The Decarboxylation of β-Keto Acids. II. An Investigation of the Bredt Rule in Bicyclo[3.2.1]octane Systems[1,2]

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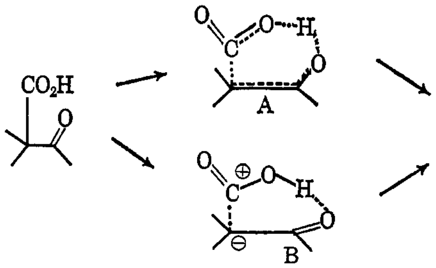
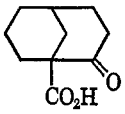
Abstract: 1-Carboxy-7-oxobicyclo[3.2.1]octane (III) and 1-carboxy-2-oxobicyclo[3.2.1]octane (IV) were prepared by reaction of the acid chlorides of hexahydrohomoisophthalic acid (VI) and 3-(3-carboxycyclopentyl)propanoic acid (VII), respectively, with triethylamine. The rates of decarboxylation of III and IV were measured. From these data and published data on the bicyclic acids I, XIV, and XV it is postulated that in bridged bicyclic keto acids the carbon atom bearing the carboxyl group maintains its sp^3 hybridization during decarboxylation and the rate of decarboxylation is proportional to the cosine of the angle between the orbital of the incipient sp^3 carbanion and the p orbital of the carbonyl group.

In our initial studies concerning Bredt's rule in bicyclo[3.3.1]nonane systems we found that the rate of decarboxylation is not a function of strain in an enolic transition state (A) but rather that it depends on the degree of overlap of the developing carbanion with the adjacent keto group (B) in a transition state with considerable ionic character.[2,3] In transition state A, which was proposed by Westheimer and Jones[4] for the concerted decarboxylation of simple β-keto acids, the carbon bearing the carboxyl group is sp^2 hybridized. This transition state is stabilized by overlap of the p orbital of the sp^2 carbon atom bearing the carboxyl group and the p orbitals of the carbonyl group. Transition state B is also stabilized by overlap but in a slightly different way. Here the extent of the overlap will be determined by the amount of p character the developing carbanion exhibits in the transition state[5] and the interacting orbital angle between this carbanion and the adjacent keto group. In rigid bicyclic systems the developing carbanion will be essentially sp^3 hybridized so that the energy of the transition state will be determined principally by the angle between the sp^3 orbital of the developing carbanion and the p orbital of the carbonyl group. The main difference between transition state A and transition state B is that the carbon atom bearing the carboxyl group is sp^2 hybridized in the former and sp^3 hybridized in the latter.

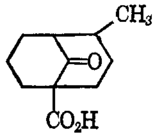


It was possible to understand the relatively facile decarboxylation of lycoctonamic acid on the basis of transition state B.[2] Inspection of models showed that transition state A was impossibly strained for lycoctonamic acid, while transition state B allowed for considerable overlap of the incipient sp^3 hybridized carbanion with the adjacent carbonyl group explaining the experimental observation.[6]

At the time we began this study lycoctonamic acid was the only compound in which it was necessary to invoke the transition state depicted in path B. For the other bridged bicyclic β-keto acids the classical mechanism for the decarboxylation of simple β-keto acids[4] (transition state A) had been applied.[7] For example, one can explain on the basis of A why the bicyclo[3.3.1]nonane derivative I decarboxylates with ease and the corresponding bicyclononane derivative II does not.[2] The strain in the enolic transition state is more readily accommodated by I because the enol double bond is in the three-carbon bridge as compared to its being in the one-carbon bridge in II.[7] However, transition state B will also explain these observations. In I the interacting orbital angle between the keto and carboxyl groups is 30° allowing for considerable overlap of the developing carbanion with the carbonyl group. The interacting orbitals are orthogonal in II and therefore one would expect little or no stabilization of the transition state by overlap of the carbanion with the carbonyl group. Although the strain in an enol intermediate (transition state A) has been used to explain



I



II

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[1] Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. Direct inquiries to J. P. F. at The Salk Institute for Biological Studies, La Jolla, Calif.

[2] Previous paper: J. P. Ferris and N. C. Miller, *J. Am. Chem. Soc.*, 85, 1325 (1963). This and the previous paper were abstracted from the Ph.D. dissertation of N. C. M., Florida State University, 1964.

[3] A brief discussion of the Bredt rule in bicyclo[3.3.1]nonane systems has been presented recently by J. P. Schaefer and J. C. Lark, *J. Org. Chem.*, 30, 1336 (1965).

[4] F. H. Westheimer and W. A. Jones, *J. Am. Chem. Soc.*, 63, 3283 (1941).

[5] In the case where the carbanion retains all its sp^3 hybridization the overlap would be three-fourths that of a p orbital.

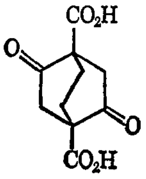
[6] A discussion of the rate of decarboxylation as a function of the stability of a bridgehead carbanion is given by V. Prelog, *J. Chem. Soc.*, 420 (1950). For a recent discussion of the effect of ring constraint on carbanion stability see D. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 52, 53.

[7] H. O. House and H. C. Muller, *J. Org. Chem.*, 27, 4436 (1962); E. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc. New York, N. Y., 1962, p 302; H. H. Wasserman, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 353.

the literature data,[7] it was our feeling that transition state B would more closely represent the actual situation in the small bridged ring systems. In these rigid systems it would be difficult to attain the sp^2-hybridized carbon atom required by A; B would be a more likely candidate. In this paper we will describe some experiments which test this postulate directly.

