the solvent was evaporated at room temperature under reduced pressure, water and benzene were added, and the aqueous layer extracted with ether. The combined organic layers were washed with water, saturated brine and then dried over anhydrous sodium sulfate. The residue obtained on evaporation of the solvent was freed of traces of pyridine by azeotropic distillation with toluene under reduced pressure. The crystalline residue was chromatographed on 100 g. of Florisil. The early fractions eluted with petroleum ether amounted to 1.08 g. of slightly oily crystalline solid, $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 316.2 mμ. Crystallization from 95% ethanol gave 0.505 g. (first crop) of colorless plates, m.p. 109–114°, and 0.029 g. (second crop), m.p. 109–113°. The first crop, after two recrystallizations from 60–80° petroleum ether and one from methanol, was obtained as colorless plates, m.p. 114–115°; $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 316.0 (ε 15,140), 227.3 (10,230).

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.5; H, 7.5.

From the later fractions of the above chromatogram a total of 0.623 g. of starting material was recovered. Crystallization from methanol gave pale yellow plates, m.p. 89–92°, undepressed on admixture with the benzylidene decalone.

Angular Methylation.—A solution of 0.201 g. of the aforementioned *trans*-2-benzylidene-Δ^3-octalone, m.p. 113.5–114.5°, in 5 ml. of benzene containing 1.2 ml. of methyl iodide was treated as described above with a solution of 0.35 g. of potassium in 15 ml. of *t*-butyl alcohol. After 5 hr. at room temperature the product was isolated as described above. The pale yellow oily residue obtained on evaporation of the solvent at reduced pressure was crystallized from 40–60° petroleum ether, to give 0.168 g. of colorless rectangular prisms, m.p. 76–77°. The residue from the mother liquors was chromatographed on 1.3 g. of Florisil, and the early fractions eluted with petroleum ether yielded, after crystallization from 40–60° petroleum ether, 0.022 g. of additional material, m.p. 75–77°. The total yield of *cis*-2-**benzylidene-9-methyl-Δ^3-1-octalone** (A isomer) was thus 0.190 g. or 89%. A sample of the 76–77.5° material after sublimation at 95° (0.2 mm.) and crystallization from methanol was obtained as colorless prisms, m.p. 77.5–78.5°; $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 319.0 mμ (ε 14,450), 229.5 (10,470).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.4; H, 7.79.

The m.p. of the product obtained by the above procedure was depressed on admixture with the *cis*-2-benzylidene-9-methyl-Δ^3-1-octalone, m.p. 82.5–83.5°, and the corresponding *trans* isomer, m.p. 101–102.5°, described below.

***cis*-2-Benzylidene-9-methyl-Δ^3-1-octalone (B Isomer).**—A 5.0-g. sample of *cis*-2-benzylidene-9-methyl-1-decalone,[7] m.p. 103–104.8°, in 50 ml. of carbon tetrachloride containing 3.9 g. of N-bromosuccinimide was irradiated as described above for the lower homolog. The crude product was dehydrobrominated with pyridine and isolated as described above. Trituration with ether gave 2.7 g., m.p. 73–81°. Crystallization from methanol afforded 2.18 g., m.p. 81–84.5°.

Comparable material from another experiment was evaporatively distilled at 7.05 mm. (120°) and recrystallized from methanol to give colorless prisms, m.p. 86.5–87.5°; $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 315 mμ (ε 14,500), 228 (10,600).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.6; H, 8.3.

***trans*-2-Benzylidene-9-methyl-Δ^3-1-octalone.**—A 5.0-g. sample of *trans*-2-benzylidene-9-methyl-1-decalone,[7] m.p. 92–93.5°, was brominated and dehydrobrominated just as described in the preceding experiment for the *cis* isomer. The crude product amounted to 4.35 g., m.p. 91–99°. After sublimation as above and recrystallization from 95% ethanol, the pure material was obtained as thick colorless prisms, m.p. 105.5–106.5°; $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 317.5 mμ ε (16,500), 229.5 (11,400).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.4; H, 7.9.

Ozonolysis of *cis*-2-Benzylidene-9-methyl-Δ^3-1-octalone. (a) B Isomer.—A solution of 0.058 g. of this ketone (see above), m.p. 72–74°, in 10 ml. of ethyl acetate was treated with excess ozone at 0°; then 5 ml. of acetic acid and 2 ml. of 30% hydrogen peroxide were added. The mixture was allowed to stand overnight at room temperature and the product was isolated as described above for the oxidation of the substituted acrylic acid. Crystallization of the crude product from a small amount of benzene gave 0.005 g. of colorless prisms, m.p. 160–162°, undepressed on admixture with authentic *cis*-1-methylcyclohexane-1,2-dicarboxylic acid described immediately below.

(b) **A Isomer.**—A 1-g. specimen of this material was ozonized as described above. After crystallization of the crude product from benzene there was obtained 0.2 g. of *cis*-1-methylcyclohexane-1,2-dicarboxylic acid, m.p. 163–165°. The reported melting points are 160,[57] and 165°.[58] The anhydride was produced by heating the diacid at 180° for 10 min. Recrystallization from 65–68° petroleum ether afforded material, m.p. 64–65° (reported[57] 60–65°).

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[57] R. P. Linstead and A. F. Millidge, *J. Chem. Soc.*, 478 (1936).

[58] F. Vocke, *Ann.*, **497**, 247 (1932).

[CONTRIBUTION FROM THE ORGANISCH-CHEMISCHES INSTITUT DER UNIVERSITÄT MAINZ, GER., AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MASSACHUSETTS, AMHERST, MASS.]

