1,3,4-Triacetoxyphenanthrene (XX).—Two milligrams of 3-hydroxy-1,4-phenanthraquinone was acetylated in one milliliter of acetic anhydride in the presence of a small amount of fused sodium acetate and zinc dust. After 10 minutes at room temperature, the zinc was filtered from the now colorless solution, and after almost complete evaporation of the solvent, dilute acetic acid was added to the warm residual solution. On dilution and further cooling the product precipitated as a white solid; weight 2 mg., m.p. 134–136°. This compound recrystallized, melted at 137–138° and gave no mixture melting point depression with an authentic sample of 1,3,4-triacetoxyphenanthrene (m.p. 137–138°) obtained from Professor L. F. Fieser.[19]

DURHAM, N. C.

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

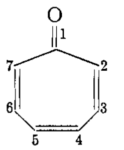
The Synthesis of Tropone and Tropolone *via* a Norcarenone → Cycloheptadienone Rearrangement

BY EUGENE E. VAN TAMELEN AND GEORGE T. HILDAHL[1]

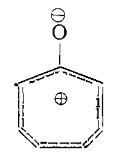
RECEIVED FEBRUARY 20, 1956

The *p*-toluenesulfonate of 5-hydroxymethyl-2-cyclohexenone, the synthesis of which is described, yields 2,4-cycloheptadienone on treatment with alkali. The latter ketone can be oxidized through a variety of techniques to tropone; or, as the enol acetate, it can be transformed to tropolone on oxidation with peracids.

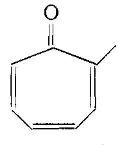
At the time this research was initiated there had been described two routes to that unusual aromatic prototype, *tropone* (cycloheptatrienylium oxide) (Ia or Ib), namely, those described by (1) Dauben and Ringold,[2] who catalytically hydrogenolyzed 2,4,7-tribromotropone, which resulted from the bromination and subsequent heating of 2-cycloheptenone and (2) Doering and Detert,[3] who brominated the product ("methoxytropilidene") obtained by irradiating a mixture of anisole and diazomethane.[4] Because of tropone's novel position in the field of aromatic chemistry and because of the occurrence of the closely related *tropolone* (II) system in various natural products, we believed it worthwhile to attempt the development of new synthesis routes promising adaptability, selectivity and general usefulness. With this purpose in mind we have undertaken two distinct approaches: one involving facile, simple elimination from a seven-membered carbocyclic system with the *direct* formation of the troponoid structure[5]; and a second, featuring the preparation of a well-defined, key *intermediate* which, approaching as closely as possible in oxidation state the tropone (or tropolone) molecule, should be transformable to the desired system through mild dehydrogenation or oxidation techniques. The present account is concerned with the second approach and is divided into three parts: the synthesis of *2,4-cycloheptadienone* (III), the conversion of III to tropone, and the preparation of tropolone from III.



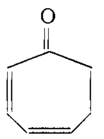
Ia



Ib

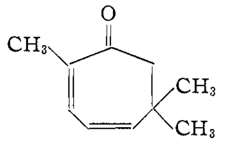


II

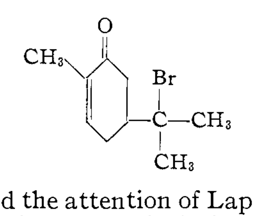


III

Synthesis of 2,4-Cycloheptadienone.—Eucarvone (IV) is an authentic 2,4-cycloheptadienone which was prepared many years ago by Baeyer[6] and, as demonstrated by Wallach,[7] evolves by a rather unusual route: the ring enlargement which accompanies the ready dehydrohalogenation of carvone hydrobromide (V) by alkali. This transformation gained the attention of Lapworth,[8] who supported Wallach's suggestion[7] that it proceeded by way of carenone (VI), which substance, however, could not be isolated and, even now, remains unknown. Nevertheless, the route involving initial ring closure to VI is eminently reasonable[9]; and



IV



V

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[1] Summer Research Assistant 1953 and 1955. Part of this work was first presented in a Communication to the Editor, THIS JOURNAL, **75**, 5451 (1953).

(2) H. J. Dauben, Jr., and H. J. Ringold, *ibid.*, **73**, 876 (1951).

(3) W. von E. Doering and F. L. Detert, *ibid.*, **73**, 876 (1951).

(4) Subsequently we learned that T. Nozoe, Y. Kitahara, T. Ando and S. Masamune (*Proc. Japan Acad.*, **27**, 415 (1951); *C.A.*, **46**, 7558 (1952)) reported the successful application of the brominative dehydrogenation technique to cycloheptanone itself, the major product being 2,4,7-tribromotropone (ref. 2).

(5) Unpublished results obtained in this Laboratory by Miss P. Barth.

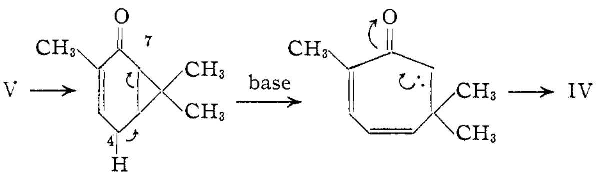
(6) A. Baeyer, *Ber.*, **27**, 810 (1894).

(7) O. Wallach and H. Kohler, *Ann.*, **339**, 94 (1905).

(8) R. W. L. Clarke and A. Lapworth, *J. Chem. Soc.*, **97**, 11 (1910).

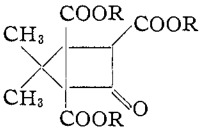
(9) N. D. Zelinsky and E. F. Dengin, *Ber.*, **55B**, 3354 (1922).

the whole process, couched in modern symbolism, becomes

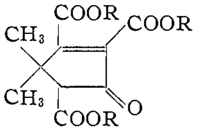


VI VII

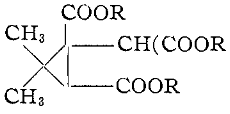
In the change VI → VII, a proton is first removed from the vinylogously activated 4-position; the anion can effect ready carbon to carbon bond breaking, leading to VII, since the resulting anion at the 7-position is in itself stabilized by interaction with the carbonyl group. Thus not one of the changes would appear to involve a high activation energy.[10] Although up until now the eucarvone case had been a unique example of this particular kind of ring enlargement, other rearrangements conform to the general pattern and probably are mechanistically similar. For example Grimwood, Ingold and Thorpe[11] have demonstrated the intervention during reaction of the forms VIIIa and VIIIb of the triester which results from the Dieckmann reaction[12] on the cyclopropane tetraester



