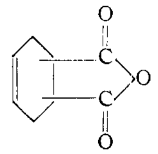
[CONTRIBUTION FROM THE B. F. GOODRICH RESEARCH CENTER]

The Diels–Alder Reactions of the Piperylene Isomers with Maleic Anhydride and Fumaric Acid

BY DAVID CRAIG

The "accumulation of unsaturation" rule[1,2] (Alder Rule II of the diene synthesis) seems not to have been applied to the *cis-* and *trans*-piperylene isomers[3] as dienes, and maleic anhydride as the dienophile. The rule, originally intended for cyclic dienes, has recently been extended to certain vinyl naphthalenes.[4] Its application to the piperylene–maleic anhydride reactions, which is the subject of this paper, obviously requires a knowledge of the configurations of the four 3-methyl-1,2,3,6-tetrahydrophthalic anhydrides.[5]

The *trans*-piperylene–maleic anhydride adduct (m. p. 63°) which is formed in nearly theoretical yield when prepared in the presence of picric acid according to Frank, Emmick and Johnson[6] has been found to undergo rearrangement to form a new anhydride (m. p. 41°). This arrangement is effected by small amounts of dibutylaniline, is reversible and reaches about 80% conversion during ten minutes at 280°. In contrast II and III, the adducts, respectively, of butadiene and isoprene, appear to undergo no such change but inspection of the formulas for these substances shows that no methyl group "tags" the upper or lower side of these molecules in the sense that a *cis*-methyl group tags one side of structure I. Hence the inversion of carbon atoms 1 and 2 cannot be detected by the structure of the products isolated after treatment with dibutylaniline.



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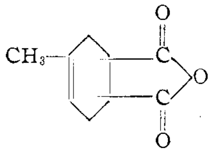
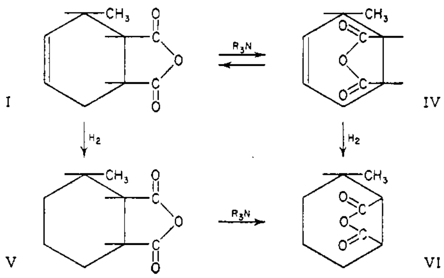


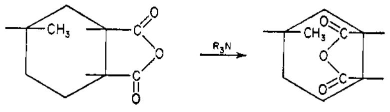
III

The study of formulas I to VI in connection with the general behavior of *cis–trans* isomers and cyclic anhydrides suggests that the rearrangement of the maleic anhydride adduct of *trans*-piperylene involves an inversion of I into IV. This interrelationship is supported by the synthesis of IV by the reaction of *cis*-piperylene with maleic anhydride and further support is found by the hydrogenation of the adduct I (m. p. 63°) since the reduced adduct (an oil) on treatment with dibutylaniline formed a product (m. p. 70°) identical with that secured by treating first with dibutylaniline and then hydrogenating. This series of reactions is shown by the scheme



Evidence that formula I actually represents the *trans*-piperylene adduct and IV the *cis*-piperylene adduct is the finding of Meek and Ragsdale[7] that *trans*-piperylene adducts with other dienophiles are *cis* and further that the *cis* form is the less stable and rearranges readily to the *trans* isomer.

Next it was found that the hydrogenation of the isoprene–maleic anhydride adduct III formed two isomeric dihydro derivatives. The one formed in larger amount was unstable in the presence of dibutylaniline and rearranged to the second. The one formed in smaller amount, unlike the other, was stable in the presence of tertiary amine. A study of the Fischer–Hirschfelder–Taylor scale model of III shows that hydrogenation, a *cis* reaction, would preferably form *cis*-4-methyl-*cis,cis*-heaxhydrophthalic anhydride VII because of steric hindrance of the anhydride ring to the formation of the *trans*-methyl isomer. Anhydride VII, by comparison to a number of well studied *cis* configurations[8] would be expected to be unstable compared to the *trans*-4-methyl-*cis,cis*-hexahydrophthalic anhydride VIII. On this basis the *trans,cis,cis* formula VIII is assigned to the stable reduced isoprene adduct, and the *cis,cis,cis* structure VII to the unstable isomer. As expected,



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(1) Norton, *Chem. Reviews*, **31**, 496 (1942).

