chlorobenzene was refluxed (124°) under nitrogen for 12 hr. Upon cooling, 17.5 g. of fine, snow white crystals of *meso*-1,2-dichlorostilbene[28] separated and were isolated (m.p. 193–194). Upon evaporation of the solution to one half its original volume and chilling, a further 8.5 g. of this compound were obtained. The remaining solution was evaporated to dryness and the residue was recrystallized from petroleum ether to yield 4.0 g. of *dl*-1,2-dichlorostilbene[28] (m.p. 90–91°).

Chlorination of Cumene.—A solution of cumene (240 g., 2 moles) and PCl_5 (208 g., 1 mole) was stirred and refluxed (110°) under nitrogen for 14 hr. Hydrogen chloride was rapidly evolved during this period. After washing with water and $NaHCO_3$ solution, the clear yellow solution which was obtained as distilled through a short packed column. There was obtained 44 g. (28.5%) of phenyldimethylcarbinyl chloride, b.p. 95–96° (15 mm.). N.m.r. showed a sharp singlet at τ 8.22; ratio of aliphatic protons to aromatic protons 6:5. There was also obtained 95 g. of a substance boiling mainly at 120–135° (15 mm.). This colorless liquid showed greatly diminished methyl peaks in its n.m.r. and infrared spectra as well as evidence in the former for $-CH_2Cl$ groups and small amounts of vinyl protons. It was not investigated further. These results were essentially reproducible. From the relative retention times in the v.p.c. analysis it was estimated that a mixture of di- and tri-chlorinated products had been formed.

Catalyzed Chlorination of Cyclohexane.—A mixture of cyclohexane (84 g., 1 mole) and PCl_5 (70 g., 0.33 mole) in 200 cc. of *o*-dichlorobenzene was refluxed (88°) under nitrogen for 7 hr. Small quantities of benzoyl peroxide were added periodically during this time and HCl was evolved. After cooling, the reaction mixture (which was a light yellow color at this point) was poured onto ice water. The organic layer was separated, washed consecutively with water and 5% $NaHCO_3$ solution, and then dried over anhydrous $CaCl_2$. Analysis by v.p.c. indicated a 70.2% yield of cyclohexyl chloride had been formed (based on PCl_5).

Acknowledgment.—We wish to thank Mr. Carl Lindemann for the gas chromatographic analyses and Mr. Paul Kaufman who helped with some of the experimental work.

The Reaction of Ethyl Azodicarboxylate with Conjugated Dienes. II[1,2]

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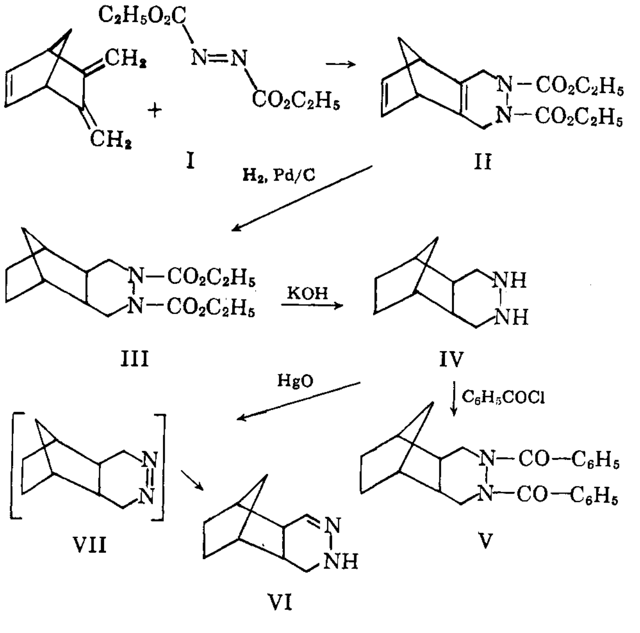
Further investigations of the reaction of ethyl azodicarboxylate (I) with conjugated dienes have been performed. The reaction of I with 5,6-dimethylenebicyclo[2.2.1]hept-2-ene gave the Diels–Alder adduct 1,2-dicarbethoxy-7,10-methano-1,2,3,6,7,10-hexahydro-4,5-benzopyridazine in 80% yield. Addition of I to bi(1-cyclohexen-1-yl) produced 1,2-dicarbethoxy-3,4,5,6-bis(tetramethylene)-1,2,3,6-tetrahydropyridazine in 80% yield. Treatment of 2,4-dimethyl-1,3-pentadiene with I proceeded by a concerted cyclic mechanism to give a mixture of isomers, 1,2-dicarbethoxy-1-[1-(4-methyl-2-methylene-3-pentenyl)]hydrazine (78.5%) and 1,2-dicarbethoxy-1-[3-(2,4-dimethyl-1,4-pentadienyl)]hydrazine (21.5%). The proofs of structure on the latter compounds were accomplished by instrumental methods and chemical degradation.