VIIIa

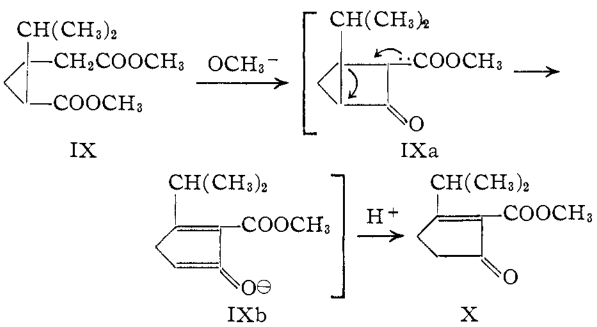


VIIIb



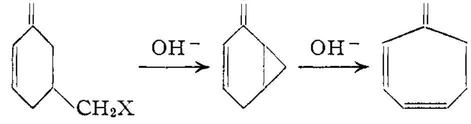
VIIIc

VIIIc.[13] In a similar vein, the Dieckmann ring closure of dimethyl α-thujadicarboxylate (IX)[14] to methyl α-tanacetonecarboxylate (X) has been viewed[15,16] as proceeding by way of the change IXa → IXb. The species represented by the formulas VI-VII, VIIIa-b and IXa-b thus constitute a class and are properly designated transannular valency tautomers.[17–19]



IX IXa IXb X

With the precedent of the eucarvone synthesis in mind, we set out to construct a suitable cyclohexenone of the type XI, which might be anticipated to eliminate, on treatment with base, the displacable group X, and, proceeding by way of the transient *norcarenone* (XII), afford the desired



XI XII

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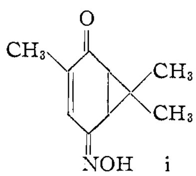
[10] The change VII → VI is implied by the observation of E. J. Corey and H. J. Burke (This Journal, **76**, 5257 (1954)) that eucarvone is transformed, by treatment with butyl nitrite–sodium ethoxide–ethanol, into the monoxime (i).

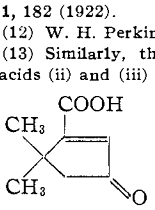


i

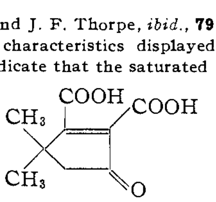
[11] R. C. Grimwood, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **121**, 182 (1922).

[12] W. H. Perkin and J. F. Thorpe, *ibid.*, **79**, 729 (1901).

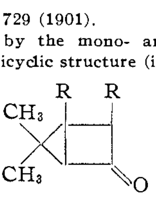
[13] Similarly, the characteristics displayed by the mono- and diacids (ii) and (iii) indicate that the saturated bicyclic structure (iv)



ii



iii



iv

contributes to the reactivity picture (E. H. Farmer, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **121**, 128 (1922)).

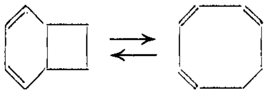
[14] O. Wallach, *Ann.*, **388**, 56 (1912).

[15] R. H. Eastman and C. R. Noller, "Organic Chemistry," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 632.

[16] Mr. Stephen Levin of this department has pointed out that the structure X for methyl α-tanacetonecarboxylate is not beyond dispute (see N. J. Toivonen, *Ann. acad. sci. Fennicae*, **A28**, 1–25 (1928); *C. A.*, **23**, 1624 (1929)).

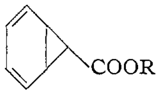
[17] J. W. Baker, "Tautomerism," D. Van Nostrand Co., Inc., New York, N. Y., 1934, p. 263.

[18] An elegant example has been provided (A. C. Cope, A. C. Haven, Jr., F. L. Ramp and E. R. Trumbull, This Journal, **74**, 4867 (1952)) in the bicyclo[4.2.0]octa-2,4-diene-1,3,5-cyclooötatriene system (v-vi), the hydrocarbons being present in an equilibrium mixture.



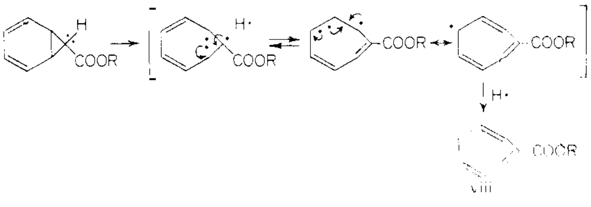
v vi

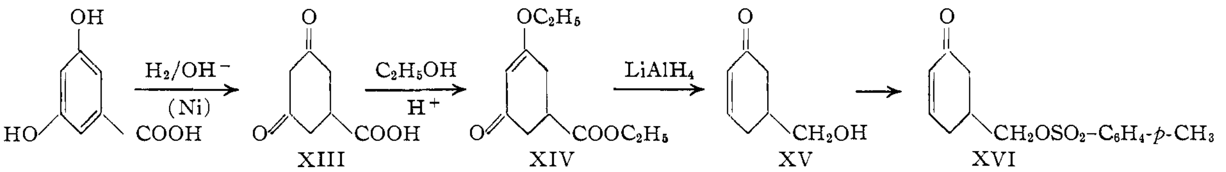
[19] Contrary to possible expectations, norcaradiene carboxylic ester (vii) is not transformed by alkali in great measure to a cycloheptatriene



vii

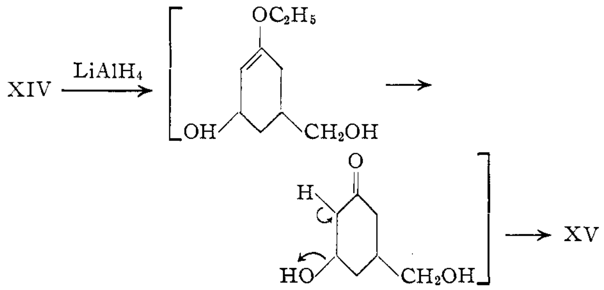
but is largely hydrolyzed to the norcaradiene carboxylic acid (C. Grundmann and G. Ottman, *Ann.*, **582**, 163 (1953); M. J. S. Dewar and R. Pettit, *Chem. and Ind.*, 199 (1955)); this behavior may be due to the difficulty in removal of an α-hydrogen from a cyclopropanecarboxylic ester (F. J. Piehl and W. G. Brown, This Journal, **75**, 5023 (1953)). On the other hand, the ester (vii) is converted to the ring enlarged ester (viii) by *heating* at 150–170°. The process may be either ionic or, more likely, radical in nature, in which case it still corresponds roughly to the general pattern set down above.