We prepared 1-carboxy-7-oxobicyclo[3.2.1]octane (III) and 1-carboxy-2-oxobicyclo[3.2.1]octane (IV) as our model compounds. If the rate of decarboxylation is principally a function of the size of the bridge in which the enol double bond is formed (transition state A), then IV should decarboxylate at only a slightly higher temperature than I. If the carbon atoms bearing the carboxyl group maintain most of the sp^3 hybrid character in the transition state, then the temperatures of decarboxylation should be proportional to the dihedral angle between the keto and carboxyl groups (transition state B).

Compounds III and IV were also chosen to explore the application of the Bredt rule in systems where the total ring size (*S*) is 6.[8] Several compounds have been studied with an *S* number of 5 or 7. The former are generally inert to decarboxylation, and the latter usually decarboxylate at moderate temperatures. It was our goal to explore this borderline region since V is the only compound in this intermediate region on which decarboxylation studies have been made.[10]

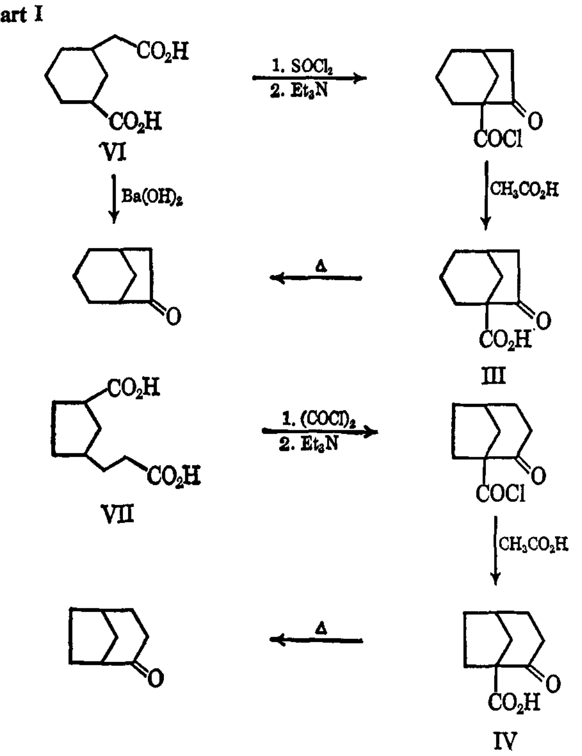


V

Synthesis

Our synthetic strategy was to prepare the diacids VI and VII and then to cyclize these to the bicyclic keto acids III and IV by the procedure of Hatchard and Schneider (Chart I).[11,12] An important advantage of this method of bridged ring synthesis is that 1,3-disubstituted cycloalkanes are the starting materials and not the more difficultly accessible 1,1,3-trisubstituted cycloalkanes required if a conventional method of cyclization (*e.g.*, Dieckmann[2]) were used. Furthermore, the mechanism of the cyclization is such that as long as one of the carboxyl groups of the diacid is directly attached to the cycloalkane ring it does not matter whether the *cis* or *trans* isomer is used.[12b] The yields in the cyclizations were low, but these advantages made this approach the method of choice for these unsymmetrical bicyclic systems. Hexahydrohomoisophthalic acid (VI) was prepared by a modification of the literature procedure[13] (see the Experimental Section). The synthesis of VII is described below. It was proved that compounds III and IV have bridgehead carboxyl groups by observing carbonyl absorption in the infrared characteristic of nonenolic β-keto acids.[14] Furthermore, the ultraviolet spectrum of III is in agreement with a bridgehead carboxyl and not with the alternative 6-carboxy derivative.[14b] The bicyclic ring structures of III and IV were proved by decarboxylation to the known bicyclooctanones.

Chart I



In the synthesis of IV two procedures were developed to synthesize the penultimate 3-(3-carboxycyclopentyl)-propanoic acid (VII) (Charts II and III). In our initial synthesis (Chart II) methyl 3-(2-oxocyclopentyl)propanoate (VIII, R = CH_3)[15] was converted into methyl 3-(2-oxo-3-carbomethoxycyclopentyl)propanoate (IX, R = CH_3) in 30% yield by reaction with methyl magnesium carbonate (MMC) followed by esterification of the intermediate β-keto acid.[16] Compound IX was reduced to the alcohol X (R = CH_3) with hydrogen and platinum and was dehydrated in low yield to a mixture of olefins. Vapor phase chromatography (vpc) indi-

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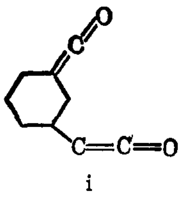
[8] The concept of *S* number was developed by Fawcett[9] and refers to the total number of atoms between the two bridghead atoms, *e.g.*, *S* = 7 in bicyclo[3.3.1]nonane.

[9] F. S. Fawcett, *Chem. Rev.*, 47, 219 (1950).

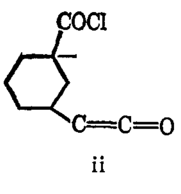
[10] P. C. Guha, *Ber.*, 72, 1359 (1939). It was not possible to determine the interacting orbital angle in V accurately because of the flexibility of the bicyclo[2.2.2]octane system. This made it unsuitable for decarboxylation studies.

[11] W. R. Hatchard and A. K. Schneider, *J. Am. Chem. Soc.*, 79, 6261 (1957).