Oxidation of N-Aminodihydroisoindoles. Synthesis of *cis*- and *trans*-1,2-Diphenylbenzocyclobutenes[1-3]

BY LOUIS A. CARPINO

RECEIVED DECEMBER 16, 1961

Oxidation of N-aminodihydroisoindole (II) by means of mercuric oxide in methylene dichloride or alkaline degradation of the corresponding *p*-toluenesulfonhydrazide (III) gave the dimer of *o*-quinodimethane, isolated as the corresponding dibromide. The related *cis*- and *trans*-1,3-diphenyl-2-aminodihydroisoindoles have been prepared from 1,3-diphenyl-1-hydroxyisoindole (XIII) by zinc–acetic acid and lithium aluminum hydride–aluminum chloride reduction, respectively. Conversion of each amine to the corresponding hydrazine through the nitroso compounds proceeded normally. Mercuric oxide oxidation of the *trans* isomer VIIb yielded the previously reported *trans*-1,2-diphenylbenzocyclobutene (XVII). Mercuric oxide oxidation of the *cis*-hydrazine VIIa was unsatisfactory, although the use of activated manganese dioxide led to isolation of the previously unknown *cis*-1,2-diphenylbenzocyclobutene (XVI) in 27% yield. N.m.r. spectral data as well as oxidation, reduction and isomerization studies support the assigned structure. A convenient synthetic route to alkyl *o*-cyanobenzoates by the one-step dehydration–esterification of phthalamic acid is reported utilizing an alkane- or arenesulfonyl chloride in the presence of pyridine and an alcohol.

Continuing a study of the oxidation of 1,1-disubstituted hydrazines, the oxidation and sulfonhydrazide degradation of N-aminodihydroisoindole and its 1,3-diphenyl derivatives is reported. It had been reported earlier[4] that the *p*-toluene-

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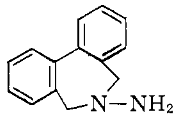
[1] Acknowledgment is made to the donors of the Petroleum Research Fund for support of this research.

[2] We are grateful to Prof. Leopold Horner who kindly provided laboratory facilities at the Organisch-Chemisches Institut in Mainz where a major portion of this work was completed.

[3] For the previous paper in this series see L. A. Carpino, A. A. Santilli and R. W. Murray, *J. Am. Chem. Soc.*, **82**, 2728 (1960).

[4] L. A. Carpino, *ibid.*, **79**, 4427 (1957).



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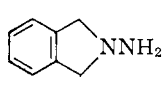
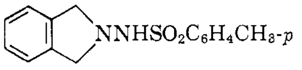
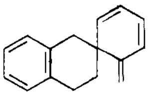


II



III

sulfonhydrazide of dibenzazepine I underwent reaction with aqueous sodium hydroxide to give, in high yield, the expected hydrocarbon 9,10-dihydrophenanthrene. The related compound, N-aminodihydroisoindole (II), was also prepared in order to study its conversion to benzocyclobutene. While this work was in progress Baker, McOmie and Preston[5] published a note on the alkaline degradation of III and showed that small amounts of benzocyclobutene (*ca.* 14%), dibenzocycloöctadiene (12%) and *o*-xylene (*ca.* 2%) were formed. These workers made no mention of the formation of the substance which, in our hands, appears to be the major product of either the mercuric oxide oxidation of II or the alkaline degradation of III. Thus oxidation of II by means of mercuric oxide in methylene dichloride solution or treatment of III with dilute aqueous potassium hydroxide solution led to the formation of the dimer (IV) of *o*-quinodimethane (VI). The dimer IV was isolated as the corresponding dibromide V. Preliminary attempts to isolate the dimer itself were unsuccessful, although Errede[6] has recently shown that IV, formed by pyrolysis of *o*-methylbenzyltrimethylammonium hydroxide, presumably through the intermediacy of VI, may be isolated in a pure state by chromatographic methods. Application of Errede's isolation technique to our reaction promises to make the interesting spiro compound IV readily obtainable. Small amounts of steam-distillable products were obtained in addition to IV, but the lack of sensitive analytic separation methods (V.P.C.) at the time this work was carried out precluded quantitative isolation and characterization.



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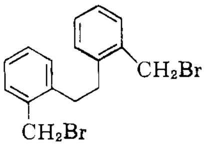
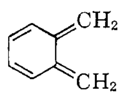
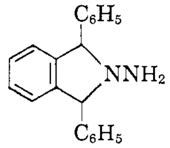


V

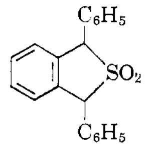


VI

Formation of IV as the major isolable reaction product in the oxidation of II suggested that this reaction might conceivably be developed into a convient source of *o*-quinodimethanes of greater stability than VI.[7] This paper reports a study of the synthesis and oxidation of *cis*-(VIIa) and *trans*-2-amino-1,3-diphenyldihydroisoindole (VIIb). Cava[8] has recently reported an unsuccessful approach to the synthesis of 1,2-diphenylbenzocyclobutene by pyrolysis of the corresponding sulfone VIII.



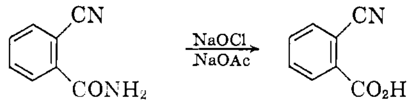
VII



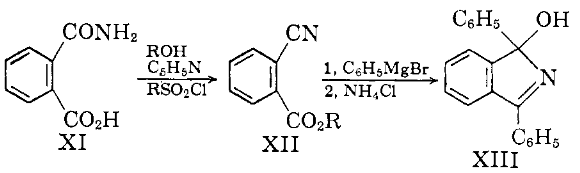
VIII

The major product (94%) proved to be 9-phenyl-9,10-dihydroanthracene, thought to be a cyclization product of the corresponding diphenyl *o*-quinodimethane.

