additional product of equal purity, m.p. 39.5–40.5° (yield 11.7 g., 96%). Recrystallization from ethanol gave m.p. 40–40.5°.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.77; H, 6.48.

Enol Ethyl Ether of 3-Carbethoxy-α-tetralone (X).—3-Carbethoxy-α-tetralone (10.9 g., 0.05 mole) was dissolved in 2 ml. (0.051 mole) of absolute alcohol and 7.6 ml. (0.051 mole) of freshly distilled ethyl orthoformate. Two drops of concentrated sulfuric acid were added and the mixture allowed to stand overnight. Triethanolamine was then added and the liquid heated on the steam-bath to remove ethyl formate and ethanol. The residual liquid was distilled under reduced pressure to give a forerun of cloudy material, b.p. 125–133° (0.35 mm.) (5 g.) and a clear fraction, b.p. 133–134° (0.35 mm.), (6 g., 50%), $n^{20}D$ 1.5400. The infrared spectrum of the latter fraction showed no carbonyl absorption; however, the material was unstable and a satisfactory analysis could not be obtained.

3-Hydroxymethyl-α-tetralone (XII).—After standing overnight, the crude enol ether reaction mixture, diluted with an equal volume of dry ether, was added over a period of two hours to a slurry of lithium aluminum hydride (7.5 g., 0.2 mole based on 18.8 g., 0.086 mole of original keto-ester) in 500 ml. of ether. The resulting mixture was stirred for two hours at room temperature, after which time the excess hydride was decomposed by adding water followed by dilute acid. The aqueous phase was separated and extracted with ether. The ether washings were combined with the original ether layer and washed with bicarbonate solution and water. The ether solution was dried over sodium sulfate and the ether then distilled off. Fractionation *in vacuo* gave fractions $n^{25}D$ 1.5765 to $n^{25}D$ 1.5780, b.p. 155–156° (0.35 mm.). The yield was 9.0 g. (59%).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 75.04; H, 6.98.

***p*-Toluenesulfonate of 3-Hydroxymethyl-α-tetralone (VII).**—The keto-alcohol (14.9 g., 0.085 mole) was dissolved in 75 ml. of dry pyridine and the *p*-toluenesulfonyl chloride (19.3 g., 0.094 mole) was dissolved in 150 ml. of pyridine. Both solutions were cooled to 0°, thoroughly mixed and kept at refrigerator temperature for 12–14 hr. The mixture was then cooled again to 0°, and several 2-ml. portions of water were added at 5-minute intervals in order to decompose excess tosyl chloride. Pouring the reaction mixture into a slurry of 75 ml. of concentrated hydrochloric acid and 200–300 g. of ice resulted in the formation of a gummy white solid which was taken up in three portions of chloroform (100, 50, 50 ml.). The chloroform solutions were washed with a relatively concentrated hydrochloric acid solution in order to remove the last traces of pyridine. After final washings with saturated salt solution until neutral, the chloroform solution was dried over sodium sulfate and the chloroform then removed by distillation under reduced pressure, affording 22.0 g. (79%) of white crystalline solid, m.p. 98–99°.

Recrystallization from ethanol afforded white prisms, m.p. 99–100°, if the ethanolic solution was cooled slowly. Rapid cooling of the ethanolic solution gave white needles, m.p. 96–96.5°. Mixed melting point showed no depression. If the needles, when mixed with the prisms, were allowed to melt and then cooled slightly, crystallization in the form of prisms (m.p. 99–100°) took place. The tosylate in ethanol exhibited the following peaks in the ultraviolet: λ_{max} 227, log ε 4.15 (ε 14,200); λ_{max} 249, log ε 4.06 (ε 11,500); λ_{max} 273, log ε 3.16 (ε 1.448); λ_{max} 292, log ε 3.23 (ε 1,710).

Anal. Calcd. for $C_{16}H_{18}O_4S$: C, 65.45; H, 5.49. Found: C, 65.60; H, 5.31.

3,4-Benzo-bicyclo(4.1.0)heptan-2-one (XIII).—The tosylate of 3-hydroxymethyl-α-tetralone (27.2 g., 0.0825 mole) was dissolved in 900 ml. of ethanol with gentle warming on the steam-bath. Sodium hydroxide (6 g., 0.15 mole) dissolved in 150 ml. of water was added and the mixture swirled to give a homogeneous solution with a slight turbid yellow color. After about five hours a qualitative ultraviolet spectrum showed a peak at 244 and 288 mμ (shift from 249 and 292 mμ). The mixture was allowed to stand overnight, neutralized with dilute hydrochloric acid and excess ethanol distilled off at reduced pressure. Solid salt was added to saturate the aqueous solution before extracting three times with ether. The ether extracts were combined and dried over sodium sulfate. Removal of the drying agent by filtration, followed by distillation of the ether, left an oily residue. Benzene was added, and distillation of the product under vacuum gave five fractions, $n^{25}D$ 1.5852 to $n^{25}D$ 1.5865, b.p. 123° (1.0 mm.). The total yield was 11.3 g. (86%). The fraction with $n^{25}D$ 1.5858 was used for analysis.