[12] (a) This procedure has been used to prepare the bicyclo[3.1.1]-heptane system in 5% yield: S. Beckmann and O. S. Ling, *Ber.*, 94, 1899 (1961). (b) Two mechanisms may be considered for this cyclization. Either the intramolecular ring closure of a diketene i or the addition of the anion of an acid chloride to a ketene ii. We prefer the latter on geometric grounds but have no evidence which bears directly on this point.



i



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[13] V. N. Ipatieff, J. E. Germain, W. W. Thomspon, and H. Pines, *J. Org. Chem.*, 17, 272 (1952).

[14] (a) Compare the infrared spectra of the enolic β-keto ester XV and the nonenolic β-keto acid VI in ref 2; (b) S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spangler, and M. J. Urbigkit, *Tetrahedron*, 19, 1625 (1963).

[15] G. Stork, A. Brizzolara, H. Landesman, J. Szmuskovicz, and R. Terrel, *J. Am. Chem. Soc.*, 85, 207 (1963).

[16] M. Stiles, *ibid.*, 81, 2598 (1959).

Chart II

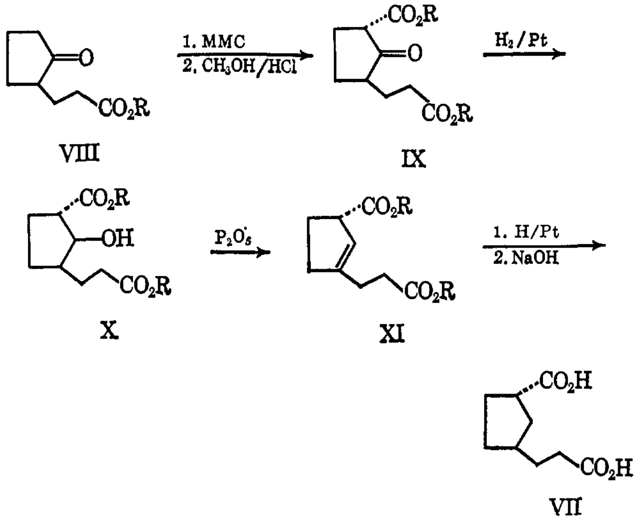
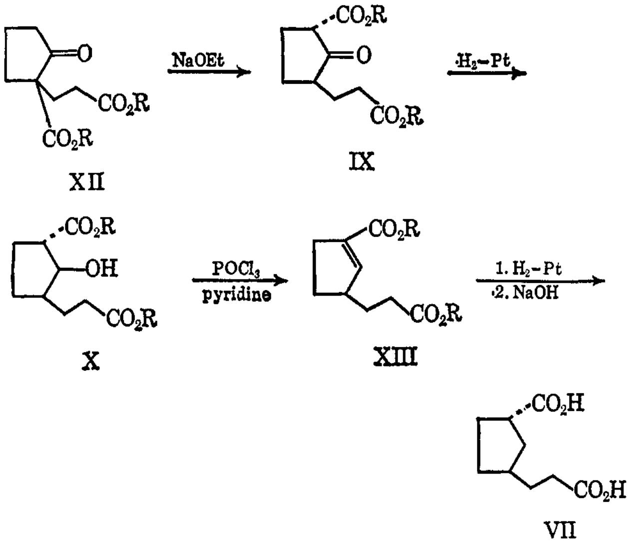


Chart III



cated that the product of the dehydration reaction consisted of a 9:1 mixture, of which 10% was the α,β-unsaturated ester, since the ultraviolet spectrum exhibited only a weak maximum at 225 mμ (ϵ 1042).[17,18] The other component of the mixture was assigned structure XI (R = CH_3) since the mixture of the two compounds was hydrogenated to a single compound, methyl *trans*-3-(3-carbomethoxycyclopentyl)propanoate as shown by a single peak in the vpc and one carbonyl absorption in the infrared spectrum at 1740 cm^{-1}.

The route to 3-(3-carboxycyclopentyl)propanoic acid outlined above did not seem to be promising due to the number of steps involved and low yields, notably in the methyl magnesium carbonate reaction and the dehydration reaction. For this reason it seemed prudent to devise an alternative synthesis (Chart III). Preliminary experiments to effect the isomerization of ethyl 3-(1-carbethoxy-2-oxocyclopentyl)propanoate (XII) to 3-(2-oxo-3-carbethoxycyclopentyl)propanoate (IX, R = Et) by the method of Chatterjee, *et al.*,[19] gave a complex mixture as evidenced by vpc analysis. However, when ethanol was removed from the reaction mixture by azeotropic distillation with toluene[20] an 80% yield of IX (R = Et) was obtained. Compound IX (R = Et) was hydrogenated to the alcohol and dehydrated in 86% yield to a mixture of olefins by reaction with phosphorus oxychloride in pyridine. The predominant olefin produced (78%) was the conjugated ester (XIII, R = Et) (infrared at 1715 cm^{-1}) and the other olefin (22%) was the nonconjugated ester (XI, R = Et) (infrared at 1740 cm^{-1}).[21] The mixture of olefins produced by the above procedures was hydrogenated to the saturated diester and this in turn was hydrolyzed to VII.

The rates of decarboxylation of III and IV were measured as before.[2] The temperatures at which III and IV decarboxylated completely in 30 min for these compounds (as well as for I, which was studied in our previous work[2]) are listed in Table I. Data from two other sources are included for comparison.