1,3-Diphenyl-3-hydroxyisoindole (XIII), previously reported by Boyd and Ladhams,[9] proved to be a key intermediate in the synthesis of both VIIa and VIIb. The isoindole (XIII) is obtainable by reaction of an alkyl *o*-cyanobenzoate with phenylmagnesium bromide. In order to prepare the large quantities of XIII required, it was necessary to develop a convenient large-scale synthesis of simple esters of *o*-cyanobenzoic acid. Prior to the present work the most convenient route to these esters involved the Sandmeyer reaction starting from the corresponding alkyl anthranilates. Alkyl *o*-cyanobenzoates were first approached in the present work through the free acid X. Although this method was abandoned in favor of a simpler method, a convenient synthesis[10] of the previously difficulty accessible acid X was developed (see Experimental section) from IX. Although it was possible to convert X to the corresponding alkyl esters by the method of Brewster and Ciotti,[11] it was subsequently found more convenient to combine the Brewster–Ciotti esterification with the Stephens–Bianco–Pilgrim[12] nitrile synthesis both of which employ the same reagents. Thus, phthalamic acid (XI) is converted in one step to the corresponding ester XII by reaction with an alcohol and a sulfonyl chloride in the presence of pyridine.[13] The



IX X



XI XII XIII

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[5] W. Baker, J. F. McOmie and D. R. Preston, *Chemistry & Industry*, 1305 (1960). A full account of this work subsequently appeared [*J. Chem. Soc.*, 2971 (1961)].

[6] L. A. Errede, *J. Am. Chem. Soc.*, **83**, 949 (1961).

[7] Both Errede and Cava [M. P. Cava and A. A. Deana, *ibid.*, **81**, 4266 (1959)] have suggested that the ultimate fate of *o*-quinodimethane (VI) generated as a short-lived species is greatly dependent on the reaction conditions prevailing during its generation. Although no definite evidence is available as to whether the *o*-quinodimethane is the actual intermediate in any of these reactions, the hypothesis is nevertheless a useful one.

[8] M. P. Cava, M. J. Mitchell and A. A. Deana, *J. Org. Chem.*, **25**, 1481 (1960).

[9] D. R. Boyd and D. E. Ladhams, *J. Chem. Soc.*, 2091 (1928); see also F. F. Blicke and R. A. Patelski, *J. Am. Chem. Soc.*, **58**, 273 (1936).

[10] Compare A. Braun and J. Tcherniac, *Ber.*, **40**, 2709 (1907), whose method had to be critically modified.

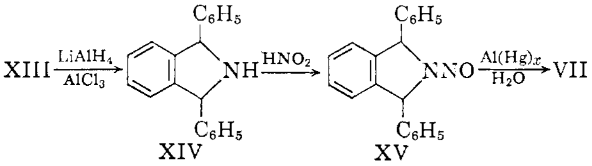
[11] J. H. Brewster and C. J. Ciotti, *J. Am. Chem. Soc.*, **77**, 6214 (1955).

[12] C. R. Stephens, E. J. Bianco and F. J. Pilgrim, *ibid.*, **77**, 1701 (1955).

[13] In an independent study C. K. Sauers and R. J. Cotter [*J. Org. Chem.*, **26**, 6 (1961)] have described a related synthesis of cyano esters from amic acids using an alkyl chloroformate and triethylamine as the dehydration–esterification reagent.

t-butyl ester, inexplicably, proved to be the most suitable of the aliphatic esters examined for conversion to XIII (31%).

Reduction of XIII to one of the isomeric 1,3-diphenyldihydroisoindoles has been reported in low yield (10–20%) by Boyd and Ladhams[9] using zinc and acetic acid. The amine was assigned the *trans* configuration. In an effort to improve the yield of reduction product, lithium aluminum hydride reduction of XIII in the presence of aluminum chloride[14] was examined. However, in this case an isomeric dihydroisoindole was obtained. Subsequent modifications of Boyd and Ladhams' original zinc–acetic acid reduction process allowed preparation of the known amine in yields of 80–90%.



XIV XV

Contrary to the suggestion of Boyd and Ladhams, we assign the *trans* structure to the amine XIVb, m.p. 126–127.5°, obtained by hydride reduction and the *cis* structure to the previously known amine XIVa, m.p. 104–105°. These configurational assignments were made on the basis of n.m.r. data by analogy with the results of Curtin and co-workers[15] who studied the 1,2-diphenylcyclopentanes and cyclopropanes and found that the isomer exhibiting greater shielding of the aliphatic ring protons is the *trans* isomer. The n.m.r. data for the series of compounds studied in the present work are given in Table I.

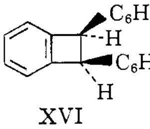
TABLE I

N.M.R. LINE POSITIONS OF α-PHENYL PROTONS IN *cis* AND *trans* ISOMERS[a]

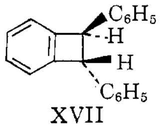
Compound	τ, p.p.m. *cis*	τ, p.p.m. *trans*
1,2-Diphenylbenzocyclobutene	4.80	5.56
1,3-Diphenyldihydroisoindole	4.25	4.46
2-Amino-1,3-diphenyldihydroisoindole	4.68	5.23

[a] Determined in deuteriochloroform using tetramethylsilane as internal standard.