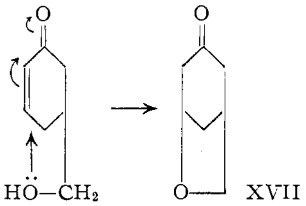




cycloheptadienone. The route chosen, starting with the available[20,21] 3,5-dihydroxybenzoic acid (α-resorcylic acid), proceeds through the stages In the first step the dihydroxyacid was catalytically hydrogenated to 3,5-diketohexahydrobenzoic acid, essentially according to the method successful for the preparation of dihydroresorcinol from resorcinol.[22] Highly active Raney nickel (W-7) led to overreduction, whereas W-1 nickel assured a smooth uptake at 50° of only one mole of hydrogen in the basic medium. This procedure ensured reproducible yields approximating 85% of product which was of sufficiently good quality for use in the succeeding step; after recrystallization, a 64% yield of purer (m.p. 178.0–178.7°) acid was obtained.[23]

It was required that the 1,3-dicarbonyl system be reduced to α,β-unsaturated ketone and the ester function to hydroxymethyl. The former transformation has been accomplished[24,25] on simpler 1,3-cyclohexandiones by first preparing the mono enol ether and subsequently reducing the single unprotected carbonyl with lithium aluminum hydride; the β-hydroxyketone secured after hydroylsis spontaneously dehydrates to the desired product. In the present case the diketoacid XII was simultaneously etherified and esterified by azeotropic distillation of water from an ethanol-benzene solution with p-toluenesulfonic acid as a catalyst. The enol ether-ester XIV, purified by distillation (86% yield), was obtained as a colorless liquid which crystallized at ice-box temperatures. The required reductions could now be accomplished in a single stroke and hydride treatment yielded, through isolation by continuous extraction with ether, a water-soluble sirup which could be neither crystallized nor distilled. The product did possess, however, spectral characteristics (λ_{max}, 226 mμ) consonant with the structure XV, and it was characterized as a bright red dinitrophenylhydrazone, m.p. 147.0–148.5° dec. Although accurate yields of products were indeterminable because we had no satisfactory gage of purity, they were estimated as roughly 65–75% and, moreover, not greatly dependent on the mode—normal or reverse—of addition.[25] Because of the propinquity of the hydroxyl group and the unsaturated carbonyl system, it was considered that at some stage cyclization to the bicyclic keto ether could—if only in part—occur. Deliberate attempts to effect (or maximize) such a cyclization by heating the keto-alcohol or treating it with mineral acid or aqueous alkali led to a certain diminution of the extinction coefficient at 226 mμ and therefore some loss of XV. Whether the latter change was due to partial conversion to XVII (possibly establishment of equilibrium between XV and XVII) or to α,β–β,γ isomerization was not determined, although it may be relevant that 5-methyl-2-cyclohexenone (prepared by the lithium aluminum hydride reduction of 5-methyl-1,3-cyclohexandione enol ether),[25,26] behaved similarly under the conditions applied to XV. In any case, XV displays no unusual facility for intramolecular conjugate addition.





In order to secure the system XI with a displaceable group-X, the sirup XV resulting from the reduction of XIV was converted, after drying but without further purification, to the p-toluenesulfonate XVI. The operation was carried out by treatment with p-toluenesulfonyl chloride at 0°,[27] the product, m.p. 75.0–75.7°, being obtained in good yield (56% over-all from XIV) after the reaction mixture had been allowed to stand for 12–24 hr.

Although the tosylate XVI, when subjected to the conditions used by Baeyer[6] for the carvone hydrobromide → eucarvone change (*viz.*, methanolic sodium hydroxide at 0°), was transformed to 2,4-cycloheptadienone, as evidenced by the presence of the desired product's characteristic ultraviolet spectrum, it was soon determined that the step could be accomplished better by stirring for some hours at room temperature a dilute ether solution of the tosylate with dilute sodium hydroxide. The progress of individual runs could be assessed by inspecting the development of the peak at 292 mμ, due to the product III; this type of assay indicated

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[20] Aldrich Chemical Company, Milwaukee, Wisconsin.

[21] R. B. Thompson, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 278.

[22] A. W. Weston and C. M. Suter, ref. 21, p. 288.

[23] Some time after this work had been completed, A. J. Birch, P. Hextall and S. Sternhell (*Aust. J. Chem.*, **7**, 256 (1954)) reported that the diketoacid XIII resulted from the sodium–liquid ammonia reduction of 3,4,5-trimethoxybenzoic acid. The reduction was reproduced in this Laboratory and afforded material which was identical with XIII obtained earlier by us.

[24] R. L. Frank and H. K. Hall, Jr., THIS JOURNAL, **72**, 1645 (1950).

[25] J. P. Blanchard and H. L. Goering, *ibid.*, **73**, 5863 (1951).

[26] Supplied by Dr. E. Silversmith.

[27] R. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

as high a yield as 85%. The product was isolated in 66% yield, after purification by distillation (b.p. 40–42° (0.5 mm.)) as a colorless liquid with a penetrating, but not unpleasant, odor reminescent of cinnamaldehyde or benzaldehyde.[28] Structural proof was provided by (1) the ultraviolet spectrum ($\lambda_{\max}$ 292 mμ (log ϵ 3.79)), which corresponded well with that of eucarvone ($\lambda_{\max}$ 303 mμ (log ϵ 3.80)), considering that the latter possesses an additional α-alkyl substituent in the chromophore and (2) catalytic hydrogenation in high yield to *suberone*, which was identified as the dinitrophenylhydrazone. Judging from the values of the extinction coefficients displayed by eucarvone and our cycloheptadienone, the latter must be substantially completely the α,β–γ,δ-dienone, uncontaminated by double bond isomers.

Synthesis of Tropone.—During the course of this investigation many oxidations designed to lead from 2,4-cycloheptadienone to tropone or tropolone were carried out. Although a number of reagents were found to afford the former material, no operation leading from III *directly* to tropolone was discovered. In one case, the tropone produced was isolated and characterized; generally, however, the crude product was assayed for tropone content by using the ultraviolet technique. The spectral assay method gives a much more accurate value for the yield in any particular reaction, since the isolation of tropone—as such or as a salt—in modest quantities seems to involve an inevitable loss of material. The sensitive ferric chloride test served to indicate the presence or absence of tropolone.

Acetic acid was the first solvent attempted in the selenium dioxide oxidation of III, and refluxing for several hours effected conversion to tropone. The nature of the product was demonstrated by formation of a monopicrylsulfonate[2] and a monopicrate,[3] the melting points of which agreed well with those reported in the literature. Furthermore, the ultraviolet spectrum of the product featured every characteristic peak previously reported for tropone.[2,3] The selenium dioxide oxidation was also carried out with water, pyridine and ethanol as solvents, the yield resulting from the use of the last-named being the highest (70%, on the basis of spectrophotometric assay). Although oxidation to tropolone might have been expected,[29] the simple dehydrogenation observed is not unprecedented.[30]

Since Willstätter had reported[31] that the product, now known to be a mixture of cycloheptadienones,[28] resulting from the Hofmann elimination of tropinone methiodide, gave a positive Tollens test, it became of interest to repeat the trial on the pure 2,4-isomer. Our dienone did indeed reduce ammoniacal silver nitrate, although neither tropone nor tropolone appeared to be among the reaction product or products.

