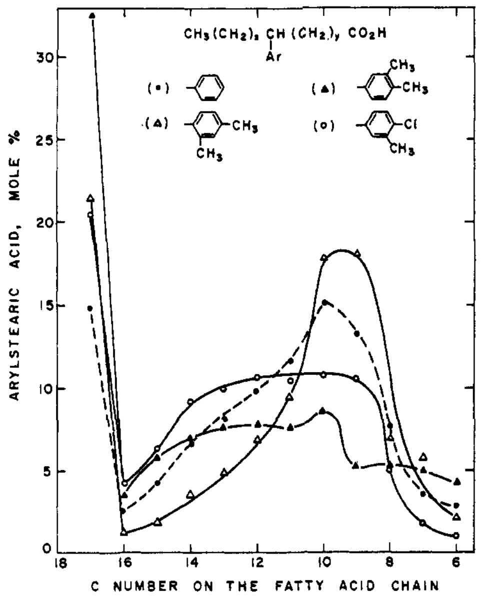

Figure 6.

number of carbon atoms gave a nearly straight line. Quantitative analysis of the mixture by gas–liquid chromatography gave the following results, % by weight: acetophenone, 18.2; propiophenone, 19.3; valerophenone, 21.0; hexanophenone, 22.2; laurophenone, 19.3. The chromatographic separation of a mixture of equal parts of three isomeric dimethylacetophenones is shown in Figure 2.

The separation of the alkyl aryl ketones obtained by chromic acid oxidation of oily arylstearic acids from benzene (aluminum chloride catalyst) and phenetole (methanesulfonic acid catalyst) is shown in Figures 3 and 4.

Distribution of isomeric arylstearic acids from benzene, *o*- and *m*-xylene, *o*- and *p*-chlorotoluene, and phenetole is shown in Table I and Figures 5 and 6. Oxidation and chromatographic separation experiments showed that the values of Table I for phenylstearic acid (aluminum chloride catalyst) could be closely duplicated with an average deviation of 0.24 mole %. As in the case of the reference acetophenone homologs, plots of the log retention time against numbers of carbon atoms gave a nearly straight line for each family of alkyl aryl ketones.

Point of Substitution on the Benzene Ring.—Chromic acid oxidation of a crystalline arylstearic acid isolated from the condensation of *p*-xylene with oleic acid[2] gave a dimethylacetophenone identical in retention time by gas–liquid chromatography with 2,5-dimethylacetophenone. The crystalline arylstearic acid is therefore 2′,5′-dimethyl-17-phenyloctadecanoic acid.

Similarly the first member of the two series of alkyl aryl ketones from oily arylstearic acids from *o*- and *m*-xylene were found to have identical and superimposable retention time with 3,4-dimethylacetophenone and 2,4-dimethylacetophenone, respectively. The point of substitution of aliphatic carbon on the benzene ring is therefore as shown in Table I.

The chlorine atom of *o*- and *p*-chlorotoluene was found to direct the point of substitution of aliphatic carbon *para* and *ortho* to itself, respectively, as shown in Table I. This is true also in the Friedel–Crafts reaction of chlorotoluenes with acetic anhydride.[8] The first member of the series of alkyl aryl ketones from the oily arylstearic acid from *o*-chlorotoluene was found identical in retention time with 4-chloro-3-methylacetophenone.

Oxidation of a crystalline arylstearic acid from *p*-chlorotoluene gave a ketone identical with 2-chloro-5-methylacetophenone in retention time and in the melting point of the oxime, 114–115°.

Reaction Products of Alloocimene and Maleic Anhydride

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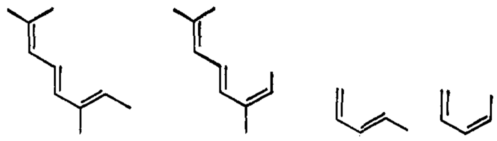
Alloocimene, a mixture of two stereoisomers of 2,6-dimethyl-2,4,6-octatriene, when treated with maleic anhydride gives two isomeric adducts, resulting from the addition of maleic anhydride to positions 4 and 7 of the alloocimene isomers. The structure of the adducts was established by n.m.r. analysis. The two acids produced by hydrolysis showed a large difference in the ionization of the second carboxyl group. A third adduct was also formed in significant amounts when traces of maleic acid were present. The latter adduct was suggested by n.m.r. analysis to be formed from a third triene produced by an acid-catalyzed isomerization of the alloocimene.