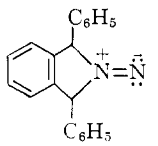
Conversion of each isomeric amine to the corresponding *cis*-(VIIa) and *trans*-(VIIb) hydrazine was carried out by reduction of the N-nitroso compound by means of aluminum amalgam in wet ether. Oxidation of the *trans*-hydrazine VIIb by means of mercuric oxide gave an 81% yield of the 1,2-diphenylbenzocyclobutene (XVII), m.p. 94–95.5°, originally reported by Jensen and Coleman.[16] This hydrocarbon is assigned the *trans* configuration on the basis of the n.m.r. data (Table I). Such an assignment is consistent with the original synthetic method of Jensen and Coleman. Baker, McOmie and Preston reported that the same hydrocarbon, m.p. 94–95.5°, was obtained by sulfonhydrazide degradation of the hydrazine obtained by nitrosation and reduction of the amine, m.p. 104–105°, of Boyd and Ladhams, to which we have assigned the *cis* configuration. Considering the conversion of these hydrazines to the corresponding hydrocarbons, it would seem that no definite prediction of stereochemistry can be made in the case of a reaction proceeding through the *o*-quinodimethane intermediate. However, if concerted expulsion of nitrogen and ring contraction occurred from an intermediate such as XVIII by analogy with the work of Overberger, Lombardino and Hiskey,[17] it would be expected that stereospecificity would be observed. Oxidation of the *cis*-hydrazine VIIa by means of mercuric oxide in methylene dichloride yielded a difficultly-resolvable mixture from which only very small amounts of both *cis*- and *trans*-1,2-diphenylbenzocyclobutenes were isolated. Oxidation of the *cis*-hydrazine by means of activated manganese dioxide[18] was more satisfactory. In this case the *cis*-hydrocarbon XVI was isolated without experimental difficulty, although in only fair yield (27%). *cis*-1,2-Diphenylbenzocyclobutene has not previously been reported. The n.m.r. spectrum is in agreement with the assigned structure (Table I). Oxidation by means of chromic acid in acetic acid gave *o*-dibenzoylbenzene. Catalytic reduction in ethanol over a palladium–charcoal catalyst at room temperature and atmospheric pressure gave *o*-dibenzylbenzene. Refluxing in carbon tetrachloride for 14 hours caused isomerization to the *trans*-hydrocarbon.



XVI



XVII



XVIII

Acknowledgment.—We are indebted to Drs. A, Melera of Varian Associates, Zürich, John Ragle, Cornell University, and Thomas Stengle, University of Massachusetts, for the n.m.r. spectra as well as aid in their interpretation.

Experimental[19,20]

Oxidation of N-Aminodihydroisoindole.—A solution of 6.1 g. of N-aminodihydroisoindole[4] dissolved in 150 ml. of methylene dichloride at room temperature was treated with 20 g. of "brown" mercuric oxide[3] in small portions, allowing gas evolution to subside between additions. The mixture was filtered and a solution of 1.4 ml. of bromine in 25 ml. of methylene dichloride added to the filtrate. Spontaneous evaporation of the methylene dichloride left a tacky black residue which was extracted with a hot mixture of nitromethane and ethanol (2:1). Cooling gave 2.2 g. (26.2%) of brown solid which on recrystallization from nitromethane–ethanol (1:1) gave 1.4 g. (17%) of cream-colored crystals, m.p. 138–139.5° (lit.[21] m.p. 137–138°). This compound was identified as 2,2′-bis-(bromomethyl)-bibenzyl by reduction using lithium aluminum hydride in tetrahydrofuran which gave an 80% yield of 1,2-di-*o*-tolylethane, m.p. and mixed m.p. 65–66° (lit.[22] m.p. 66.5°).

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[14] R. F. Nystrom and C. R. A. Berger, *J. Am. Chem. Soc.*, **80**, 2896 (1958).

[15] D. Y. Curtin, H. Gruen and B. A. Shoulders, *Chemistry & Industry*, 1205 (1958).

[16] F. R. Jensen and W. E. Coleman, *J. Am. Chem. Soc.*, **80**, 6149 (1958).

[17] C. G. Overberger, J. G. Lombardino and R. G. Hiskey, *ibid.*, **79**, 6430 (1957).

[18] H. Morrison, S. Danishefsky and P. Yates, *J. Org. Chem.*, **26**, 2617 (1961).

[19] Melting and boiling points are uncorrected.

[20] Elemental analyses are by Drs. Weiler and Strauss, Oxford, Eng., and Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.

[21] E. D. Bergmann and Z. Pelchowicz, *J. Am. Chem. Soc.*, **75**, 4281 (1953).

In one case when an attempt was made to distil under vacuum the oxidation product of N-aminodihydroisoindole, rapid polymerization occurred. This is in accord with the experience of Errede[6] who isolated the pure *o*-quidodimethane dimer by chromatographic methods. The infrared spectrum of the crude material corresponded to that published by Errede[6] for the dimer IV. Sulfonhydrazide degradation of N-*p*-toluenesulfonamidodihydroisoindole[4] by means of aqueous alkali also led to the isolation of the dibromide of the *o*-quinodimethane dimer, m.p. and mixed m.p. 138–139.5.

o-**Cyanobenzoic Acid.**—A suspension of 14.6 g. of *o*-cyanobenzamide[10] (recrystallized from dimethylformamide–nitromethane (1:1), m.p. 177–179°, resolidification and new m.p. 206–208°) and 40 g. of anhydrous sodium acetate in 400 ml. of commercial sodium hypochloride solution contained in a 1-l. erlenmeyer flask and having a thermometer immersed in the liquid was heated on a hot-plate with continuous rapid swirling at such a rate that the temperature rose to 57° in 3 minutes. The mixture was removed from the hot-plate and vigorously swirled for 60 sec. during which time the temperature rose to 59°. Immediately thereafter the mixture was plunged in an ice-bath and cooled rapidly to 20–25°. The insoluble material was filtered off and the filtrate stored in an ice-bath until a second run had been made. Generally less than 1–2 g. of material remains undissolved if the reaction is successful. The filtrates of two such runs were combined and acidified with 120 ml. of concentrated hydrochloric acid. The white brei which retained a large amount of water was filtered and the wet material transferred to a beaker and 100 ml. of ethyl acetate added. The mixture was warmed on a hot-plate to the boiling point of ethyl acetate and stirred well to extract as much of the acid as possible into the organic layer which was decanted into a flat dish. An additional 100 ml. of ethyl acetate was added and the treatment repeated. A two-phase liquid system formed which was separated in a separatory funnel. Spontaneous evaporation of the combined organic layers left a white crystalline solid (20 g.) which was recrystallized from about 400 ml. of ethyl acetate to give 16–18 g. (55–61%) of white needles, m.p. 178–183° (resolidifies and remelts at 229–230°); lit.[23] m.p. 187–188° followed by resolidification and remelting at 220°.