Anal. Calcd. for $C_{11}H_{10}O$: C, 83.51; H, 6.37. Found: C, 82.97; H, 6.29.

2,3-Benzo-4-cycloheptenone (XIV).—The tricyclic compound XIII (6.04 g., 0.038 mole), dissolved in a small amount of benzene, was rapidly added through a pressure-equalized dropping funnel into a stirred benzene slurry of potassium *t*-butoxide prepared in the following manner. Potassium (28 g., 0.72 mole) was dissolved, with stirring, in a three-liter three-necked flask containing 550 ml. of dry *t*-butyl alcohol and a nitrogen atmosphere. The excess alcohol was distilled off until a slurry started to form at which time benzene was added to act as solvent and to azeotrope out the last traces of alcohol; 2.5 l. of benzene were distilled off before the boiling point of pure benzene was reached. The flask then contained 1000–1500 ml. of benzene.

The flask with dropping funnel and condenser in place and charged with ketone was evacuated four times and refilled with nitrogen. The compound was then added to the potassium *t*-butoxide slurry with stirring. The mixture was refluxed for 2.5 minutes, after which time it was made acidic with dilute hydrochloric acid and then brought back to *p*H 6 with 10% sodium hydroxide. The water layer was separated and the benzene layer washed with 5% alkali until the basic solution remained essentially colorless. The benzene solution was then washed to neutrality with saturated salt solution and the benzene distilled off. Distillation of the product gave six fractions $n^{25}D$ 1.6039 to 1.6052, b.p. 80–83° (0.22 mm.). The total weight obtained was 4.94 g. (82%). A seventh fraction $n^{25}D$ 1.6029 weighed 0.23 g. A fraction of $n^{25}D$ 1.6052 was analyzed.

Anal. Calcd. for $C_{11}H_{10}O$: C, 83.51; H, 6.37. Found: C, 83.86; H, 6.30.

β-(2-Carboxybenzoyl)-propionic Acid.—A solution of XIV (0.997 g., 0.0063 mole) in 100 ml. of methylene dichloride, cooled in an ethylene dichloride–Dry Ice-bath, was treated with ozone. A Welsbach ozonizing machine was used (oxygen pressure, 7.5 lb., scale reading 0.06, 92 volts). Ozone was bubbled through the solution until the appearance of a distinct blue color (10 min.) followed by oxygen (20 min.). The solvent was distilled off under reduced pressure. Water (80 ml.), acetic acid (20 ml.) and 30%

(15) N. D. Zelinsky and E. F. Dengin, *Ber.*, **55B**, 3360 (1922).

hydrogen peroxide (10 ml.) were added, and the solution was then refluxed for 3 hours. After refluxing, the solution was cooled and extracted several times with ether. The ether extracts were washed with a 10% bicarbonate solution, leaving some yellow neutral material in the ether layer. The bicarbonate washings were strongly acidified and extracted with ether. The ether was evaporated down leaving a yellow, oily residue of acidic material. Chloroform was added to the residue; the precipitate which formed was filtered off and washed with chloroform, leaving 0.401 g. (28.6%) of acid, m.p. 130–135°. Two recrystallizations from ether–petroleum ether raised the m.p. to 134.5–135.5° (0.35 g., 25%). An authentic sample of β-(2-carboxybenzoyl)-propionic acid[16] melted at 135–136.8°. The mixed melting point was 134.5–135.5°.

The neutral material from the first ether extraction, amounting to 81 mg., was identified as the dilactone of the above acid.

Norcarenone (XX).—The tosylate of 5-hydroxymethyl-2-cyclohexenone (9.2 g., 0.0328 mole), was dissolved in 450 ml. of 95% ethanol and cooled to 0°. Barium hydroxide (0.0892 *N*, 330 ml., 0.0295 equivalent) was added dropwise and with stirring over a period of 40 min. The base was added at such a rate as to maintain an average *p*H of 7.6–7.8. At no time was the *p*H allowed to go above *p*H 8. After all the base had been added, the solution was stirred until the *p*H of the solution fell to 6. The ethanol was then removed under reduced pressure. The aqueous solution was extracted three times with ether and the combined ether extracts washed with saturated salt solution. The ether was dried over sodium sulfate, which was removed by filtration, after which the ether was distilled off under reduced pressure. The residue was transferred to a small distillation flask with the aid of a small amount of benzene and distilled, giving the following fractions.