Table I. Orbital Angles and Temperature of Decarboxylation

Compd	Orbital angle, deg	T, °C
I	30	145^a
IV	50	260^b
III	60	320^b
XIV	60^c	350^d
XV	90	500^{e,f}

^{a} See ref 2. ^{b} This work. ^{c} The angle is an estimate since it is difficult to make a model of this compound. ^{d} See ref 12. ^{e} See ref 24. ^{f} No decarboxylation was observed.

Discussion

As shown in Table I the decarboxylation temperatures for the compounds we studied increase in the order I < IV < III. One cannot distinguish between transition states A and B on the basis of decarboxylation temperatures alone since this is just the order that would be predicted by A, if one considers the size of the bridge which contains the enolic double bond, or by B, if one considers the orbital angle between the incipient carbanion and the keto groups. However, if transition state A were operative, one would predict on the basis of strain considerations that I and IV would have close to the same decarboxylation temperature since the enolic double bond would be in the three-carbon bridge in both. Compound III would be expected to decar-

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[17] A. T. Nielsen, *J. Org. Chem.*, **22**, 1539 (1957).

[18] The resistance to dehydration and the formation of the nonconjugated olefin as the major isomer indicates that the stereochemistry of the cyclopentyl alcohol is unfavorable for *trans* elimination. Thus, the keto form (and not the enol form) of IX must be hydrogenating from the side opposite to the methyl propionate side chain resulting in the formation of an alcohol group which is *trans* to the carbomethoxy group and *cis* to the methyl propionate group. If the enol form of IX were being hydrogenated, one would expect *cis* addition of the two hydrogen atoms to the double bond to yield the all *cis* product. Very little of this product is formed since it would be expected to eliminate with ease to form the α,β-unsaturated ester, a result that was observed only to the extent of 10%.

[19] N. N. Chatterjee, B. K. Das, and G. N. Barpujani, *J. Ind. Chem. Soc.*, **17**, 161 (1940).

[20] K. Sisido, K. Utimoto, and T. Isida, *J. Org. Chem.*, **29**, 2781 (1964).

[21] The conjugated isomer was the major product of this dehydration in contrast to the previous results with phosphorus pentoxide because a proton in a *cis* configuration to the leaving group is removed preferentially to one which is *trans*, if the *cis* proton is activated by an electron-withdrawing group, and therefore results in a stabilized carbanion.[22] In this reaction pyridine serves as the base to remove the *cis* proton from the carbon bearing the carbethoxy group, while in the phosphorus pentoxide dehydration no base was present.

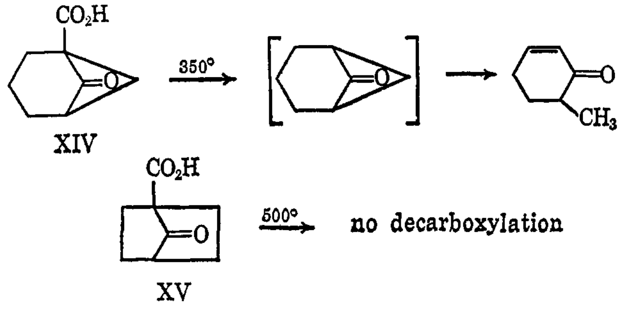
[22] S. J. Cristol and E. F. Hoegger, *J. Am. Chem. Soc.*, **79**, 3438 (1957).

boxylate at a much higher temperature since the enolic double bond must be accommodated in a two-carbon bridge. In fact, the decarboxylation temperature of IV is closer to the decarboxylation temperature of III than it is to I, a situation which is difficult to understand on the basis of A.

These data are well accommodated by transition state B. In this mechanism one would predict that the temperature of decarboxylation would be proportional to the cosine of the orbital angle between the carboxyl and the keto groups. In fact, one finds that these qualities are not only proportional, but that a linear relationship exists between them (Figure 1). This linear correspondence depicted in Figure 1 provides strong support to the postulate that the decarboxylation of these keto acids proceeds *via* transition state B.[23]

Decarboxylation studies on a pair of bicycloheptanones (XIV[12a] and XV[24]) became available while our work was in progress. As shown in Chart IV, XIV decarboxylates at 350° to the intermediate bicyclic ketone which rearranges to the cyclohexenone derivative. Exhaustive efforts were made to decarboxylate XV with no success. It sublimes cleanly at 350°, and it sublimes with charring at 500°.[24] This is exactly the result that would be predicted by transition state B on the basis of the orbital angles given in Table I. The strain in an enolic intermediate (transition state A) should be the same for both XIV and XV. Therefore, the same rate of decarboxylation would be expected for each; a result that was not observed.

Chart IV



On the basis of our studies it seems reasonable to conclude that transition states for the decarboxylation of lycoctonamic acid and compounds I, III, XIV, and XV are better depicted by transition state B than by transition state A. Since it is necessary to invoke transition state B in these instances to explain the decarboxylation behavior, one can now assume that it represents the transition state for the decarboxylation of the highly strained (*S* numbers 3 to 7)[8] bridged bicyclic β-keto acids. Furthermore, the demonstration of a linear relationship between the cosine of the interacting orbital angle and decarboxylation temperature should be useful in predicting the rates of other bridgehead carbanion reactions.[24a]

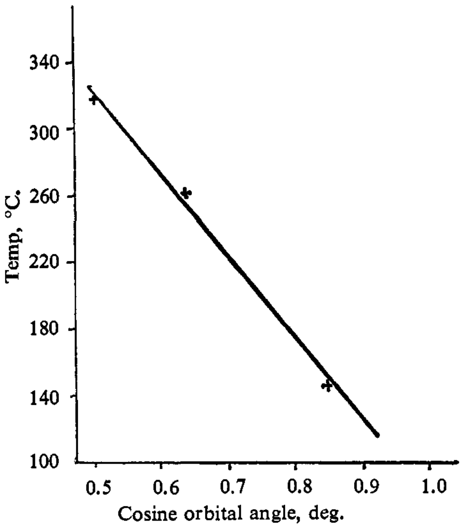


Figure 1. Plot of decarboxylation temperature against the cosine of the angle between the interacting orbitals.