(2) Kloetzel, "Organic Reactions," edited by Adams, John Wiley & Sons, New York, N. Y., 1948, Vol. IV, p. 1.

(3) Craig, THIS JOURNAL, **65**, 1006 (1943).

(4) Bachmann and Chemerda, *ibid.*, **70**, 1468 (1948).

(5) Arnold and Coyner, *ibid.*, **66**, 1542 (1944), found that certain 1-arylbutadiene adducts had the *cis,cis,cis* configuration.

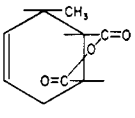
(6) Frank, Emmick and Johnson, *ibid.*, **69**, 2315 (1947).

(7) (a) Meek and Ragsdale, *ibid.*, **70**, 2502 (1948); (b) Meek, Lorenzi and Cristol, *ibid.*, **71**, 1830 (1949); (c) Ropp and Coyner, *ibid.*, **71**, 1832 (1949); (d) Reich and Becker, *ibid.*, **71**, 1834 (1949).

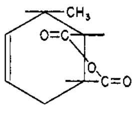
(8) Marvel, in Gilman's "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1943, pp. 450–454, discussed several pairs of open-chain *cis–trans* isomers which illustrate the rule that a hydrocarbon group *trans* to a carbonyl group confers greater stability than the same group *cis* to the carbonyl group. In the alicyclic series a similar rule seems to apply. Thus *cis*-hexahydro-*p*-toluic acid is more unstable than *trans*, according to Delépine and Bodoche (*Ann. chim.*, **17**, 179 (1942)) and the rearrangement of *cis* Diels–Alder adducts to the *trans* forms has been recorded by several workers; compare references 4 and 7.

cis-hexahydrophthalic anhydride failed to rearrange with dibutylaniline.

The base catalyzed inversions of I undoubtedly proceed through the intermediate *trans* anhydrides. Both of these were formed from both piperylenes by reaction with fumaric acid in acetic anhydride solution. Under the conditions used acetic anhydride, though it reacts with fumaric acid to form mixed anhydrides, does not effect the formation of maleic anhydride. From *trans*-piperylene the crude anhydride reaction product melted at 104–105° and consisted of about three parts of one isomer (m. p. 121°) and one part of the other (m. p. 133°). From *cis*-piperylene the crude mixture (m. p. about 108°) of anhydrides contained about one part of the 121° melting isomer to three of the 133° melting isomer. Mixtures of the two anhydrides appear to form mixed crystals and are difficult to separate. On the basis of Meek's[7] studies of *trans*-piperylene with open-chain dienophiles as well as our own work with fumaric acid and maleic anhydride with both piperylenes, it seems likely that the 121° melting anhydride has the methyl group *ortho* and *cis* to one of the carbonyl groups. Therefore, structure IX is assigned to it and X is assigned to the 133° melting adduct. Both of the anhydrides rearranged to IV when they were heated with dibutylaniline as did I.



IX



X

A controlling factor in such rearrangements appears to be the greater stability of the *cis* anhydride structure in comparison to that of the *trans*.[9] Another factor, based on general experience with geometric isomers,[8] is that greater stability is achieved by having the methyl group *trans* rather than *cis* to a carboxyl group.

It is often found that *cis* and *trans* isomers can coexist[8] in equilibrium with each other. In the present work an equilibrium mixture which was approachable from either side was found to contain about 80% of IV and 20% of I. Further study may show that the rearrangements of V and VII also lead to mixtures containing minor amounts of *cis,cis,cis* isomers. It is also reasonable to suspect the presence of only very small amounts of *trans* anhydride isomers in such rearrangements.