Alloocimene (2,6-dimethyl-2,4,6-octatriene), a terpene produced from the thermal isomerization of α-pinene exists in two geometric forms,[1,2] I and II. In two separate studies[1,3] both isomers were reported to give the same addition product (m.p. 84°) when treated separately with maleic anhydride. Only this adduct was isolated from the reaction of maleic anhydride and a mixture of the isomers.[4,5] Recently, however, Alder and co-workers[2] reported that the alloocimene isomers gave different adducts. The adduct which melted at 84° was derived from the 4:5-*trans*-6:7-*cis* isomer[6] I, and a different adduct which melted at 38° was produced from the 4:5-*trans*-6:7-*trans* isomer[6] II.



I II III IV

trans-Piperylene (III) and *cis*-piperylene (IV), which are related to I and II in the steric configuration of the terminal methvl group, differ markedly in their reactivity with maleic anhydride. With a mixture of the two piperylenes only the *trans* isomer gives an isolable

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[1] J. J. Hopfield, S. A. Hall, and L. A. Goldblatt, *J. Am. Chem. Soc.*, **66**, 115 (1944).

[2] K. Adler, A. Drieke, H. Erpenbach, and U. Wicker, *Ann.*, **609**, 1 (1957).

[3] J. Wolinsky, B. Chollar, and M. D. Baird, *J. Am. Chem. Soc.*, **84**, 2775 (1962).

[4] Y. Chrétien-Bessière, *Ann. chim.* (Paris), **13**, 301 (1957).

[5] B. A. Arbuzov and A. R. Vil'chinskaya, *J. Gen. Chem. USSR*, **25**, 168 (1955).

[6] This nomenclature, based on the relationship of like groups, was adopted to permit further characterization of each triene according to ref. 1, 14, and O'Connor and Goldblatt, *Anal. Chem.*, **26**, 1726 (1954). Alder and co-workers employ a different convention and refer to isomer I as 4:5-*trans*-6:7-*trans*, or alloocimene, and to isomer II as 4:5-*trans*-6:7-*cis*, or neoalloocimene.

adduct.[7,8] The pure *cis* isomer gives mainly polymeric material, but a small amount of the addition product is produced under forcing conditions.[8]

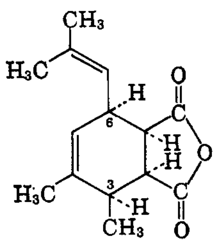
In view of the difference in reactivity of the piperylene isomers and the conflicting reports on the products from alloocimene, the identity of the reaction products of the latter with maleic anhydride were re-examined.

Results and Discussion

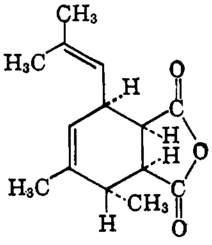
When a mixture of the alloocimene isomers consisting of 64% I and 32% II was heated with maleic anhydride, two adducts were produced as shown by v.p.c. analysis. The amount of each was 72% and 25%, respectively, of the distilled reaction mixture. The same adducts were produced from the reaction of maleic anhydride with a mixture containing 7% I and 93% II and the composition of the mixture after distillation was 23% and 73% of each adduct, respectively.

Thus, in agreement with Alder and co-workers, two different adducts are formed from the alloocimene isomers. An n.m.r. analysis of the mixtures demonstrated that both adducts were stereoisomers of a structure resulting from the addition of maleic anhydride to positions 4 and 7 of the alloocimene isomers. The spectra of the mixtures exhibited proton resonance lines for two vinyl hydrogens at τ 4.4, nine hydrogens for three methyl groups on doubly bonded carbon atoms at 8.0–8.35, and three hydrogens for one methyl group on a saturated carbon atom at 8.53–8.74.

Structures V and VI were assigned to the adducts from the *trans-cis*-alloocimene isomer (I) and the *trans-trans*-alloocimene isomer (II) on the basis of the *cis* addition rule of Alder and Stein.[9] The existence of the two stereoisomers was readily discerned from the n.m.r. spectra by the presence of two separate doublets, each of which resulted from a splitting of the C-3-methyl resonance by the adjacent C-3 hydrogen. The assignment of the doublets at τ 8.53 to V and 8.74 to VI was straightforward from a comparison of the peak areas of the doublets with the composition of the mixtures as measured by v.p.c.