Phthalamic Acid.—A mixture of 740 g. of phthalic anhydride and 1.1 l. of concentrated ammonium hydroxide was stirred in a 3-l. round-bottomed flask for 8 hours at room temperature. The temperature rose spontaneously during the first 2 hours and the phthalic anhydride was replaced by a second granular solid. After air-drying, the unwashed solid was added to 2.2 l. of water at room temperature and the mixture shaken until most of the solid dissolved. Filtration of insoluble material followed by addition of 400 ml. of concentrated hydrochloric acid and storage overnight gave 459 g. (56%) of tiny white crystals, m.p. 140–143° (resolidifies at about 160°); lit.[24] m.p. 149° followed by resolidification and melting at 231°.

Ethyl *o*-Cyanobenzoate.—In a 2-l. round-bottomed flask fitted with a mechanical stirrer, dropping funnel and thermometer there was placed 606 ml. of pyridine, 138 ml. of commercial absolute ethanol and 165.5 g. of phthalic acid monoamide. While cooling in an ice-bath there was added dropwise with stirring over a period of 2 hours 233 ml. of methanesulfonyl chloride. The inner temperature remained at 8–15°. The ice-bath was removed and stirring was continued for 4 hours (the temperature rose to 55–60°), 100 ml. of commercial absolute ethanol was added and stirring continued for an additional 4 hours. The mixture was diluted with water to a total volume of 4 l., cooled in an ice-bath and the tacky white crystalline solid filtered and air-dried overnight. Distillation gave 124 g. (71%) of the ester, b.p. 103–105° (0.1 mm.), m.p. 63–65.5°. Recrystallization from 30–60° ligroin–benzene (2:1) gave 112.5 g. (64%) of large white crystals, m.p. 64.5–66° (lit.[9] m.p. 68–69°). There was no depression of melting point on admixture with an authentic sample.

Methyl *o*-Cyanobenzoate.—Substitution of methanol for ethanol in the above reaction led to a 71% yield of the corresponding methyl ester, m.p. 49.5–51.5° (lit.[9] m.p. 51°). Essentially the same process was used to esterify *o*-cyanobenzoic acid except that only 2 equivalents of methanesulfonyl chloride was used. Benzene- and *p*-toluenesulfonyl chloride could be substituted for the methanesulfonyl chloride in each of these reactions.

***t*-Butyl *o*-Cyanobenzoate.**—There was added 89.6 g. of phthalamic acid to a stirred solution of 134 ml. of *t*-butyl alcohol and 329 ml. of pyridine. The resulting solution was cooled in a tap-water-bath and 210 ml. of benzenesulfonyl chloride added over a period of 1 hour, the internal temperature remaining at 35–40°. The mixture was allowed to stand at room temperature overnight, diluted with water to a total volume of 2 l. and the oil extracted with 3–4 50-ml. portions of ether. The ether extracts were washed with three 50-ml. portions of water, four 50-ml. portions of dil. hydrochloric acid (10%) and three 50-ml. portions of dil. sodium carbonate solution. Removal of solvent from the dried ether extracts left 90 g. (81%) of an orange colored oil. The crude liquid was suitable for reaction with the phenyl Grignard reagent. Distillation through a short-stem Claisen flask gave 62 g. (56%) of the ester, b.p. 83–84° (0.05 mm.).

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45. Found: C, 70.45; H, 6.32.

1,3-Diphenyl-3-hydroxyisoindole.—A solution of 180 g. of crude *t*-butyl *o*-cyanobenzoate dissolved in 560 ml. of benzene was added to a stirred solution of phenylmagnesium bromide prepared from 52.5 g. of magnesium, 230 ml. of bromobenzene and 700 ml. of ether at a rate to maintain gentle refluxing (*ca.* 1.5 hr.). The mixture was refluxed for 1 hour and the complex decomposed by dropwise addition of 190 ml. of saturated ammonium chloride solution. The resulting solid was filtered, divided into two equal portions and each portion extracted with 500 ml. of boiling toluene. The hot extract was filtered by suction and the filtrate cooled in an ice-bath for several hours or overnight and the yellow-green crystals of pure isoindole filtered (m.p. 190–192°). The spent filtrate was used to extract the original solid in the same way two additional times.

The original ether–benzene filtrate was allowed to evaporate in a flat dish to about one-fifth of the original volume, the greenish-black mixture filtered and the solid recrystallized from toluene which gave additional pure isoindole, m.p. 190–192°. The combined amount of pure isoindole obtained, m.p. 190–192°, was 78 g. (31%).

Substitution of methyl or ethyl *o*-cyanobenzoate for the *t*-butyl ester gave, in our hands, extremely poor yields (3–10%) of the hydroxyisoindole in spite of the fact that previous workers[9] obtained high yields using these esters. Although the reactions were repeated scores of times the difficulty was not traced to any one factor although it might have been caused by impurities (or lack thereof) in the magnesium used. The highest yields (30–35%) using the *t*-butyl ester were obtained consistently using normal samples of magnesium as commonly obtainable in West Germany. Upon repeating the reaction with the type of magnesium normally obtainable in the United States much lower yields (10–15%) were obtained, although attempts were made to duplicate conditions exactly.