It seemed that a potentially efficient technique for effecting the cycloheptadienone→tropone conversion is catalytic dehydrogenation. Accordingly the action of (1) Raney nickel and (2) palladium, with maleic acid or maleate anion,[32] on III in an aqueous medium was evaluated. Spectral examination of the product showed that in each of the runs tropone was formed but not in any encouraging amount. Reaction times beyond 2 hr. did not serve to increase the yields.

Recently, Braude, Linstead, *et al.*,[33] reported that certain quinones of high oxidation potential were effective as hydrogen transfer agents, useful for converting hydroaromatic substances to the corresponding aromatic materials. 2,3-Dicyano-5,6-dichlorobenzoquinone, one of the more effective agents, did bring about the dehydrogenation of III, but did not give, under any of several different conditions, higher than a 10% spectral yield of tropone. The time-honored chloranil was no more rewarding. It is interesting to note that these failures are consistent with the concept of quinone dehydrogenation supplied by Braude, Jackman and Linstead:[34] ". . . . a two-step heterolytic mechanism involving a rate-determining transfer of a hydrogen atom with its pair of bonding electrons from the hydrocarbon to the quinone, followed by a rapid transfer between the resulting conjugate acid of the aromatic hydrocarbon and the quinol anion

$$RH_2 + Q \xrightarrow{\text{slow}} R\cdot H^+ + QH^- \xrightarrow{\text{fast}} R + QH_2,\text{"}$$

Clearly, for electrostatic reasons, the removal of hydride from either of the methylene carbons in 2,4-cycloheptadienone would be difficult.

Perhaps the most novel tropone preparation encountered is that involving the action of air in a basic aqueous solution of III, observed quite by chance while carrying out routine spectral analyses. Subsequent control runs showed that III in a dilute solution (*p*H 11–12) was slowly oxidized over a period of days, as evidenced by a fair spectral yield of tropone. The autoxidation was not observed in the *p*H range of 6–10; with much stronger bases (alkoxide or more concentrated aqueous alkali) the ketone appears to decompose.

Treatment with molecular bromine constituted the most satisfactory method for the preparation of tropone from III. The addition of the reagent at 0° to a carbon tetrachloride solution of the starting ketone resulted in the formation of an unisolated addition product, which, on being refluxed in the same solvent for some hours, evolved hydrogen bromide and was transformed into the nearly pure, insoluble tropone hydrobromide,[3] which was isolated in a 79% yield. N-Bromosuccinimide in carbon tetrachloride was completely ineffectual in producing the desired change.

2,4-Cycloheptadienone can be transformed in good yield to an *enol acetate* (XVIII), the reagent

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[28] J. Meinwald, S. L. Emerman, N. C. Yang and G. Buchi (*Chem. and Ind.*, 1063 (1953); THIS JOURNAL, **77**, 4401 (1955)) have reported the formation of isomeric cycloheptadienones, including II, in the basic decomposition of tropinone methiodide.

[29] E. Dane, J. Schmitt and C. Rautenstrauch, *Ann.*, **532**, 29 (1937).

[30] E. Borgwardt and E. Schwenk, THIS JOURNAL, **56**, 1185 (1934).

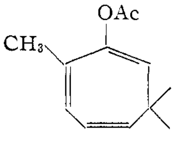
[31] R. Willstätter, *Ber.*, **29**, 393 (1896).

[32] R. Majima and S. Murahashi, *Chem. and Ind.*, **35**, 372 (1936).

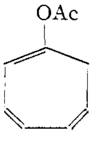
[33] E. A. Braude and R. P. Linstead, *J. Chem. Soc.*, 3544 (1954), and succeeding articles.

[34] E. A. Braude, L. M. Jackman and R. P. Linstead, *ibid.*, 3548 (1954).

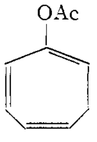
being isopropenyl acetate with *p*-toluenesulfonic acid as the catalyst. The ester, a liquid (b.p. 68–69° (2 mm.)), possessed a peak in the ultraviolet at 266 mμ (log ϵ 3.52), which, after allowance (5 mμ) for an alkyl substituent, tallies well with the observed value of 273 mμ (log ϵ 3.42) for eucarvone enol acetate (XIX).[35] The correspondence does not imply the preferability of structure XVIIIb over XVIIIa, however, since the presence of an acetoxyl substituent on a conjugated, unsaturated chromophore has been claimed[36] to have little effect on the position of the maximum, apart from having an effect because of its *position* on the chromophore.[37] The following reagents were effective in converting the enol acetate to tropone: (1) selenium dioxide in pyridine, (2) lead tetraacetate and (3) N-bromosuccinimide in allyl bromide, although the spectral yield was in no case greater than 29%. One equivalent of perbenzoic acid was found to give, after 6 hr. at room temperature, an intermediate—probably the oxide—which, on mineral acid hydrolysis, afforded an over-all yield of tropone amounting to 55%.[38]



XIX



XVIIIa

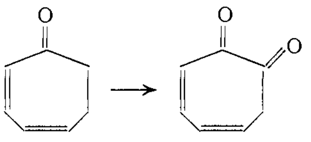


XVIIIb

In appraisal of the various results reported in this section, it seems that there is less similarity between the formal change 2,4-cycloheptadienone-2H → tropone and *e.g.*, the change 1,3-cyclohexadiene-2H → benzene or cyclohexenone-2H → phenol,[39] than one might have anticipated, considering that both lead to an aromatic structure. A dehydrogenation to a benzenoid aromatic can be best brought about by dehydrogenation catalysts or hydrogen transfer agents; these techniques are of no great value, however, in effecting the III → I transformation. Rather, for the purpose, true chemical reagents, acting presumably through direct oxidation or bromination, followed by elimination, are definitely more efficacious.

Since tropone itself has been converted to tropolone,[40a] the transformations described herein constitute new routes to the latter substance and should be considered to supplement those already reported by other workers[40] as well as the route detailed in the following section.

Synthesis of Tropolone.—As emphasized above, the direct conversion of III to tropolone was never accomplished, dehydrogenation to tropone taking precedence in all cases studied. The obtention of tropolone by direct means implies the change (or its equivalent), but reagents generally recognized to be effective in this respect, *e.g.*, alkyl nitrite (leading to an α-oximino ketone), *p*-dimethylaminonitrosobenzene or selenium dioxide produced no tropolone when acting on the ketone III. Certain of the results become understandable by assuming that the increase in resonance energy involved in going to tropone is sensibly greater than that involved in the formation of the (non-aromatic) dione XIX and that, barring decisive mechanistic differences, oxidation will therefore afford the aromatic material.