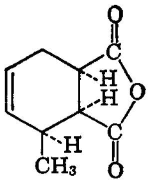


V

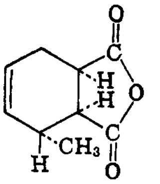


VI

The maleic anhydride adducts (VII, VIII) from *trans*-piperylene and *cis*-piperylene, respectively, could also be characterized by n.m.r. analysis. Adduct VII exhibited a doublet for the C-3-methyl hydrogens at τ 8.66, and adduct VIII a doublet at 8.73. These values support the assignments made to the stereochemistry of the adducts from alloocimene, since for both pairs of adducts a higher field position was found for the proton resonance lines of the C-3-methyl hydrogens when the methyl group was *trans* to the anhydride ring.



VII

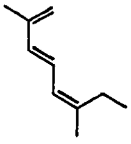


VIII

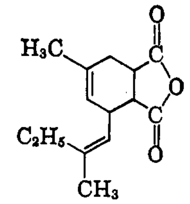
Although the adduct V from *trans-cis*-alloocimene could be isolated as a solid which melted at 80–82° and exhibited a single doublet at τ 8.53 in the n.m.r. spectrum, adduct VI from the *trans-trans*-alloocimene isomer could not be isolated from the reaction. Crystalline mixtures of the two adducts were obtained.

Based on the n.m.r. spectrum, the solid with m.p. 80–82° consisted of a single isomer, and no absorption lines were present to indicate any additional stereoisomers or structural isomers. An analysis by v.p.c., however, showed the presence of a small amount of a second component (8%) which could not be removed by recrystallization. From the n.m.r. data, accordingly, the impurity is probably a third stereoisomer since a structural isomer would be expected to be detectable at the concentration present.

Appreciable amounts of a structural isomer were found, however, when alloocimene was not completely dry, or when maleic anhydride was contaminated with maleic acid. The adduct could be resolved on a v.p.c. column but could not be separated from V and VI by distillation. Structure IX was assigned to the adduct on the basis of its n.m.r. spectrum and its probable mode of occurrence. Thus, a mixture containing 60% of the adduct, as measured by v.p.c., exhibited new absorption lines for olefinic hydrogens at τ 4.8, and for ring CH_2 hydrogens at 7.5. The presence of an ethyl group was established by a triplet for the methyl hydrogens at τ 9.01 and a nearly resolved quartet at 7.93 of which the two center lines were clearly visible for the methylene hydrogens. Integration of the peak areas gave a value of 2:18 for the vinyl hydrogen to total hydrogen ratio as required for a mixture of V, VI, and IX. The ratio of methyl hydrogens on doubly bonded carbon atoms to total hydrogen for this mixture of adducts was 6.8:18. Structure IX requires a ratio of 6:18 compared with 9:18 for adducts V and VI.



X



IX

It is reasonable to presume that IX is formed from the octatriene X. The structure of the octatriene, in addition, is indicative of an acid-catalyzed isomerization of alloocimene. The known ease of polymerization of alloocimene by acids and the occurrence of the adduct through the presence of maleic acid supports this contention.

The measured dissociation constants of the dicarboxylic acids from V and VI are shown in Table I, together with the values for the acids from VII and VIII

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[7] R. L. Frank, R. D. Emmick, and R. S. Johnson, *J. Am. Chem. Soc.*, **69**, 2313 (1947).

[8] D. Craig, *ibid.*, **72**, 1678 (1950).

[9] J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).

TABLE I

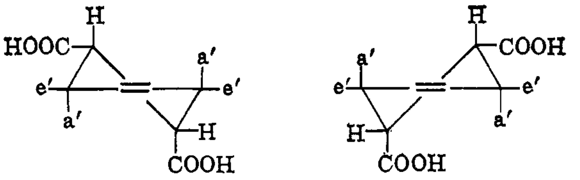
ACID DISSOCIATION CONSTANTS OF *cis*-Δ^4-TETRAHYDROPHTHALIC ACID DERIVATIVES

	pK_1	pK_2	$K_1 \times 10^4$	$K_2 \times 10^9$	K_1/K_2
V acid	3.10[a]	8.45[a]	7.95	3.55	224,000
VI acid	3.65[b]	6.70[b]	2.24	200	1,120
VII acid	3.85	6.75	1.41	178	792
VIII acid	3.85	6.70	1.41	200	705

[a] The same values were found for both the isolated acid (m.p. 163–165°) and the acid prepared *in situ* by hydrolysis of the adduct, m.p. 80–82°, containing 8% of an isomer. [b] pK values were calculated from the measured pK values for the acid mixture derived from 23% adduct V and 73% adduct VI (pK_1 = 3.50; pK_2 = 7.20) and the pK values of the acid from V.

for comparison. Inspection of the data shows that the acid from V differs significantly in the K_1/K_2 ratio and this is due almost entirely to the smaller K_2-value.