The four possible piperylene adducts having thus been synthesized and configurations assigned to each, we may examine the Alder rules. This is facilitated by use of scale models with which it can be seen that the configurations independently assigned to the adducts are those predicted from these rules, provided that the hyperconjugation of the methyl group with the diene system in piperylene is considered as unsaturation to be accumulated in the Alder complex. Concordance with Rule II is evident even though three of the adducts, I, IX and X, are unstable with respect to the fourth, IV. This concordance is especially convincing in the case of the maleic anhydride reactions. Thus, IV was secured as the expected isomer by the reaction of *cis*-piperylene with maleic anhydride. The formation of the two *trans* adducts from each of the two dienes and fumaric acid indicates that with each diene there are two orientation complexes having nearly the same accumulation of unsaturation. This is clearly analogous to the formation of *exo* and *endo* isomers from certain cyclic dienes[2] and is suggested by models of probable complexes. The orientation complexes from *cis*-piperylene cannot be planar because of the steric hindrance to the formation of the *cis*oid[8] form of this diene. Probably for this reason the diene reactions with it are slow, but there is no doubt now that they occur.

We were led to test the effects of organic bases on the structure of Diels–Alder adducts during an earlier study of the effects of low concentrations of bases such as diamylamine and dibutylaniline on the rate[10] of reaction in diene analysis. In this work these bases had no measurable qualitative effect on the rate of reaction of butadiene or of *trans*-piperylene with maleic anhydride at 50 to 100°. Also, it appeared that *cis*-piperylene did not become reactive in the presence of dibutylaniline. The reaction of the *trans* isomer appears to be purely stereoselective and to be uncatalyzed.

Acknowledgment should be made to E. W. D. Huffman and J. R. Kubik for microanalyses and to A. K. Kuder for some of the hydrogenations. Thanks are also due W. L. Semon, J. E. Jansen and S. J. Averill for several helpful discussions.

Experimental

The anhydrides in this series of compounds sometimes formed mixed crystals or were liquids not easily characterized. The corresponding acids were solids and in all such cases were used for identification of the anhydrides.

1,2,3,6-Tetrahydro-*trans*-3-methyl-*cis,cis*-phthalic Anhydride, IV.—Thirty-three and two-tenths grams (0.2 mole) of the *trans*-piperylene adduct I prepared according to Frank, *et al.*,[6] was heated with 0.33 g. of dibutylaniline for four hours at 175°. Ten minutes at 280° also seemed satisfactory. The reaction mixture was found to melt at about 30°. It was distilled at 4 mm. pressure. After a small forerun 27 g. (81%) distilled at 122–134°. This fraction melted at 35–38°. A viscous residue of 3.3 g. was obtained. The distilled anhydride was analyzed though it was known to be a mixture.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.14, 65.06; H, 6.10, 6.06.

The anhydride (5.9 g.) was boiled with 35 ml. of water for fifteen minutes and cooled. Crystals appeared which were filtered off and washed with water, giving a yield of 4.4 g. (68% on the rearranged anhydride or 54% on adduct I), m. p. 161–162° or 135–140° mixed with the acid similarly obtained by the hydrolysis of I.

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.66; H, 6.57. Found: C, 58.73, 58.74; H, 6.61, 6.54.

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(9) Hückel and Goth, *Ber.*, **58**, 447 (1925).

(10) Compare Woodward, THIS JOURNAL, **64**, 3058 (1942).

The distillation at atmospheric pressure of a mixture of 9.2 g. of the acid, m. p. 161–162°, with 18 g. of acetic anhydride produced acetic acid and a residue which was distilled at 5 mm. The main fraction, Compound IV, amounted to 7.8 g. (94%) of a solid, m. p. 40–41°. The m. p. was not changed by crystallization from cyclohexane and was depressed by admixture with I.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.93, 64.89; H, 6.26, 6.16.

A similar distillation with acetic anhydride of the acid, m. p. 156–158°, from I reformed the anhydride in nearly theoretical yield.

The filtrate from the acid of m. p. 161–162° by careful evaporation yielded the acid m. p. 156–158° corresponding to anhydride I. The complete working up of the rearrangement mixture yielded the two acids in the ratio of five parts of the higher melting isomer to one of the lower melting. The two acids were similarly isolated in the same ratio from mixtures prepared by heating IV with dibutylaniline.