XIX

The observation that the action of *two* moles of perbenzoic acid on 2,4-cycloheptadienone enol acetate gave a small yield (4%) of tropolone provided the impetus for further peracid attempts. Although the yield in the perbenzoic acid reaction could not be raised beyond the value cited, peroxytrifluoroacetic acid[41] proved reasonably satisfactory. Two equivalents of the oxidizing agent, acting in methylene dichloride at 0°, furnished an intermediate, which was not isolated; acid hydrolysis led to a 26% yield of tropolone, isolated as the copper salt. Regeneration from the metallic derivative gave tropolone (m.p. 49.0–50.5°), which was identical with an authentic sample. Again, several possible routes accounting for the change XVIII → II can be envisioned, of which one is outlined below.

The major share of the starting material was not accounted for; a search did not uncover either of the possible tropolone isomers, β- or γ-hydroxy tropone, which might have been expected to result from a course of oxidation and elimination different from that presented above.

Acknowledgment.—This investigation was supported by a grant from the Research Corporation.

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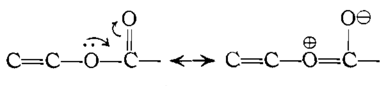
[35] E. J. Corey, H. J. Burke and W. A. Remers, This Journal, **77**, 4941 (1955).

[36] L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, p. 188.

[37] We favor structure XVIIIb, however, for the following reasons: (1) it more readily accounts for the peracid oxidation to tropolone (*vide infra*) and (2) in applying the proposed mechanism (W. G. Dauben, J. F. Eastham, R. A. Micheli, K. H. Takemura, L. Mandell and J. M. Chemerda, This Journal, **75**, 3255 (1953)) for enol acetylation with isopropenyl acetate, it is apparent that the transition state leading to XVIIIb is unstrained, whereas that leading to XVIIIa implies partial double bond character at both bridgeheads. In spite of admitted dubiety, structure XVIIIb will be used, for the sake of clarity, when discussing reactions of 2,4-cycloheptadienone enol acetate.

[38] Attack by peracid at a double bond bearing an acyloxy substituent appears to proceed at a very much slower rate than attack on a double bond with only hydrogen or alkyl substitutions (R. B. Moffett and G. Slomp, Jr., This Journal, **76**, 3678 (1954)). This behavior may be ascribed to the partial positive charge on the enolic oxygen



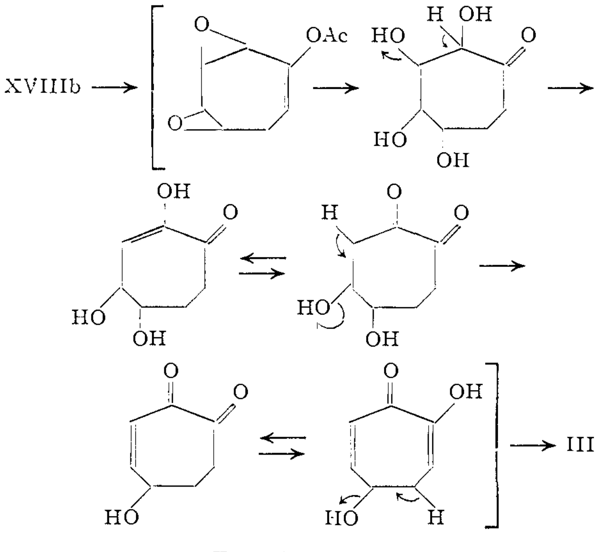
$$\mathrm{C{=}C{-}O{-}\overset{\overset{O}{\|}}{C}{-}} \longleftrightarrow \mathrm{C{=}C{-}\overset{\oplus}{O}{=}\overset{\overset{O^{\ominus}}{|}}{C}{-}}$$

its effect being to render the double bond area more positive and therefore to retard attack by the electrophilic reagent. The observation of Moffett and Slomp that a 1-acyloxy-1,3-diene is epoxidized at the 3,4-double bond is reasonable, since the electrostatic effect of the charged oxygen should fall off with distance, thereby implying—other factors being equal—preferential attack at the more distant olefinic link.

[39] E. C. Horning and M. G. Horning, This Journal, **69**, 1359 (1947).

[40] (a) W. von E. Doering, Abstracts of American Chemical Society Symposium, June, 1953, p. 1; W. von E. Doering and L. H. Knox, This Journal, **73**, 837 (1951); (b) P. L. Pauson, *Chem. Rev.*, **55**, 30 (1955).

[41] W. D. Emmons and A. S. Pagano, This Journal, **77**, 89 (1955).



Experimental[42]

3,5-Diketohexahydrobenzoic Acid (XIII).—A steel hydrogenation bomb was charged with the following: (1) 3,5-dihydroxybenzoic acid (m.p. 236–238°), 308 g. (2.0 moles); (2) 900 ml. of water; (3) 176 g. (4.4 moles) of sodium hydroxide; and (4) 3 teaspoonsful of W-1 Raney nickel. The hydrogenation was carried out at 50° under about 1400 p.s.i. with shaking. Hydrogen uptake stopped after about 3.5 hr., at which point one mole had been consumed. With the aid of about 100 ml. of water, the bomb content was removed and the catalyst filtered off. The pale gray-green solution was iced and acidified slowly to congo red with about 300 ml. of concentrated hydrochloric acid; the diketo acid appears to be sensitive to the acid medium at higher temperatures. During the acidification the solution became turbid but later clear, when more strongly acidic; at the same time a color change from green to yellow took place. The acid solution is subject to supersaturation, although scratching induces crystallization. After crystallization at refrigerator temperature, the yellowish, sandy crystals of 3,5-diketohexahydrobenzoic acid were isolated by filtration. This product, which was contaminated by a small amount of sodium chloride, weighed 289 g. (83%) and melted at 165–168° (after previous yellowing at about 150°). The material isolated by continuous ethyl acetate extraction amounted to 8 g. and raised the yield to 86% of material which was suitable for the preparation of the enol ether XIV. Recrystallization can be accomplished using water, acetic acid or ethyl acetate, the melting point thereby being raised to 178.5–180°; a single crystallization gives a 64% yield of acid melting at 178.0–178.7°.

The acid does not give a color with ferric chloride solution.

Anal. Calcd. for $C_7H_8O_4$: C, 53.86; H, 5.16. Found: C, 53.60; H, 5.33.

3-Ethoxy-5-carboethoxy-2-cyclohexenone (XIV).—To a five-liter round-bottomed flask equipped with a Dean-Stark water separator was added 156 g. (1 mole) of 3,5-diketohexahydrobenzoic acid (XIII), 400 ml. of absolute ethanol, 2400 ml. of benzene and 5 g. of *p*-toluenesulfonic acid monohydrate. The solution was refluxed rapidly for 36 hr., during which period about 100 ml. of aqueous condensate collected. After the solution had been concentrated at atmospheric pressure to about one liter and allowed to cool, it was freed from some precipitated solid by filtering. Removal of the toluenesulfonic acid was accomplished by washing the benzene solution with dilute aqueous bicarbonate and saturated salt solution. Distillation gave a colorless liquid boiling at about 125–130° (0.4 mm.). The refractive indices of eight fractions fell within the range 1.4911–1.4923 ($n^{25}D$), and material with the index 1.4920 was used for analysis. The total yield was 183 g. (86%).