***trans*-1,3-Diphenyldihydroisoindole.**—A 1-l. round-bottomed flask containing 270 ml. of ether was cooled in an ice-bath and there was added slowly with stirring 15 g. of anhydrous aluminum chloride followed by 4.26 g. of lithium aluminum hydride. The mixture was stirred at room temperature for 5 min. and 16 g. of 1,3-diphenyl-3-hydroxyisoindole added through a rubber solid-addition tube (Gooch) over a period of 10 min. The mixture was refluxed for 17 hr., cooled in an ice-bath and decomposed by the cautious addition of 27 ml. of water followed by 13 ml. of a solution prepared by dissolving 8 g. of sodium hydroxide in 20 ml. of water. The mixture was stirred at room temperature for 10 min., filtered and the ether solution allowed to evaporate in a flat dish. A yellow solid (3 g.) remained.

The complex aluminum salts filtered above were added to a solution of 30 g. of sodium hydroxide in 150 ml. of water. There was added 100 ml. of ether and the mixture shaken vigorously; the ether layer was decanted through Celite into a suction filter. The milky alkaline liquid was extracted in the same manner with four additional 50-ml. portions of ether and the extracts allowed to evaporate in a flat dish. The combined residues (8.9 g.) were recrystallized from ethanol–nitromethane (1:1) which gave 9.2 g. (64.8%) of long yellow-white needles, m.p. 125–127°. The analytical sample (ethanol) had m.p. 126–127.5°.

Anal. Calcd. for $C_{20}H_{17}N$: C, 88.52; H, 6.32; N, 5.16. Found: C, 88.64; H, 6.65; N, 4.87.

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(22) C. Moritz and R. Wolffenstein, *Ber.*, **32**, 2531 (1899).

(23) O. Allendorf, *ibid.*, **24**, 2348 (1891).

(24) E. Chapman and H. Stephen, *J. Chem. Soc.*, *127*, 1791 (1925).

Oxidation of *trans*-1,3-Diphenyldihydroisoindole.—To a solution of 0.54 g. of the *sec*-amine in 3 ml. of boiling acetic acid there was added 0.27 g. of chromic oxide. After 2–3 min. the solution was diluted with 25 ml. of water, heated to boiling, filtered and the solid recrystallized from ethanol–nitromethane which gave 0.1 g. of cream-colored crystals, m.p. 146–147.5°, mixed m.p. with an authentic sample[9] of *o*-dibenzoylbenzene 146–147.5°.

***trans*-1,3-Diphenyl-2-nitrosodihydroisoindole.**—A solution of 9.2 g. of 1,3-diphenyldihydroisoindole in 24 ml. of water and 24 ml. of acetic acid was prepared by brief warming. The solution was cooled in an ice-bath and a solution of 2.62 g. of sodium nitrite in the minimum amount of water added. An oily solid which soon became granular separated at once. After the addition of 50 ml. of water the mixture was heated to the boiling point briefly, cooled in an ice-bath and filtered. There was obtained 9 g. (88%) of yellow-cream powder, m.p. 131.7–134.5°. Recrystallization from ethanol–nitromethane (2:1) gave 7.5 g. (73.5%) of yellow-white flakes, m.p. 133–134°.

Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 79.97; H, 5.37. Found: C, 79.92; H, 5.17.

***trans*-1,3-Diphenyl-2-benzoyldihydroisoindole.**—Acylation of 1,3-diphenyldihydroisoindole by means of benzoyl chloride in dimethylformamide in the presence of triethylamine gave the benzoyl derivative as small white crystals, m.p. 146–148° (ethanol).

Anal. Calcd. for $C_{27}H_{21}NO$: C, 86.37; H, 5.64. Found: C, 86.33; H, 6.01.

***trans*-1,3-Diphenyl-2-aminodihydroisoindole.**—A suspension of 9 g. of aluminum amalgam[25] in 300 ml. of ordinary ether was stirred gently and 7.5 g. of 1,3-diphenyl-2-nitrosodihydroisoindole was added all at once. The reaction mixture was warmed briefly in order to start the reaction which proceeded by gentle spontaneous refluxing for about 10 minutes. There was added 0.25 ml. of water and the mixture refluxed with stirring for 30 min., 0.2 ml. of water was again added and refluxing continued for another 2 hr. after which another 0.2 ml. of water was added and refluxing continued for 3 hr. longer. The ether and colloidal sludge was decanted from the unreacted aluminum into a solution of 20 g. of sodium hydroxide in 200 ml. of water. Fresh ether was used to wash the aluminum. The dried (magnesium sulfate) ether solution was evaporated from a water-bath with the aid of a water aspirator. The oil became glassy on standing in a refrigerator. Trituration[26] with a small amount of ethyl alcohol converted the glassy material to a yellowish solid. Additional alcohol was then added with heating to dissolve the substance (10–12 ml.). Cooling at room temperature followed by standing in a refrigerator overnight gave 4.5 g. (63%) of the hydrazine, m.p. 98–100°. Recrystallization from ethyl alcohol gave 4.0 g. (56%) of yellowish crystals, m.p. 100–103°. The analytical sample had m.p. 104–106° (benzene-ligroin, b.p. 60–70°).

Anal. Calcd. for $C_{20}H_{18}N_2$: C, 83.88; H, 6.34. Found: C, 84.13; H, 6.25.

The benzal derivative, prepared in the usual manner and recrystallized from an equivolume mixture of ethanol, nitromethane and dimethylformamide, had m.p. 188–189.5°.

Anal. Calcd. for $C_{27}H_{22}N_2$: C, 86.59; H, 5.92. Found: C, 86.96; H, 6.24.