Experimental Section[25]

Ethyl *m*-Bromomethylbenzoate. N-Bromosuccinimide (478 g) was mixed with 1 g of benzoyl peroxide and added slowly with stirring to a refluxing solution of 438 g of ethyl *m*-toluate in 400 ml of carbon tetrachloride. After the addition was completed, the reaction mixture was refluxed for 1 additional hr; then the succinimide was removed by filtration and washed with carbon tetrachloride. The filtrates were concentrated by distillation at reduced pressure, and the residue was distilled at 108° (0.3 mm) (lit.[26] bp 174–176° (30 mm)) to yield 502 g (77%) of product, $\nu\nu_{max}$ 1730 and 1695 cm^{-1} (CCl_4).

Ethyl *m*-Cyanomethylbenzoate. Ethyl *m*-bromomethylbenzoate (388 g) was added dropwise over a period of 2 hr to a refluxing solution of 77 g of sodium cyanide in 1500 ml of ethanol and 450 ml of water. The solution was concentrated at reduced pressure, extracted with ether, and dried over sodium sulfate. Distillation at 130° (0.25 mm) yielded 249 g (78%) of product; $\nu\nu_{max}$ 3030 and 1740 cm^{-1} (CCl_4). There was no absorption in the infrared at 2250 cm^{-1}. The nmr spectrum exhibited a singlet at τ 7.25 (CCl_4).

Homoisophthalic Acid. A mixture of 100 g of ethyl *m*-cyanomethylbenzoate, 400 ml of water, 1 l. of acetic acid, and 400 ml of sulfuric acid was refluxed for 12 hr, then concentrated at reduced pressure and poured onto ice. The crystals were suction filtered and washed with three 200-ml portions of water. Recrystallization from water after boiling with Norit yielded 48 g (50%) of product, mp 182–183° (lit.[13] mp 184–185°).

Hexahydrohomoisophthalic Acid (VI). Homoisophthalic acid (25 g) dissolved in 300 ml of acetic acid was hydrogenated over 0.5 g of platinum oxide at an initial pressure of 70 psi of hydrogen. When the pressure had dropped to 35 psi, the solution was filtered and hydrogenated again over 0.5 g of fresh platinum oxide. About 48 hr was required. Recrystallization from water gave 16 g (62%) of product, mp 147–149° (lit.[13] mp 150–152°).

Hexahydrohomoisophthalic Acid Chloride. Hexahydrohomoisophthalic acid (49 g), 150 ml of thionyl chloride (distilled from cottonseed oil), and 2 ml of dimethylformamide were combined and stirred at room temperature for 12 hr. The excess thionyl chloride was removed at reduced pressure at room temperature, and the residue was flash distilled at approximately 160° (2.0 mm). The yellow distillate was redistilled at 95° (0.5 mm) to yield 38.6 g (65.8%) of product; ν_{max} 1800 cm^{-1} (CCl_4).

1-Carboxy-7-oxobicyclo[3.2.1]octane (III). Triethylamine (19 g, dried over sodium wire) was added dropwise with stirring to a re-

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(23) The data obtained for 1-carboxy-2-oxo-3-ethylazobicyclo[3.3.1]-nonane[2] do not lie on the linear plot. However, one would expect a different linear plot with lactam acids because of the intrinsic difference between the lactam carbonyl and ketone carbonyl.

(24) C. F. H. Allen, G. A. Reynolds, S. K. Webster, and J. L. R. Williams, *J. Org. Chem.*, **27**, 1447 (1962).

(24a) Note Added in Proof. For a recent application see A. T. Nielsen, *J. Org. Chem.*, **31**, 1053 (1966).

(25) Infrared spectra were measured in chloroform unless indicated otherwise on Perkin-Elmer Model 137 spectrophotometer and ultraviolet spectra were determined on a Cary 14 spectrophotometer in ethanol. Nmr spectra were run in carbon tetrachloride on a Varian A-60 spectrometer. An F and M Model 500 gas chromatograph was used with helium flow of 60 cc/min, and the column temperature was programmed at 11°/min starting at 90°. A 2-ft silicone rubber column of 0.25-in. diameter was used except where noted otherwise.