Anhydride IV from *cis*-Piperylene and Maleic Anhydride.—The *cis*-piperylene[3] used in this preparation had been treated with cuprous chloride, then fractionated, refluxed with maleic anhydride, then refractionated and treated again with cuprous chloride and finally refluxed again with maleic anhydride. The b. p. at 745 mm. was 43.2° and the refractive index $n^{20}D$ 1.4366. The corresponding values for a Bureau of Standards standard sample containing 0.08 mole % impurity when measured in the same apparatus were 43.2° and 1.4370. According to J. J. Shipman of this Laboratory the infrared spectra of the two samples were essentially identical between two and sixteen microns. The sample used was believed to be nearly free of the *trans* isomer.

cis-Piperylene, 2.04 g. (0.03 mole), maleic anhydride, 2.94 g. (0.03 mole) and 15 g. of acetic anhydride were heated at 94–100° during eight hours. During this period much polymeric material formed and the piperylene was nearly used up. The acetic anhydride and most of the unreacted maleic anhydride were removed at reduced pressure. Evaporative distillation[4] provided a distillate of 0.34 g. (m. p. 0 to 10°) which was boiled with water. The hydrolysate was concentrated until crystallization took place. The first crop of crystals weighed 0.19 g. These melted at 160–162° alone or when mixed with the acid from IV. The second crop weighed 0.05 g. and melted at 148–150° dec. alone or mixed with maleic acid. The total yield of the acid of IV was 0.22 g. or 4%.

Hexahydro-*cis*-3-methyl-*cis*,*cis*-phthalic Anhydride, V.—The adduct I, 31.2 g. (0.188 mole), dissolved in 75 ml. of ethyl acetate absorbed 0.20 mole of hydrogen during thirty-five minutes at 3 atmospheres pressure and at 25°. The catalyst was 5 g. of Raney nickel which had been washed with alcohol and then with ethyl acetate. The catalyst was filtered off and the reaction mixture distilled at 0.2 mm. The yield of oil (V) distilling at 105–125° was 27.3 g. (86%).

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.25; H, 7.19. Found: C, 64.18; H, 7.01.

Anhydride V hydrolyzed in contact with water with great speed compared to the other anhydrides in this series to form the expected dibasic acid. The yield after crystallization from water and washing with a benzene–cyclohexane mixture amounted to 91%. This acid was also prepared in nearly theoretical yield by hydrogenating the acid corresponding to I in acetic acid over PtO_2. It melted at 169–170°.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.03; H, 7.55. Found: C, 58.02; H, 7.46.

Hexahydro-*trans*-3-methyl-*cis*,*cis*-phthalic Anhydride, VI.—Crude anhydride IV, under the hydrogenation conditions used for V absorbed nearly an equimolar amount of hydrogen at about the same rate as compound I. The yield of product which distilled at 100–122° at 0.2 mm. amounted to 83%. It crystallized nicely from cyclohexane. A 67% yield of colorless crystals of VI melting at 70° was isolated. The same product was secured in 68% yield by heating 5.0 g. of V with 0.05 g. of dibutylaniline to reflux at 290–292° for ten minutes.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.25; H, 7.19. Found: C, 64.33; H, 7.26.

The dibasic acid corresponding to VI was formed in nearly theoretical yield by boiling a mixture of VI and water as well as by hydrogenating the dibasic acid of IV in acetic acid over PtO_2. It melted at 129° when crystallized from water.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.03; H, 7.55. Found: C, 58.14; H, 7.57.

Hexahydro-*cis*-4-methyl-*cis*,*cis*-phthalic Anhydride, VII.—This was obtained in admixture with minor amounts of the isomeric *trans*-4-methyl anhydride VIII by the hydrogenation of III under the conditions used for hydrogenating I except that PtO_2 was used in place of nickel. Raney nickel was tried but gave an impure product and caused the slow absorption of less than the expected amount of hydrogen. PtO_2 in contrast caused the expected amount of hydrogen to be taken up in fifteen minutes. A 90% yield of product, b. p. 125–128° at 6 mm. was secured.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.25; H, 7.19. Found: C, 64.42; H, 7.11.