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.76; H, 7.36.

5-Hydroxymethyl-2-cyclohexenone (XV).—A solution of 38 g. (1.0 mole) of lithium aluminum hydride in 700 ml. of dry ether was used to reduce in the usual fashion 106 g. (0.5 mole) of 3-ethoxy-5-carboethoxy-2-cyclohexenone (XIV), dissolved in 100 ml. of dry ether. After the addition of XIV to the reducing agent was complete (3 hr.), the excess reagent was decomposed by the addition of ethyl acetate in ether. The reaction mixture was then poured, with stirring, into a mixture of 50 ml. of concentrated sulfuric acid, 200 ml. of water and about 500–600 g. of ice. After the ether layer clarified, it was decanted and allowed to stand over dry sodium bicarbonate for a short time before filtering. Sodium bicarbonate was added in small increments to the aqueous phase resulting from the workup of the hydride reduction mixture until aluminum hydroxide began to precipitate, at which time sodium sulfate sufficient to saturate the solution was added. Ether extraction, carried out with a continuous extractor over a period of 40 hours and with several changes of solvent, afforded, after removal of solvent under reduced pressure, a residue, which was dried by distilling from it about 2 liters of benzene. The remaining benzene was removed by adding chloroform and distilling; finally, as much of the latter solvent as possible was removed under 1.0 mm. of pressure. The red-brown sirup displayed a peak at 226 mμ, and in the assumption that the pure 5-hydroxymethyl-2-cyclohexenone would possess an extinction coefficient of around 10,000, the amount of product present constituted about a 65–75% yield. An attempt to distil this water-soluble sirup resulted in extensive resinification; no tendency to crystallize was observed.

In an attempt to effect cyclization to the bicyclic compound XVII, portions of the material were subjected to various conditions of heat and *p*H. In all cases, a slow diminution, ceasing after about a 33–38% decrease in the height of the peak at 226 mμ, was observed. 5-Methyl-2-cyclohexenone exhibited a similar behavior.

The 2,4-dinitrophenylhydrazone was prepared by adding 0.6 ml. of the crude XV to a solution of 0.5 g. of DNP, 10 ml. of concentrated sulfuric acid and 10 ml. of 95% ethanol, which had previously been brought to boiling. After the reaction mixture had cooled, the crystalline product was separated from some oil which had formed and was crystallized from absolute ethanol. The bright red derivative, m.p. 147.0–148.5°, possessed λ_{max} 252 mμ (log ε 4.20), 374.5 mμ (log ε 4.43).

Anal. Calcd. for $C_{13}H_{14}O_4N_4$: C, 50.97; H, 4.61. Found: C, 50.94; H, 4.90.

The *p*-toluenesulfonate (XVI) of 5-hydroxymethyl-2-cyclohexenone was secured according to the method of Tipson.[27] The reaction mixture began, after several hours at 0°, to deposit pyridinium chloride. After a total reaction time of 12–24 hr. at the same temperature, 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 125 ml. of concentrated hydrochloric acid and 300–400 g. of ice resulted in the separation of an oil, which was taken up in 3 successive 100-ml. portions of chloroform or, perhaps better, ether. After being washed with saturated salt solution, the combined extracts were concentrated at room temperature by evaporation in a stream of air; cooling and seeding induced crystallization of the residue. The semi-solid cake thus obtained was triturated with a small amount of ether and filtered, after which procedure there was obtained a mass of fine needles, m.p. 72.5–73.5°, weighing 15.7 g. (56% over-all from XIV). Of the solvents suitable for recrystallization (95% ethanol, absolute ethanol, ether and acetic acid), 95% ethanol was most frequently used, and tosylate purified through its use melted at 75.0–75.7°.

Anal. Calcd. for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 60.21; H, 5.54.

2,4-Cycloheptadienone (III).—Initial attempts to effect the rearrangement of the tosylate XVI to 2,4-cycloheptadienone were carried out under the conditions used by Baeyer for the preparation of eucarvone. The reaction developed a brilliant red color, and spectral assay showed that a certain amount (ε 600–4000 at 292 mμ) of III had formed, the quantity depending on reaction time, temperature, etc. The following modified procedure was found to give the highest and most reproducible yields. To a solution of 19.6 g. (0.07 mole) of the tosylate XVI (m.p.

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[42] All melting points are corrected.

73.5–75.0°) in a liter of good quality ether was added 3.4 g. (0.085 mole) of sodium hydroxide dissolved in 250 ml. of water, and the mixture was stirred at room temperature for about 16 hr. During this time, the ether layer turned an intense yellow, and the aqueous phase became reddish-brown. From time to time, an aliquot was assayed in the ultraviolet; when the extinction coefficient at 292 mμ reached about log ε 3.72 (85% conversion) the reaction was worked up. The ether layer was removed, and the aqueous portion, after acidification with sodium bisulfate, was extracted with three portions of ether. The combined ether solutions were washed with saturated boric acid solution and then with saturated sodium chloride solution. In order to isolate the product, the ether was carefully removed under diminished pressure, and the dark red oil remaining was distilled. Three fractions

		n^{25}D	
1.	Below 39.5° (0.5 mm.)	1.5335	1.07 g.
2.	40–42° (0.5 mm.)	1.5337	1.51 g.
3.	42° (0.5 mm.)	1.5333	2.44 g.

were taken; the refractive indices indicated essential homogeneity of the colorless product, which was obtained in a total yield of 66%.

Anal. Calcd. for C_7H_8O: C, 77.73; H, 7.46. Found: C, 77.65; H, 7.56.

Reduction of III to Cycloheptanone.—The dienone III (0.442 g., 0.0041 mole) was reduced catalytically with Adams catalyst (0.07 g.) at atmospheric pressure and room temperature with ethanol distilled from Raney nickel as the solvent. The ketone took up in one hour 95% of the calculated amount of hydrogen. After being freed from catalyst, the solution of cycloheptanone was added to a solution of 0.8 g. of DNP in 1.6 ml. of sulfuric acid and 15 ml. of 95% ethanol. Digestion for a few minutes was followed by cooling overnight in the refrigerator. The pale yellow product, after isolation by filtration and subsequent drying, weighed 1.02 g. (85%) and melted at 144.5–145.0°. Elemental analysis and a mixed melting determination with authentic cycloheptanone DNPH (m.p. 148.0–148.5°) served to identify our material, which, after recrystallization from ethanol, melted at 148.5–149.0°.