(26) W. Davies and W. H. Perkin, *J. Chem. Soc.*, **121**, 2202 (1922).

fluxing solution of 34.7 g of hexahydrohomoisophthalic acid chloride in 500 ml of dry ether under nitrogen pressure over a period of 2 hr. Reflux was continued for 2 hr after the addition was completed, then the reaction mixture was filtered under nitrogen pressure without exposure to air and concentrated at reduced pressure. The residue was distilled at 110° (0.5 mm) to yield 6.5 g of the acid chloride of 1-carboxy-7-oxobicyclo[3.2.1]octane. This product was immediately dissolved in 30 ml of acetic acid and heated at reflux for 1 hr, then concentrated by freeze drying. On dissolving the residue in ether and cooling, 1.2 g of hexahydrohomoisophthalic acid (mp 145°) crystallized from solution. After separation of additional crops of the hexahydrohomoisophthalic acid by crystallization, the filtrates were combined and concentrated at reduced pressure. The residue was sublimed ten times at 60° (0.05 mm) to yield a white solid, mp 99–104°, which was contaminated by an enolic compound as evidenced by its ultraviolet spectrum ($\lambda_{\max}$ 240 mμ (ϵ 342)). Four additional sublimations at 60° (the portion that sublimed during the first 30 min was discarded) yielded 0.335 g (1.2%) of product, mp 104.5–106.5°; $\lambda_{\max}$ 290 mμ (ϵ 33). The ultraviolet spectrum did not exhibit a maximum at 240 mμ (ϵ is 97 at 240 mμ); $\nu\nu_{\max}$ 2950, 1760, 1710 cm^{-1}.

Anal. Calcd for $C_9H_{12}O_3$: C, 64.26; H, 7.19. Found: C, 63.92; H, 7.07.

6-Oxobicyclo[3.2.1]octane. A. From Hexahydrohomoisophthalic Acid. Hexahydrohomoisophthalic acid (10 g) was ground with 1 g of barium hydroxide and the mixture was heated at 330–350° in a Wood's metal bath. The product distilled from the reaction mixture and was dissolved in ether and extracted with 40 ml of a saturated sodium bicarbonate solution, then washed twice with water and dried over sodium sulfate. Concentration of the ether solution in a stream of dry air yielded 3.6 g (51.4%) of product. The product was purified by sublimation at atmospheric pressure, mp 148–150° (sealed capillary) (lit.[27] mp 157–158°); $\nu_{\max}$ 1740 cm^{-1}.

The **semicarbazone** of 6-oxobicyclo[3.2.1]octane was prepared by dissolving 90 mg of the ketone in 8 ml of ethanol and adding a solution of 134 mg of semicarbazide hydrochloride, 200 mg of sodium acetate, and 3 ml of water in 10 ml of ethanol then refluxing for 1 hr. The product crystallized when the reaction mixture was cooled and diluted with water. One recrystallization from ethanol–water gave a product melting at 184–184.5° (lit.[27] mp 183–183.5°); $\nu\nu_{\max}$ 1700, 1570 cm^{-1}.

Anal. Calcd for $C_9H_{15}N_3O$: C, 59.65; H, 8.34; N, 23.18. Found: C, 59.94; H, 8.33; N, 23.05.

B. From 1-Carboxy-7-oxobicyclo[3.2.1]octane. 1-Carboxy-7-oxobicyclo[3.2.1]octane (0.125 g) was heated at 325° for 0.5 hr in a nitrogen-filled sealed tube. The infrared spectrum of the product without further purification was identical in all respects with that of the ketone obtained from the barium salt method.

The **semicarbazone** of this ketone was prepared in the same manner as in part A above, mp 185–186°. The melting point of an intimate mixture of this semicarbazone and that from the ketone prepared by the barium salt method was not depressed. The infrared spectra of the semicarbazones were identical in all respects.

Methyl 3-(2-Oxo-3-carbomethoxycyclopentyl)propanoate (IX, R = Me). A mixture of 25 g of methyl 3-(2-oxocyclopentyl)propanoate and 350 ml of a 2 *M* solution of methyl magnesium carbonate in dimethylformamide[16] was heated at 120–125° for 2 hr. Methanol was distilled from the reaction mixture as it was formed with the aid of nitrogen which was bubbled through the solution slowly. The reaction mixture was cooled to 0° and added slowly to 500 ml of dry methanol saturated with anhydrous hydrochloric acid at Dry Ice temperature. The mixture was stirred for 12 hr as the solution was allowed to slowly warm to room temperature. It was then concentrated under reduced pressure and extracted twice with 200-ml portions of ether. The ether extracts were dried over sodium sulfate and concentrated under reduced pressure and then distilled at 130° (0.5 mm) to yield 10.5 g (30.7%) of product. The vapor phase chromatogram exhibited a single peak with retention time of 8.0 min, and the product gave a positive ferric chloride test.

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.06. Found: C, 58.12; H, 7.24.

Methyl 3-(2-Hydroxy-3-carbomethoxycyclopentyl)propanoate (X, R = Me). Methyl 3-(2-oxo-3-carbomethoxycyclopentyl)propanoate (17 g) was dissolved in 200 ml of ethyl acetate and hydrogenated over 1.7 g of platinum dioxide. The catalyst was filtered and the solution was concentrated under reduced pressure. The product was used in the next step without further purification; $\nu\nu_{\max}$ 3540, 1750, 1730 (shoulder) cm^{-1} (CCl_4). The vapor phase chromatogram exhibited a single peak with retention time of 8.2 min, and the product gave a negative ferric chloride test.