This anhydride (mostly VII) was hydrolyzed by boiling with a small amount of water for fifteen minutes. Enough alcohol to make the solvent 50% alcohol was added. By careful cooling and evaporation to secure successive crops of crystals, the hydrolyzate was separated into a mixture of seven parts of an acid melting at 173–175° with decomposition to three parts of one melting at 175–177°. The higher melting acid is described more completely below. The lower melting acid corresponds to VII.

Anal. Calcd. for $C_{19}H_{14}O_4$: C, 58.03; H, 7.55. Found: C, 58.09; H, 7.57.

Hexahydro-*trans*-4-methyl-*cis*,*cis*-phthalic Anhydride, VIII.—This compound was prepared by heating the above acid (2.00 g.) in the presence of 0.02 g. of dibutylaniline to just above the m. p. to split out water and then heating the mixture to 280–290° for ten minutes to effect the rearrangement. The mixture was distilled at 0.2 mm. to provide 1.34 g. (50%) of an oil, VIII. This oil (0.81 g.) when titrated with 1 *N* sodium hydroxide required 9.1 ml. (calcd. 9.65 ml.). The titration solution was acidified and the crystals which came down were filtered off and dried; yield 0.64 g. (72%). The crystals (the acid of compound VIII) melted at 177–179° with decomposition or at 165–170° when mixed with the starting acid.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.03; H, 7.55. Found: C, 58.15, 58.13; H, 7.61, 7.58.

1,2,3,6-Tetrahydro-*cis*-3-methyl-*cis*,*trans*-phthalic Anhydride, IX.—Fumaric acid (5.8 g., 0.05 mole), 25 ml. of acetic anhydride and 4.00 g. (0.059 mole) of pure *trans*-piperylene were refluxed for one and one-half hours. During this period the fumaric acid dissolved and the temperature rose from 70 to 130°. Distillation at 15 mm. produced an acetic acid–acetic anhydride fraction followed by 8.2 g. (99%) of a fraction which came over at 150° and which melted at 104–105°. Crystallization from hexane containing a little benzene produced 7.1 g. of colorless needles, m. p. 105–106°.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.11; H, 6.09.

This product appeared homogeneous under the microscope and the melting point was not raised by crystallization from alcohol or cyclohexane. However, hydrolysis with water or dilute alkali led to a mixture of acids. One of these was isolated in about 30% yield by crystallization from benzene. It melted at 156–158° and strongly depressed the melting points of the acids from I and IV.

Anal. Calcd. for $C_9N_{12}O_4$: C, 58.66; H, 6.57. Found: C, 58.71; H, 6.57.

This acid was refluxed for a few minutes with excess acetic anhydride which was then removed along with acetic acid in a stream of nitrogen. The residue crystallized from cyclohexane as needles of IX, m. p. 120–121°.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.04; H, 6.07.

Mixtures of these needles with those melting at 105–106° melted between 106 and 121°. The 105–106° melting needles thus appear to be mixed crystals containing IX.

1,2,3,6-Tetrahydro-*cis*-3-methyl-*trans,cis*-phthalic Anhydride, X.—The mother liquor from the needles melting at 105–106° was concentrated and crystallized from hexane. In this way 0.53 g. of fine needles was secured which melted at 125–126°. This product appeared homogeneous. Titration of 0.4753 g. required 5.67 ml. (calcd. 5.73 ml.) of 1 *N* sodium hydroxide. The titration solution was acidified with 0.5 ml. of concd. hydrochloric acid and the mixture extracted with ether. The ether layer was evaporated and the residue crystallized from benzene. In this way 0.38 g. (72%) of crude acid, m. p. 115–120°, was obtained. Recrystallization from benzene gave a colorless product, m. p. 127–128°.

Anal. Calcd. for $C_9H_{12}O_4$: C, 58.66; H, 6.57. Found: C, 58.82; H, 6.57.

Cyclizing this acid with acetic anhydride gave needles melting at 133°, believed to be pure X. Mixtures with 125–126° melting needles all melted between 126 and 133°.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.11; H, 6.09.

The product melting at 125–126° thus indicated to be mixed crystals containing X and, presumably, IX was also prepared in 1% yield by the reaction of pure *cis*-piperylene (4.5 g.), fumaric acid (5.8 g.) and 25 g. of acetic anhydride at 100–124° during twenty-four hours. The volatile product m. p. about 108° was separated from the polymeric materials by sublimation at 0.15 mm. The only product isolated was that melting at 125–126° though small amounts of unidentified substances were present.