2,4-Cycloheptadienone Enol Acetate (XVIII).—The reaction between 2,4-cycloheptadienone (III) (16.2 g., 0.15 mole) and isopropenyl acetate (30 ml.) was carried out with 1.0 g. of *p*-toluenesulfonic acid monohydrate as a catalyst. The round-bottomed flask used for the operation was attached to a Vigreux column, and, while the reaction mixture was boiled, the distillate (acetone) boiling up to 69° was collected. After approximately the theoretical amount of acetone had been collected, the catalyst was neutralized with 1.0 g. of fused sodium acetate. Distillation of the excess reagent was carried out at water pump pressure, and fractionation of the residue afforded 17.1 g. (76%) of 2,4-cycloheptadienone enol acetate, b.p. 68–69° (2 mm.), n^{25}D 1.5117.

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.94; H, 6.67.

Conversion of 2,4-Cycloheptadienone to Tropone. Selenium Dioxide Oxidation.—The product III resulting from the rearrangement and detosylation of 2.8 g. (0.01 mole) of XVI was taken up directly in 15 ml. of glacial acetic acid and added to a solution of 2.4 g. (0.02 mole) of freshly sublimed selenium dioxide in 10 ml. of the same solvent. While the reaction mixture refluxed for 2.5 hr., red selenium precipitated. After the addition of 10 ml. of water, refluxing was continued for 0.5 hour. Precipitated selenium was removed by filtration with the aid of Filter-Cel, and the acetic acid solution was treated with sulfur dioxide gas in order to reduce the excess selenium dioxide, after which the filtration was repeated. Two 10-ml. portions of water were added while the volume of the solution was reduced under diminished pressure; when the volume reached 15 ml., the solution was divided into two parts. One portion was reserved for preparation of tropone picrylsulfonate, while the other was used to make tropone picrate.

A. Tropone Picrate.—A 10-ml. portion of the above solution was treated with 30 ml. of saturated aqueous picric acid. The solution was extracted with three successive portions of chloroform (total volume, 100 ml.). Excess solvent was removed from the yellow-colored extracts through the application of a stream of air. Slow evaporation left a crystalline mass, consisting of picric acid crystals mixed with darker colored rhombs of tropone picrate. The latter were separated manually and when collected, weighed 0.47 g. (21%) and melted at 100–101.2°. The melting point reported for a monopicrate is 99–100°.[3] Attempts to recrystallize led to extensive decomposition and therefore the picrate was analyzed without further purification.

Anal. Calcd. for $C_{13}H_9N_3O_8$: C, 46.65; H, 2.84; N, 12.54. Found: C, 46.45; H, 2.98; N, 12.88.

In order to regenerate tropone for spectral identification, a solution of 0.100 g. of tropone picrate in 10 ml. of 50% ethanol was put through a column prepared by placing in a 25-ml. buret about 8 g. of IR-45 resin in the hydroxyl phase. The ultraviolet spectrum of the eluate revealed all the peaks (λ_{max} 224, 228, 232, 239, 303 (infl.) and 312 mμ) with appropriate extinctions reported for tropone.[2,3]

B. Tropone Picrylsulfonate.—Five ml. of the aqueous solution containing tropone produced by the selenium dioxide oxidation in acetic acid was mixed with a solution of 1.0 g. of picrylsulfonic acid in 5 ml. of water. After being allowed to stand overnight in the cold, the reaction mixture was filtered and the salt recrystallized five times from water, after which it melted at 268–270° (reported m.p. 266–267°[2]).

Selenium dioxide oxidation in ethanol proceeded smoothly according to the following method. A mixture obtained by adding a solution of 0.554 g. (0.00514 mole) of III in 5 ml. of 95% ethanol to a solution of 0.568 g. (0.00514 mole) of selenium dioxide in 5 ml. of ethanol was refluxed for 0.75 hour, during which time black selenium deposited. The cooled mixture was poured into 100 ml. of water and neutralized with sodium bicarbonate. After removal of selenium by filtration, the tropone solution was extracted with four portions of chloroform (total volume 250 ml.). Spectrophotometric assay at two wave lengths in the ultraviolet (232 and 312 mμ) indicated yields of 71 and 72%, respectively, of tropone.

Catalytic Dehydrogenation.—To each of three flasks was added 50 ml. of water containing 0.108 g. (0.01 mole) of 2,4-cycloheptadienone. To one flask was added *ca.* 0.5 g. of W-1 Raney nickel; to a second, 0.5 g. of palladium black and 0.235 g. of maleic acid[32] and to the remaining flask, the same quantities of palladium black and maleic acid plus 1 g. of sodium bicarbonate. Each mixture was refluxed and aliquots removed periodically to check the progress of reaction; each aliquot was run into water (treated, if acidic, with sodium bicarbonate) and extracted with ether. The ether extract was diluted with ethanol and the ultraviolet spectral determination made. After three hours, the nickel experiment had produced no detectable amount of tropone. After 2 hr., the yield in the palladium–maleic acid run amounted to 18%; an additional hour's reflux did not raise the yield. The palladium–sodium maleate experiment gave a somewhat smaller amount of tropone, which sensibly diminished after an additional hour's reaction time.

Quinone Dehydrogenation.—Of the sets of conditions tried, the following produced the best yields, which in other cases fell as low as 1%.

2,3-Dicyano-5,6-dichloroquinone (1.025 g.) was added to a solution of 0.485 g. of the dienone III; on warming the reagent dissolved to give a bright red solution, which was refluxed for 2 hr. During this time a dark, heavy precipitate formed. The mixture was cooled and filtered, and the filtrate freed of benzene by distillation under diminished pressure. Trituration of the remaining oil with hot water gave a brownish solution which was assayed by the ultraviolet method, which indicated a 9–10% yield of tropone.

Air Oxidation.—A solution containing 2.5 × 10^{-4} mole of III and 5 × 10^{-4} mole of sodium hydroxide in 100 ml. of water was allowed to stand at room temperature; periodically the absorption in the ultraviolet was measured and the yield of tropone determined (starting material: λ_{max} 292 mμ; ε 5900).

Time, hr.	λ_{max}, mμ	ε	λ_{max}, mμ	ε
2	298	5700		
6	300	5600	232	2700
96	311	3960	232	8600 (also: λ_{max} 224, ε 8200; 227, ε 8500; 239, ε 5500)

The spectral values after 96 hr. indicated a 38% conversion to tropone. Attempts to carry out the oxidation at *p*H 6, *p*H 8 and *p*H 10 were unsuccessful.