Dehydration of Methyl 3-(2-Hydroxy-3-carbomethoxycyclopentyl)propanoate. Phosphorus pentoxide (12 g) was added in 2-g portions to a refluxing solution of 9.3 g of methyl 3-(2-hydroxy-3-carbomethoxycyclopentyl)propanoate dissolved in 50 ml of dry benzene at 0.5-hr intervals with vigorous stirring. Reflux with sitrring was continued overnight, then the benzene solution was decanted from the phosphorus pentoxide residue and concentrated under reduced pressure. Distillation yielded a 0.66 g fraction boiling at 103° (0.25 mm). Vapor phase chromatography of this fraction on a 4-ft diethylene glycol succinate column indicated the presence of two isomers in a 10:1 ratio with retention times of 10.2 and 11.0 min, respectively. This mixture had $\lambda_{\max}$ 225 mμ (ϵ 1042).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.28; H, 7.97. Found: C, 61.86; H, 7.44.

Methyl 3-(3-Carbomethoxycyclopentyl)propanoate. The mixture of olefin isomers formed from the dehydration of methyl 3-(2-hydroxy-3-carbomethoxycyclopentyl)propanoate (0.66 g) was dissolved in 100 ml of ethyl acetate and hydrogenated over 0.2 g of platinum dioxide. The catalyst was filtered and the solution was concentrated under reduced pressure and used directly in the next step without further purification. The vapor phase chromatogram exhibited a single peak with retention time of 6.5 min.

3-(3-Carboxycyclopentyl)propanoic Acid (VII). A mixture of 6 ml of Claisen's base (3.5 g of potassium hydroxide and 2.5 ml of water, diluted to 10 ml with methanol) and 4 ml of water was added to 0.66 g of methyl 3-(3-carbomethoxycyclopentyl)propanoate dissolved in 6 ml of methanol. The mixture was refluxed for 4 hr, then concentrated under reduced pressure and acidified to pH 2 with hydrochloric acid. The product was extracted with ether, dried over sodium sulfate, and concentrated under reduced pressure. The residue was taken up in ether and crystallized from ether–cyclohexane, mp 78–87°; sublimation at 70° (0.05 mm) brought the melting point to 88.5–90.5°.

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.23; H, 7.59.

Ethyl 3-(2-Oxo-3-carbethoxycyclopentyl)propanoate (IX, R = Et). Ethyl 3-(1-carbethoxy-2-oxocyclopentyl)propanoate (250 g) was added to a solution of 23 g of sodium in 340 ml of dry ethanol and refluxed under a nitrogen atmosphere for 8 hr. After removing 200 ml of ethanol by distillation, 500 ml of toluene was added and distillation was continued until the temperature reached 110°.[20] The residue was dissolved in 400 ml of toluene and poured into 1 l. of ice-cold 10% acetic acid solution. The toluene layer was separated and washed with water, 7% sodium carbonate solution, and again with water, then dried over sodium sulfate. After concentration under reduced pressure, the product was distilled at 138° (0.5 mm) to yield 22 g (80%) of product. The product gave a positive ferric chloride test and the vapor phase chromatogram exhibited a single peak with retention time of 9.2 min.

Ethyl 3-(2-Hydroxy-3-carbethoxycyclopentyl)propanoate (X, R = Et). Ethyl 3-(2-oxo-3-carbethoxycyclopentyl)propanoate (20 g) was dissolved in 150 ml of ethyl acetate and hydrogenated over 2 g of platinum oxide. Filtration of the catalyst and concentration of the solution under reduced pressure yielded 19.1 g (95%) of product; $\nu\nu_{\max}$ 3500, 1740, 1720 cm^{-1} (CCl_4). The product gave a negative ferric chloride test and the vapor phase chromatogram exhibited a single peak with retention time of 9.5 min.

Dehydration of Ethyl 3-(2-Hydroxy-3-carbethoxycyclopentyl)-propanoate. Phosphorus oxychloride (50 ml) was added dropwise to a stirred solution of 25.7 g of ethyl 3-(2-hydroxy-3-carbethoxycyclopentyl)propanoate dissolved in 250 ml of pyridine cooled to 0° in an ice-salt bath. The solution was stirred at room temperature for 24 hr, then cooled to 0°. Water was added cautiously until there was no further reaction, then the solution was transferred to a separatory funnel and extracted with 500 ml of ether. The ether extracts were washed with water, 10% hydrochloric acid, and again with water, then dried over sodium sulfate and concentrated under reduced pressure to yield 20.8 g (86%) of ethyl (3-carbethoxy-3-cyclopentenyl)propanoate; $\nu\nu_{\max}$ 1740, 1715, 1625 cm^{-1} (CCl_4). The vapor phase chromatogram exhibited a major peak (72.6%) with retention time of 8 min, and smaller peaks with retention times of 7.25 (16%) and 8.5 min (11%). The product was used directly in the next step without further purification.

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Ethyl 3-(3-Carbethoxycyclopentyl)propanoate. The product of the dehydration of ethyl 3-(2-hydroxy-3-carbethoxycyclopentyl)-propanoate (34 g) was dissolved in 400 ml of ethyl acetate and hydrogenated in two 17-g portions over 1.7 g of platinum dioxide. After filtration of the catalyst and concentration of the solution, the product was used directly in the next step without further purification.

3-(3-Carboxycyclopentyl)propanoic Acid (VII). Ethyl 3-(3-carbethoxyclopentyl)propanoate (32 g) was hydrolyzed in the same manner as described for methyl 3-(3-carbomethoxycyclopentyl)propanoate to yield 20.4 g (73%) of product, mp 69–79°. One recrystallization from ether–cyclohexane raised the melting point to 79–82°. On mixture of a sample of this product with an authentic sample of the diacid (from the methyl ester series) the melting point was not depressed. The infrared spectrum of this product was identical in every respect with that of the diacid from the methyl ester series.