***trans*-1,2-Diphenylbenzocyclobutene.**—A solution of 1.8 g. of 1,3-diphenyl-2-aminodihydroisoindole in 15 ml. of methylene dichloride was treated with 2.2 g. of mercuric oxide over a period of 5–7 min. The oxidation was initiated by slight warming. When ebullition became very slow the mixture was allowed to stand for 10 min. and filtered through very retentive filter paper. The filtrate and washings were allowed to evaporate spontaneously in a flat dish. There remained 1.3 g. (80.8%) of a cream-tan solid, m.p. 75–78.5°. Recrystallization from about 10 ml. of ethanol[27] gave 1 g. (62.1%) of small white needles, m.p. 94–95.5° (lit. m.p. 94.5–95.2°).

***cis*-1,3-Diphenyldihydroisoindole.**—Zinc dust was weakly coppered by adding 150 g. in one portion to a solution of 5 g. of copper sulfate in 500 ml. of water, swirling for 5 min., filtering, washing twice with water, twice with methanol and twice with ether. The resulting black powder was air-dried for about 1 hour and used at once.

In a 3-neck flask cooled by a tap-water-bath there was placed 400 ml. of glacial acetic acid, the temperature allowed to drop to 16–17° and 24 g. of 1,3-diphenyl-3-hydroxyisoindole added with stirring. The resulting solution was then treated with 86 g. of the coppered zinc dust with vigorous stirring over a period of 0.5 hour while keeping the temperature between 24–26°. The mixture was stirred mechanically for an additional 10 min., diluted with 1 l. of water, treated with several grams of decolorizing charcoal and filtered after about 3 hours. The filtrate was neutralized with solid sodium hydroxide to the neutral point (universal indicator paper, 243 g. of sodium hydroxide). The mixture was extracted with six 100-ml. portions of ether and the extracts filtered into a flat dish and allowed to evaporate. The cream-colored solid remaining amounted to 18.2 g. (80%). The amine was pure enough for conversion to the nitroso compound. Recrystallization of a small portion from 75% ethanol or ligroin gave small white crystals, m.p. 104–105° (lit.[9] m.p. 109°).

***cis*-1,3-Diphenyl-2-nitrosodihydroisoindole.**—The method described for the corresponding *trans* isomer was used. The crude nitroso compound was recrystallized from ethanol–dimethylformamide to give 70% of the nitroso derivative, m.p. 175–177° (lit.[9] m.p. 175–175.5°).

***cis*-1,3-Diphenyl-2-aminodihydroisoindole.**—A mixture of 12 g. of aluminum amalgam and 200 ml. of water-saturated ether was stirred vigorously and 7.9 g. of the nitroso compound added in one portion. The reaction was initiated by warming and continued gently when the heating bath was removed. After about 20 min., 0.2 ml. of water was added and also after the subsequent three 20-min. periods. If the spontaneous reaction slowed down too much the mixture was gently heated. After 3–5 hours the ether–sludge mixture was decanted from the unreacted aluminum into an aqueous solution of sodium hydroxide. The ether layer was separated and the aqueous phase extracted with an additional 100 ml. of ether. The dried ether solution was evaporated in a flat dish and the resulting yellow solid triturated with ethanol and filtered. Recrystallization from ethanol–nitromethane (1:1) gave 4.2 g. (56%) of white crystals, m.p. 130–137°. Three additional recrystallizations from ethanol–nitromethane and nitromethane gave 2.75 g. (32.5%) of the pure hydrazine, m.p. 140–142.5°.

Anal. Calcd. for $C_{20}H_{18}N_2$: C, 83.88; H, 6.34. Found: C, 83.83; H, 6.43.

The *benzal* derivative prepared in ethanol solution in the presence of a few drops of acetic acid and recrystallized from ethanol–dimethylformamide (1:1) had m.p. 186–186.5°. The melting point was depressed 30–40° on admixture with the benzal derivative, m.p. 188–189.5°, prepared from the isomeric hydrazine.

Anal. Calcd. for $C_{27}H_{22}N_2$: C, 86.59; H, 5.92. Found: C, 86.66; H, 5.82.

***cis*-1,2-Diphenylbenzocyclobutene.**—A solution of 1.8 g. of *cis*-1,3-diphenyl-2-aminodihydroisoindole in 190 ml. of methylene dichloride was cooled in an ice-bath and there was added over a 20-min. period with continuous swirling 2.6 g. of activated manganese dioxide. The mixture was allowed to stand in the ice-bath for 1.5 hr., filtered and treated in a separatory funnel with dilute aqueous sodium bisulfite in order to remove the last of the brown color. The filtered, dried (magnesium sulfate) solution was allowed to evaporate slowly from a crystallizing dish which left a greenish-yellow sirup. Trituration with cold methanol gave 1 g. of yellow amorphous solid, m.p. 58–87°. This solid was extracted with 10 ml. of hot methanol and a small amount of tough polymer-like material filtered off. Cooling in an ice-bath gave 0.43 g. (26.8%) of long white needles, m.p. 85.5–87.5°. Several recrystallizations from methanol gave an analytical sample, m.p. 85.5–87.5°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.72; H, 6.28. Found: C, 93.86; H, 6.26.

Isomerization of *cis*-1,2-Diphenylbenzocyclobutene.—A solution of 100 mg. of *cis*-1,2-diphenylbenzocyclobutene in

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(25) I. Vogel, *J. Chem. Soc.*, 594 (1927).

(26) If trituration with ethanol did not yield crystalline material, a small amount of the glassy product was dissolved in methylene dichloride whereupon crystals appeared at the edge of the solution as the solvent evaporated. These crystals were then used to seed the main mass of material.

(27) In one case only recrystallization from ethanol gave shimmering white flakes, m.p. 77–79°. Attempts to convert the high melting form into the low melting form were unsuccessful.