Two half-chair conformations which are interconvertible can be adopted for a cyclohexene ring.[10] In view of the well-known nonbonded interactions between 1,3-substituents which are axial in a six-membered ring, the reduced acidity of the second carboxyl of the acid from V is probably due to this interaction, resulting from either the C-3-methyl group or the C-6-(2-methylpropenyl) group in the respective conformations. For each of the other acids a conformation is possible where no interaction of these groups with either carboxyl occurs.



The steric influence of a group on the ionization of a carboxyl has been attributed to both the consequent effect of the group on the ease of hydration of the carboxylate ion,[11] and the increased steric interaction resulting from the larger effective volume of the hydrated carboxylate ion compared with the carboxyl group.[12] However, the possible occurrence of intramolecular hydrogen bonding of the carboxyl groups in the acid from V, which would result in a larger K_1 and a smaller K_2,[13] could also reconcile the data.

Experimental

Proton chemical shifts expressed in τ-units were determined at 56.4 Mc. on a Varian Associates DP60 n.m.r. spectrometer for 10% solutions in deuterated chloroform ($CDCl_3$) and completely deuterated dimethyl sulfoxide (DMSO-d_6) with tetramethylsilane as an internal standard. Dissociation constants of the dicarboxylic acids were determined from the half neutralization point of each carboxyl group, using a Model N Beckman pH meter for potentiometric titration of an alkaline solution.

Dry commercial alloocimene was prepared by distillation from calcium hydride or sodium. Analysis by v.p.c. on a 11.5-ft. column of 20% Dow Corning high vacuum silicone grease on 60–80-mesh Gas Chrom CLA at 125° and 28-p.s.i. helium pressure showed two principal peaks[14]: 4:5-*trans*-6:7-*trans*-alloocimene[6] (32–36%) and 4:5-*trans*-6:7-*cis*-alloocimene[6] (62–64%), with relative retention times (R.R.T.) of 1.11 and 1.21, respectively, compared with *t*-amylbenzene.

Piperylene (Matheson Coleman and Bell) and maleic anhydride (Eastman Organic, White Label) were used as received.

Reaction Products of Alloocimene and Maleic Anhydride.—Equimolar amounts of pure maleic anhydride and an anhydrous mixture of the alloocimene isomers (64% *trans-cis*, 32% *trans-trans;* and 7% *trans-cis*, 93% *trans-trans*) were heated with a few crystals of hydroquinone for 3 hr. on a steam bath. The reaction products were distilled under reduced pressure to separate first residual alloocimene and maleic anhydride, and then the adduct mixtures from resinous material. Analyses were made by v.p.c. on a 10-ft. analytical silicone column at 180° using 30-p.s.i. helium pressure and 18.5-p.s.i. hydrogen pressure, and a flame-ionization detector. The solid adduct mixture from 64% I and 32% II was isolated in 72% yield and showed two main peaks using *n*-hexadecane as a marker (R.R.T.): adduct V, 72%, (1.85), and adduct VI, 25% (1.46). The liquid adduct mixture from 7% I and 93% II was isolated in 67% yield and consisted of 23% V and 73% VI. Both mixtures contained a trace of an adduct with R.R.T. 1.54. When commercial maleic anhydride containing maleic acid was used for the reaction, two additional peaks were present with R.R.T. 1.66 and 1.75.

Commercial maleic anhydride and moist alloocimene (64% I, 32% II), when heated at reflux temperature in benzene for 5 hr., gave the following yield of adducts based on alloocimene (R.R.T.): V, 57% (1.85); VI, 10% (1.46); IX, 14% (1.75); unknown, 5% (1.54); unknown, 1% (1.66); and unknown, 1% (2.05).

Maleic Anhydride Adduct of *trans-cis*-Alloocimene (V).—The adduct was isolated from mixures by several recrystallizations to a constant melting point of 80–82° (lit.[2] m.p. 84°), using petroleum ether–hexane (3:1) as solvent.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.80. Found: C, 71.34; H, 7.56.

A doublet in the n.m.r. spectrum of the C-3-methyl group was present at τ 8.53 for a solution in $CDCl_3$, and at 8.67 with DMSO-d_6 as solvent.

An analysis by v.p.c. showed two completely separated peaks (R.R.T.): 92% V (1.85) and 8% unknown (1.54).