3-(3-Carboxycyclopentyl)propanoic Acid Chloride. A solution of 92 ml of oxalyl chloride in 100 ml of dry benzene was added dropwise to a stirred solution of 39.5 g of 3-(3-carboxycyclopentyl)-propanoic acid in 200 ml of dry benzene. After the addition was completed, the solution was warmed to 40° and stirred for 1 hr. The solution was concentrated under reduced pressure, then distilled at 97–105° (0.03 mm) to yield 42.7 g (79%) of product; $\nu_{\max}$ 1795 cm^{-1} (CCl_4).

1-Carboxy-2-oxobicyclo[3.2.1]octane (IV). A solution of 30 ml of triethylamine (distilled from potassium hydroxide) in 100 ml of dry ether was added dropwise with stirring to a refluxing solution of 42.7 g of 3-(3-carboxycyclopentyl)propanoic acid chloride in 500 ml of dry ether under nitrogen pressure over a period of 0.5 hr. Reflux was continued for 1.5 hr after the addition was completed, then the reaction mixture was filtered under nitrogen pressure without exposure to air and concentrated at reduced pressure. The residue was distilled in a short-path apparatus at approximately 175° (2 mm), then redistilled at 85–90° (0.03 mm) to yield approximately 5 g of the acid chloride of 1-carboxy-2-oxobicyclo[3.2.1]-octane. This product was dissolved in 50 ml of acetic acid and warmed on the steam bath for 1 hr, then concentrated by freeze drying, to yield 1 g of residue. The residue was dissolved in a small amount of benzene and placed on a chromatography column of 30 g of silica gel (powder, Baker reagent grade) prepared in cyclohexane and eluted with cyclohexane, then mixtures of cyclohexane–benzene (3:1, 2:2, 1:3, 0:1) and then benzene–ether mixtures (9:1, 8:2, 7:3, 6:4). The fractions (20 ml) were examined by thin layer chromatography on silica gel. The plates were developed with a mixture of 80 ml of ethanol and 5 ml of 29% ammonia, then dried at 100° for 15 min and sprayed with a solution of bromcresol purple. The acids were indicated by yellow spots on a dark blue background. No acids were present in fractions prior to elution with benzene–ether. A fraction eluted with benzene–ether (8:2) gave a major spot with R_f 0.25, and crystallized (needles) on removal of the solvent, to yield 70 mg (0.2%) of product, mp 90–100°. Two sublimations at 60° (0.03 mm) raised the melting point to 109.5–112.5°. Thin layer chromatography as described above gave one spot, R_f 0.34; $\nu\nu_{\max}$ 2950, 1750, 1710 cm^{-1}.

Anal. Calcd for $C_9H_{12}O_3$: C, 64.26; H, 7.19. Found: C, 64.14; H, 7.44.

2-Oxobicyclo[3.2.1]octane. 1-Carboxy-2-oxobicyclo[3.2.1]octane (4 mg) was heated at 260–265° for 0.5 hr in a sealed tube. The infrared spectrum of the product was identical with that of an authentic sample of 2-oxobicyclo[3.2.1]octane kindly donated by Professor H. M. Walborsky.

The Decarboxylation Studies. Weighed samples of the β-keto acids were heated for 0.5-hr periods in a stirred oil bath or a stirred Wood's metal bath at temperatures where approximately one-half of the sample was decarboxylated. The temperature was controlled to within 1° by turning the oil bath heater off and on manually as necessary. After the samples were heated, a known amount of Spectrograde chloroform was added by a pipet so that the concentration of the resulting solution was approximately 10 mg/ml, depending on the amount of decarboxylation at the chosen temperature. In all cases, the sample dissolved rapidly and completely. The amount of acid remaining in the sample after heating was determined by the intensity of the acid carbonyl band in the infrared spectrum.

The Measurement of Dihedral Angles. Dreiding models were used to construct molecular models of the compounds prepared in this work. At least two molecular models were constructed for each compound and five angle measurements were made from each model. The average value of the orbital angle is listed for each compound in Table I. The previous angle[2] listed for compound I is in error and the correct value is given in Table I.

Sigmatropic Reactions in the 1,4-Bis(cycloheptatrienyl)benzene Isomers

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Abstract: The preparation of the 1,4-bis(cycloheptatrienyl)benzene isomers is described. Thermal and photochemical sigmatropic reactions have been observed in these materials, and the kinetics of one of these processes have been measured. The activation energy, *A* factor, and transition state parameters have been calculated for this process and compared with those for similar systems. The nmr and ultraviolet spectra of the isomers are reported and discussed. An analysis of the proton spin–spin coupling in the 7,7 isomer leads to the conclusion that it exists in a preferred conformation.

As part of a continuing study of the chemistry of compounds containing more than one diazo group,[1–3] we have photolyzed and thermolyzed 1,4-bis-(α-diazomethyl)benzene (I) in the presence of benzene in hopes of obtaining the interesting hydrocarbon, 1,4-bis(7-cycloheptatrienyl)benzene (IIa). This reaction would be analogous to that reported by Gutsche, Bachman, and Coffey for phenyldiazomethane which gives phenylcycloheptatriene when photolyzed in benzene.[4] The desired hydrocarbon (IIa) was of interest as a potential precursor to the dicarbonium ion, *p*-phenylenebis(cycloheptatrienylium cation) (III).

Despite numerous attempts, including a number of experimental variations, IIa was never obtained in

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