25 ml. of carbon tetrachloride was refluxed for 14 hours. Evaporation of the yellowish solution left a yellow sirup which crystallized upon trituration with methanol. Recrystallization from ethanol gave 50 mg. (50%) of tiny white needles, m.p. 93.5–94.5°. There was no melting point depression on admixture with a sample of the *trans*-hydrocarbon prepared by oxidation of the *trans*-hydrazine VIIb.

Hydrogenation of *cis*-1,2-Diphenylbenzocyclobutene.—A stream of hydrogen was passed for 8 hours at room tempera-through a solution of 200 mg. of *cis*-1,2-diphenylbenzocyclobutene in 50 ml. of ethanol to which 150 mg. of palladium-charcoal catalyst (10%) was added. Filtration and evaporation of the solvent gave, after recrystallization from ethanol, 100 mg. (49.5%) of *o*-dibenzylbenzene as white crystals, m.p. 76.5–78° (lit.[28] m.p. 78°). It had been reported previously by Jensen and Coleman[16] that the *trans* isomer was reduced to *o*-dibenzylbenzene under similar conditions. This was verified by reduction of a sample of the *trans*-hydrocarbon obtained by oxidation of VIIb.

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[28] A. Bistrzycki and B. Brenken, *Helv. Chim. Acta*, **5**, 20 (1922).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY, DETROIT 2, MICH.]

Conformational Analysis. XXVIII. The 3-Alkylketone Effect[1,2]

BY NORMAN L. ALLINGER AND LESLIE A. FREIBERG

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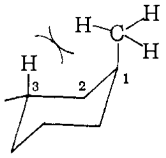
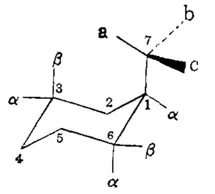
The energy of an axial methyl group relative to an equatorial in the position 3 to a ketone was measured by equilibrating the *cis* and *trans* isomers of 3,5-dimethylcyclohexanone, and the value found was 1.4 kcal./mole. The reduction of energy due to the 3-alkylketone effect was therefore 0.6 kcal./mole. This value is consistent with that predicted by van der Waals interactions.

Robins and Walker, in their study on the stability relationships of the 1,4-dioxophenanthrenes,[3] found their results were most easily interpretable if certain interactions, which had been ignored up until that time, were taken into account. Klyne[4] generalized these interactions as the 2-alkylketone and the 3-alkylketone effects. Recent studies, both theoretical and experimental, have indicated that the 2-alkylketone effect of a methyl group should be and is negligibly small.[5] The present work was aimed at evaluating, both theoretically and experimentally, the 3-alkylketone effect.



The evaluation of the 3-alkylketone effect by Klyne was based on the idea that the energy of the axial methyl group, in other words the energy of a gauche interaction, resulted mainly from the van der Waals repulsion between the hydrogen on the methyl and the axial hydrogens at C-3 and C-5 as indicated. If C-3 is converted to a carbonyl group, then one of these interactions would be eliminated, and the energy of the methyl axial should be reduced to half the value it has on the saturated ring.

It has recently been shown in a number of cases[6] that a semi-quantitative evaluation of the energies involved in such van der Waals interactions can be carried out using the general method developed by Hill.[7] Unfortunately, precise calculations are not now possible because neither the van der Waals functions nor the molecular geometry is known with sufficient accuracy. It is possible to calculate the energy of an axial methyl (relative to an equatorial one) on a cyclohexane ring by this method by summing the interaction energies for each pair of atoms for which the distance differs in the two conformations, and most of the pertinent data are given in Table I.



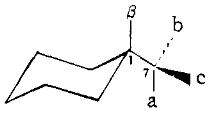


TABLE I

DATA FOR VAN DER WAALS ENERGY CALCULATION[a]

Interaction	Distance, Å.	Times Axial	Times Equatorial	Energy Axial	Energy Equatorial
3βH-aH	1.85	2	0	+1.04	...
3C-7C	2.95	2	0	+ .22	....
7C-3βH	2.60	2	0	− .03	....
3C-aH	2.60	2	0	− .03	....
aH-2αH	2.55	0	2	....	−0.09
3C-1βH	2.70	0	2	....	− .11
7C-2αH	2.70	0	2	....	− .11
1βH-3βH	2.55	0	2	....	− .09
1αH-2αH	2.45	2	0	−0.10	....
7C-3C	3.85	0	2	....	−0.19
7C-3βH	4.2	0	2	....	−0.03
1αH-3C	3.50	2	0	−0.09	....
				+1.01	−0.62

[a] Other data required for the calculations: van der Waals radii; C = 1.70 Å., H = 1.20 Å., ϵ = 42 cal./mole (H–H repulsion); ϵ = 67 cal./mole (C—H repulsion) and ϵ 107 cal./mole (C–C repulsion). These quantities are either those of Hill,[7] or from unpublished work of the authors.

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[1] Paper XXVII, N. L. Allinger and H. M. Blatter, *J. Org. Chem.*, **27**, 1523 (1962).

[2] This work was supported by the U. S. Army Research Office under Grant Number DA-20-018-ORD 22743.

[3] P. A. Robins and J. Walker, *Chemistry & Industry*, 772 (1955); *J. Chem. Soc.*, 1789 (1955); 3960 (1954).

[4] W. Klyne, *Experientia*, **12**, 119 (1956).

[5] N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, **83**, 994 (1961).

[6] (a) N. L. Allinger, J. Allinger, L. A. Freiberg, R. Czaja and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960); (b) N. L. Allinger and W. Szkrybalo, *J. Org. Chem.*, **27**, 722 (1962).

[7] T. L. Hill, *J. Chem. Phys.*, **16**, 399 (1948).