Brominative Elimination.—To a solution of 0.812 g. (0.0075 mole) of 2,4-cycloheptadienone in 20 ml. of carbon tetrachloride was added dropwise with stirring a solution of one equivalent of bromine in 38 ml. of carbon tetrachloride. The addition was carried out at 0° over a period of 2 hr.; disappearance of the bromine color was immediate. Although the intermediate bromination product was not investigated, it was noted to be somewhat volatile and extremely irritating. The brominating mixture was then refluxed, with the exclusion of atmospheric moisture, overnight, during which time a felt-like mass of tropone hydrobromide was deposited. The product, which weighed 1.04 g. (79%), was contaminated by a small amount of black powder; spectral analysis showed that the salt was, however, 95% pure (obsd. log ϵ 4.32 $\lambda_{\max}$ 224 mμ), reported log ϵ 4.43).

Conversion of 2,4-Cycloheptadienone Enol Acetate to Tropone. Elimination with N-Bromosuccinimide.—Using an infrared lamp as a heat source, a mixture of 0.25 g. (0.005 mole) of XVIII, 0.9 g. (0.005 mole) of N-bromosuccinimide and 25 ml. of allyl bromide was refluxed for 2 hr. After this time a mixture of solids had precipitated, spectral assay of which indicated a quantity of tropone, presumably as the hydrobromide, which corresponded to about 16% yield. The allyl bromide filtrate was extracted with dilute hydrochloric acid; the extract revealed on spectral analysis an additional amount of tropone which raised the total spectral yield to 29%.

Perbenzoic Acid Oxidation.—A chloroform solution of 0.75 g. (0.005 mole) of XVIII was made up in a 50-ml. volumetric flask with 14.5 ml. of a chloroform solution containing one equivalent of perbenzoic acid. The consumption of perbenzoic acid was complete after 6 hr. at room temperature. Twenty-five milliliters of the reaction mixture was extracted with 5% sodium carbonate; neither the aqueous extract nor the chloroform solution gave a test for tropolone (ferric chloride). The latter solution was mixed with a solution of 1 ml. of concentrated hydrochloric acid in 20 ml. of water, after which the chloroform was distilled off. Neutralization of the aqueous tropone hydrochloride solution with sodium carbonate, followed by spectral assay, indicated a 55% yield of I.

Small yields of tropone were also obtained as a consequence of the action of the following reagents on 2,4-cycloheptadienone enol ether: (1) selenium dioxide in pyridine, (2) lead tetraacetate.

Conversion of 2,4-Cycloheptadienone to Tropolone.—Through the action of two moles of perbenzoic acid on the enol acetate XVIII, tropolone was obtained, although in small yield (4.3%). The oxidation proper was carried out as described in the XVIII to tropone conversion, using perbenzoic acid, except that two equivalents of the reagent were used. The rate of consumption of the second mole was slower than that of the first. Again, a 25-ml. portion of the chloroform solution was extracted with 5% sodium carbonate, which removed no tropolone (ferric chloride test); 1 ml. of concentrated hydrochloric acid and 20 ml. of water was added to the chloroform solution and the organic solvent removed by evaporation. The aqueous solution remaining was decanted from a tarry, brown residue and then extracted with chloroform. The extract was mixed with 20 ml. of concentrated aqueous cupric acetate, the mixture warmed and the chloroform separated. After several repetitions of the hot chloroform extraction, the combined extracts were concentrated to give 33 mg. of pale green needles, m.p. 318° (lit. 320°[43]). A portion of the salt was converted to tropolone by treatment with hydrogen sulfide; sublimation of the recovered aromatic gave product which melted at 50–51°.

The yield of tropolone could be raised to 26% by oxidation with peroxytrifluoroacetic, rather than perbenzoic, acid. A solution of 3.0 g. (0.02 mole) of the enol acetate XVIII in 25 ml. of dry methylene chloride was introduced into a suspension of 25 g. of vacuum dried, powdered sodium carbonate in 80 ml. of dry methylene chloride protected from moisture. While the flask was cooled in ice, a methylene dichloride solution containing, by assay, 0.04 equivalent of peroxytrifluoroacetic acid (about 10% of the solvent was distilled from the solution before its standardization, as an aid toward drying) was added dropwise with rapid stirring. The supernatant, which did not give any coloration with ferric chloride, was decanted from the buffer, which had coalesced after about three-quarters of the peracid had been added. The methylene chloride solution, combined with three washings of the residue made with the same solvent, was mixed with 20 ml. of 20% hydrochloric acid. Evaporation of the organic solvent left a reddish-brown pungent solution, which was filtered and extracted with portions of chloroform until the extracts failed to give the green color, characteristic of tropolone, with alcoholic ferric chloride. Removal of the solvent under reduced pressure gave about 1.3 g. of a dark liquid which was converted to a precipitate of crude tropolone copper enolate on treatment with 25 ml. of saturated cupric acetate solution. The precipitate was taken up in hot chloroform; after filtration, the solvent was blown off to yield 0.807 g. of the enolate, m.p. 319–320°. The metallic derivative could be converted by the hydrogen sulfide method in 93% yield of sublimed tropolone, m.p. 50.4–51.6°. A mixed melting point taken with authentic tropolone (m.p. 50.8–51.6°) was found to be 50.6–51.6°.

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[43] W. von E. Doering and L. Knox, THIS JOURNAL, **73**, 828 (1951).

MADISON, WISCONSIN

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Studies with the Amine Adducts of β-Benzoylacrylic Acid and its Methyl Ester[1]

BY NORMAN H. CROMWELL, PAUL L. CREGER AND KENNETH E. COOK

RECEIVED APRIL 2, 1956

Evidence is presented to show that amines add to both β-benzoylacrylic acid and its methyl ester to produce the α-amino-γ-ketoacids and esters. Reduction of the methyl α-amino-β-benzoylpropionates with lithium aluminum hydride produced a new class of amino diols while catalytic hydrogenation led to the new γ-phenyl-α-amino-γ-butyrolactones. γ-Phenyl-γ-butyrolactone reacted with morpholine to give γ-phenyl-γ-morpholinobutyric acid while γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide under similar conditions resulted in β-benzoylpropionmorpholide. The infrared spectra of these materials were determined and analyzed.

Several investigators have reported studies of the reactions of β-benzoylacrylic acid and its esters with ammonia and amines.[2] Little or no evidence for the structures of the resulting products have been offered by these investigators and disagreement as to assignment of structures is apparent from a reading of the literature. Nevertheless, Bougault[2a] seems to have made the most logical structural assignments for the amine adducts.

The present investigation of the reactions of

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[1] Presented in part at the 128th meeting of the American Chemical Society, Minneapolis, Minn., Sept., 1955.

[2] (a) J. Bougault, *Ann. chim. phys.*, [8] **15**, 491 (1908); (b) P. Chabrier, *et al.*, *Compt. rend.*, **230**, 212 (1950); **226**, 1378 (1948); **237**, 1420 (1953).