The acid was isolated by heating the solid in 0.5 *N* sodium hydroxide, acidifying the solution with concentrated hydrochloric acid, and recrystallizing the product to a constant melting point of 163–165° (lit.[2] m.p. 170°). The n.m.r. spectrum of the acid in DMSO-d_6 as solvent exhibited a single doublet for the C-3-methyl group at τ 8.92.

Attempted Isolation of the Maleic Anhydride Adduct of *trans-trans*-Alloocimene (VI).—The distillate from the reaction of alloocimene containing 93% of the *trans-trans* isomer was a liquid which partly crystallized on standing. After several recrystallizations by cooling the mixture in hexane below 0° a crystalline fraction was isolated which melted at 36–42° (melting point expected,[2] 38°). An analysis by v.p.c. (R.R.T.) showed the presence of 34% V (1.85), 60% VI (1.46), and 6% unknown (1.54).

The n.m.r. spectrum of the mixture showed a doublet for the C-3-methyl hydrogens in VI at τ 6.74 and at 6.83, using $CDCl_3$ and DMSO-d_6 as solvents, respectively. The accompanying doublet for the C-3-methyl hydrogens in V was also present, and was approximately one-half to two-thirds as large.

A crystalline acid could not be isolated on work-up of the product obtained by hydrolysis of the mixture with alkali and acidification with hydrochloric acid.

Characterization of Adduct IX.—Distillation of a noncrystallizable mixture of the adducts from alloocimene through a 24-in. spinning-band column gave a liquid fraction boiling at 131–133° (0.25 mm.). The composition of the distillate as determined by v.p.c. analysis (R.R.T.) was 60% IX (1.75), 18% V (1.85), 14% VI (1.46), and 4% each of two adducts with R.R.T. 1.54 and 1.66.

The n.m.r. spectrum of the mixture in $CDCl_3$ as solvent exhibited as new absorption lines a large triplet at τ 9.01 and a nearly resolved methylene quartet at 7.93, absorption lines for ring CH_2 hydrogens at 7.5, and additional lines at 4.8 for olefinic hydrogens.

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(10) D. H. R. Barton, R. C. Cookson, W. Klyne, and C. W. Shoppee, *Chem. Ind.* (London), 21 (1954).

(11) G. S. Hammond and D. H. Hogle, *J. Am. Chem. Soc.*, **77**, 338 (1955).

(12) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 744.

(13) L. Eberson, *Acta Chem. Scand.*, **13**, 211 (1959).

(14) P. E. Kiener, Ph.D. Thesis, Department of Chemistry, University of Illinois, 1961; C. Cappas, Ph.D. Thesis, Department of Chemistry, University of Florida, 1962.

Maleic Anhydride Adduct of *trans*-Piperylene (VII).—A solution containing maleic anhydride (1 mole), 0.5 g. of picric acid, and a mixture of *cis*- and *trans*-piperylene (2 moles) in 500 ml. of benzene was heated to reflux.[7] Attempts to purify the product by recrystallization, after removing benzene and *cis*-piperylene, were not successful, but the pure adduct melting 61–62° (lit.[7] m.p. 61°) could be obtained by two distillations at 127–129° (0.5 mm.).

The n.m.r. spectrum of the adduct in CDCl$_3$ as solvent exhibited a doublet for the C-3-methyl hydrogens at τ 8.66, slightly nonequivalent vinyl hydrogens at 4.09, C-1 and C-2 hydrogens at approximately 6.6, and the C-3 and C-6 hydrogens at approximately 7.5. The doublet for the C-3-methyl hydrogens using DMSO-d_6 as solvent occurred at τ 8.74.

The acid from VII, m.p. 154–157° (lit.[8] m.p. 156–158°), was isolated by heating 6 g. of the adduct in 35 ml. of boiling water for 10 min. and allowing the solution to stand overnight at room temperature.

The n.m.r. spectrum of the acid in DMSO-d_6 as solvent exhibited a doublet for the C-3-methyl hydrogens at τ 8.97.

Maleic Anhydride Adduct of *cis*-Piperylene (VIII).—A mixture of 33.2 g. of VII from *trans*-piperylene and 0.33 g. of dimethylaniline was heated 4 hr. at 190° (bath temperature).[8] Dimethylaniline was removed by distillation under reduced pressure, and the product was collected at 108° (0.75 mm.). The n.m.r. spectrum of a CDCl$_3$ solution indicated that only 40% isomerization had occurred as measured by the ratio of the peak areas for the C-3-methyl group in VIII at τ 8.73 and in VII at 8.66 using CDCl$_3$ as solvent.