Fraction	B.p. °C.	Mm.	$n^{25}D$	Wt., g.
1	44	0.25	1.5150	0.1693
2	44	.25	1.5148	.3379
3	44–46	.25	1.5130	.3384
4	46–45	.25	1.5130	.4224
5	46–45	.25	1.5150	.2060
6	Forced over		1.5110	.2703

The ultraviolet showed λ_{max} 292, log ε 2.79; λ_{max} 218, log ε 4.94. These values indicate 10% of the 2,4-dienone and therefore the true value for pure norcarenone is log ε 4.98 (ε 9,530).

Anal. Calcd. for C_7H_8O: C, 77.75; H, 7.46. Found: C, 78.03; H, 7.47.

(16) W. Roser, *Ber.*, **17**, 2770 (1884).

Rearrangement of XX to Cycloheptadienone.—Norcarenone containing about 26% of the dienone (2.0 g., 0.0185 mole) was dissolved in ether; sodium hydroxide (0.8 g., 0.02 mole), dissolved in 25 ml. of water, was then added and the solution stirred. The aqueous layer turned red-brown almost immediately, while the ether layer became orange-yellow. The mixture was stirred for 5.5 hours, after which time the peak at 218 mμ had disappeared and the value for the peak at 292 mμ had increased markedly. The aqueous layer was then separated, acidified to *p*H 2 with dilute hydrochloric acid, and extracted three times with ether. The ether extracts were combined with the original ether layer and washed with saturated boric acid solution, followed by saturated salt solution. The ether solution was dried over sodium sulfate, the sodium sulfate removed by filtration, and the ether distilled under reduced pressure. The residue was transferred with the aid of a little ether and distilled into a Dry Ice–acetone cooled receiver. The material distilled at 34–36° at 0.8 mm., and amounted to 1.16 g. (58%), $n^{26}D$ 1.5305. The ultraviolet spectrum showed a peak at 292 mμ (log ε 3.81), indicating essentially complete purity.

Isolation of a Eucarvone Intermediate from Basic Treatment of Carvone Hydrobromide.—The carvone hydrobromide was treated under the conditions used for the conversion of tosylate XVIII to norcarenone. Nineteen grams (0.088 mole) of hydrobromide was dissolved in 200 ml. of 95% ethanol, and a 0.2 *N* solution of barium hydroxide was added at such a rate that the *p*H remained below 8.5 and above 8. The temperature of the reaction was maintained at about 20°.

After evaporating the alcohol, washing and extracting the aqueous layer with three 75-ml. portions of ether, 9.5 g. of crude material was obtained. After solvent evaporation, the material was distilled at 0.18–0.2 mm. Redistillation of the first fraction afforded 750 mg. of product, b.p. 52–54° (0.03 mm.), which was analyzed.

Fraction	B.p., °C.	Wt., g.
1	63–73	0.98
2	75–125	4.36
3	Residue	2.50

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.94; H, 9.41. Found: C, 79.45; H, 8.97.

Treatment of the first fraction (λ_{max} 235 mμ, ε 7200) with potassium hydroxide in methanol (1 *M*) gave a 36% spectral yield of eucarvone in 30 minutes (λ_{max} 303 mμ, ε 1880). It was found that eucarvone undergoes 45% deterioration in 2.5 hours under the same conditions, whereas carvone undergoes virtually no change.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MONSANTO CHEMICAL COMPANY]

The Preparation and Bacteriostatic Activity of Substituted Ureas

BY DAVID J. BEAVER, DANIEL P. ROMAN AND PAUL J. STOFFEL

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The preparation and *in vitro* bacteriostatic activity of some ureas, carbanilides and related compounds against *Micrococcus pyogenes* var. *aureus* are described and the physical data of the compounds are tabulated. A discussion of the relation of antimicrobial action to structure is included.

Introduction

The present paper is a continuation of work described previously[1,2] on the relationship of chemical structure to bacteriostatic properties. The search for compounds more stable to light and less soluble in alkaline soap solutions than the previously described bis- and tris-phenols prompted the present study and it was found that certain substituted ureas overcame these limitations of the phenols. The parent compound urea[3] was first mentioned as a bacteriostat in 1906 and reviewed[4] in 1944 and the anthelmintic[5] and bac-

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(4) L. Weinstein and A. McDonald, *Science*, **101**, 44 (1944).
(5) M. Shimotani, *J. Pharm. Soc. Japan*, **72**, 440 (1952).