Isomerization of IX and X.—These anhydrides when heated to 280° with traces of dibutylaniline rearranged as did I to form a mixture of I and IV. Hydrolysis of this mixture yielded the acids, melting at 156–158° and 161–162°, respectively. Anhydrides IX and X also isomerized merely by heating. Thus during ten minutes at 150° the melting point of IX dropped 16° and that of X dropped 12°. Similar treatment of I resulted in no change in the melting point. In view of the tendency of IX and X to isomerize it is somewhat surprising that they could withstand distillation. Therefore, a repetition of the reaction (this time conducted for six hours at 78–94°) of *trans*-piperylene, fumaric acid and acetic anhydride was run. Low pressure evaporation of the acetic anhydride provided the theoretical yield of crude anhydride, m. p. 105–106°. This was fractionally crystallized from mixtures of benzene and cyclohexane. The higher melting anhydride is much more soluble in these solvents than the other isomer and benzene is a much better solvent for both of them than is cyclohexane. The highest melting point for a sample rich in IX was 115° (or at 117–119° mixed with IX) and this was from pure benzene. Similarly the highest melting point for a fraction rich in X was 126° (or at 128–130° mixed with X) and this was from pure cyclohexane. Only a trace of material melting below 100° was secured after 4 stages of the fractionation. Mixtures of IX with X melted at about 104–108° over a wide range of intermediate concentrations.

Summary

1. The well-known maleic anhydride adduct of *trans*-piperylene, m. p. 63°, was found to have the *cis,cis,cis* configuration.
2. The two *trans* anhydride isomers, m. p. 121° and 133°, were both synthesized by the reaction of the *trans* diene with the *trans* dienophile fumaric acid. The higher melting anhydride corresponds to *cis*-piperylene from which it was also prepared.
3. These three anhydrides rearrange in the presence of an organic base to the fourth possible racemic anhydride, m. p. 41°, which was also synthesized by the reaction of *cis*-piperylene with maleic anhydride.
4. The configuration of the Diels–Alder adducts reported on were found to be those predicted on the basis of Alder Rules I and II.
5. *cis*- and *trans*-3-methyl and *cis*- and *trans*-4-methylhexahydro-*cis,cis*-phthalic anhydrides were synthesized.

BRECKSVILLE, OHIO RECEIVED MAY 16, 1949

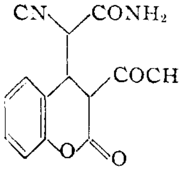
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Condensations of 3-Acetocoumarin with Amides, and with Amides and Ketones[1]

BY C. F. KOELSCH AND S. A. SUNDET

Contrary to expectation and to published report,[2] 3-acetocoumarin does not react with cyanoacetamide to yield a normal Michael product (I) or the cyclized anhydro-derivative (II) of such a substance. Instead, two molecules of 3-acetocoumarin unite with a molecule of ammonia furnished by the amide to form III.

No plausible reason can be advanced for the preferential reaction of the acceptor (3-acetocoumarin) with the ketonic addendum (3-acetocoumarin), rather than with cyanoacetamide acting as an addendum.[3] But such preference appears to be characteristic. When 3-acetocoumarin is treated with cyanoacetamide and a different ketonic addendum, the latter substance



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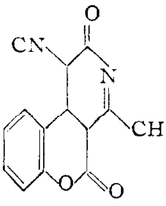
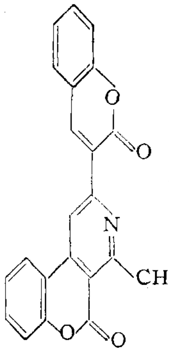


II



III

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[1] From the Ph.D. Thesis of Sherman A. Sundet, June 1948.

[2] Sastry and Seshadri, *Proc. Indian Acad. Sci.*, **16A**, 29 (1942).

[3] Speculations regarding this and other phases of the mechanism of the reaction are found in Dr. Sundet's Thesis.