Repetition of the base-catalyzed isomerization at 280–290° for 10 min. gave 22.2 g. of product, isolated by distillation at 134–136° (3.5 mm.), which consisted of 75% VIII and 25% unchanged VII.

The pure acid from VIII, m.p. 160–162° (lit.[8] m.p. 161–162°), was isolated by hydrolyzing 22 g. of the adduct mixture in 120 ml. of boiling water for 5 min., collecting the insoluble product after cooling, and recrystallizing the acid from 70 ml. of water at room temperature.

The n.m.r. spectrum of the acid in DMSO-d_6 as solvent exhibited only one doublet corresponding to the C-3-methyl group at τ 8.92.

Acknowledgment.—We wish to thank Mrs. M. T. Neglia for the n.m.r. spectra and Dr. R. Feinland for the v.p.c. data.

Synthesis and Study of Pseudo-Aromatic Compounds. IV. A Synthetic Approach to Anthrazulene[1]

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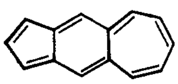
The synthesis of 5,7-diphenyl-1-anthrazulenium ion and attempts to convert this ion to 5,7-diphenylanthrazulene are described. The limited data available indicates that the anthrazulene ring system is extremely reactive to electrophilic attack.

The theoretical relevence of anthrazulene (1) lies in the fact that this molecule should serve as a criterion for the validity of applying empirical rules to predict aromatic character. Both Craig's rule[2] and the $4n + 2$ rule[3] are commonly used as a basis for predicting the presence or absence of stabilization in the ground state due to π-electron delocalization in cyclic conjugated polyenes. Since anthrazulene is predicted to possess a high π-electron delocalization energy from molecular orbital calculations (2.254 γ, 74.1 kcal./mole)[4] and has a $4n + 2$ periphery and totally symmetrical ground state, as predicted by Craig's rule, it would be expected to be aromatic. However, both these empirical rules and quantum mechanical approximation methods fail to take into account a high reactivity which might be associated with certain structural characteristics. Thus anthrazulene may possess a substantial π-electron delocalization energy in accordance with prediction, but may be highly reactive due to facile conversion to a benzenoid aromatic system by reaction with its environment, or it may possess essentially no π-electron delocalization energy and be unstable for the same reason.



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It has been established that dehydrogenation of indano[5′,6′:1,2]cyclohepta-1,3-diene does not lead to anthrazulene and that it is not aromatic from a classical standpoint[5,6] (*i.e.*, it does not possess a high π-electron delocalization energy which is associated with a lowering of the ground-state energy in relation to its environment). Also it has been demonstrated that the anthrazulene ring system is a substantially higher energy species than related systems in which the central ring is formally benzenoid.[7]

In order to attempt to determine the ground-state properties of anthrazulene the synthesis of 5,7-diphenylanthrazulene has been investigated and the results of this investigation are reported herein.

Indane-5,6-dialdehyde[7] readily condenses with 1,3-diphenylacetone in the presence of base to give the corresponding indano[5′,6′:4,5]-2,7-diphenyltropone (2). This procedure has been shown to be a general method for the synthesis of 4,5-benzotropones.[8] The experimental molecular weight indicated that the product resulted from condensation of 1 mole of aldehyde and 1 mole of ketone. The n.m.r. (Figure 1) and infrared spectra are completely consistent with the proposed structure 2.

This indanotropone reacted with N-bromosuccinimide to give an unstable bromination product which lost hydrogen bromide upon attempts to recrystallize

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(1) Part III: D. J. Bertelli and C. Golino, *J. Org. Chem.*, **30**, 368 (1965).

(2) D. P. Craig, *J. Chem. Soc.*, 3175 (1951).

(3) E. Huckel, *Z. Physik*, **70**, 204 (1931); *Z. Electrochem.*, **43**, 752 (1937).

(4) G. Berthier, B. Pullman, and J. Baudet, *J. Chim. Phys.*, **50**, 209 (1953).

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(6) S. Gupta, *Current Sci.* (India), **5**, 133 (1936); S. Dev, *J. Indian Chem. Soc.*, **30**, (1953); *Chem. Abstr.*, **49**, 3116 (1955).

(7) D. J. Bertelli, *J. Org. Chem.*, **29**, 3032 (1964).

(8) J. Thiele and J. Schneider, *Ann.*, **369**, 287 (1909); J. Thiele and E. Weitz, *ibid.*, **377**, 1 (1910); W. Reid and H. Bender, *Ber.*, **89**, 1574 (1956).