In a previous report from this laboratory,[2] it was shown that ethyl azodicarboxylate added to simple conjugated dienes by Diels–Alder or 1,4-addition, whereas, with more highly substituted conjugated dienes addition occurred by a different mechanism with a shift of the double bond.[2,4] The present report describes the results of an extension of these studies to other conjugated diene systems.

The addition of ethyl azodicarboxylate (I) to 5,6-dimethylenebicyclo[2.2.1]hept-2-ene took place with an evolution of heat and gave an 80% yield of the Diels–Alder adduct, 1,2-dicarbethoxy-7,10-methano-1,2,3,6,-7,10-hexahydro-4,5-benzopyridazine (II). The adduct II was hydrogenated over palladium-on-charcoal catalyst in ethanol to form 1,2-dicarbethoxy-7,10-methanodecahydro-4,5-benzopyridazine (III) in 82% yield. Hydrolysis of III was accomplished by refluxing in ethanolic potassium hydroxide solution for 11.5 hours. The cyclic hydrazine, 7,10-methanodecahydro-4,5-benzopyridazine (IV), was thus obtained in 84% yield. The dibenzoyl derivative of IV, 1,2-dibenzoyl-7,19-methanodecahydro-4,5-benzopyridazine (V) was prepared in 80% yield. Oxidation of IV was performed under a nitrogen atmosphere using yellow mercuric oxide in anhydrous ether. The only compound isolated was the cyclic hydrazone, 7,10-methano-Δ^2-octahydro-4,5-benzopyridazine (VI) in 63.5% yield, which was characterized by its infrared and ultraviolet spectra. The isolation of VI indicated that the azo compound VII had probably formed, but facile isomerization to the more stable structure VI, had taken place under the reaction conditions.



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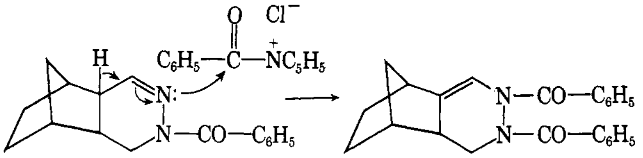
[1] This research was carried out under Grant No. 17836 from the National Science Foundation, whose support is gratefully acknowledged.

[2] For the previous report on this topic see B. T. Gillis and P. E. Beck, *J. Org. Chem.*, **27**, 1947 (1962). The literature pertinent to this subject and leading references to prior investigations can be found in this reference.

[3] Abstracted in part from a thesis by P. E. Beck submitted in partial fulfillment of the requirements for the degree Doctor of Philosophy, to Duquesne University, June, 1963.

[4] B. Franzus and J. H. Surridge, *J. Org. Chem.*, **27**, 1951 (1962).

Preparation of the benzoyl derivative of VI was attempted in pyridine. Instead of the desired monobenzoyl derivative, a compound was isolated, m.p. 179–180°, whose analysis corresponded to $C_{23}H_{22}N_2O_2$. The infrared spectrum of the compound was undefinitive except that it showed no N–H band, and a benzoyl type of carbonyl peak was present. The compound discolored permanganate and absorbed bromine. Further, it easily absorbed one molar equivalent of hydrogen catalytically to produce V. Thus, this compound was formulated as 1,2-dibenzoyl-7,10-methano-Δ^3-octahydro-4,5-benzopyridazine (VIII), which could arise by the following mechanism.

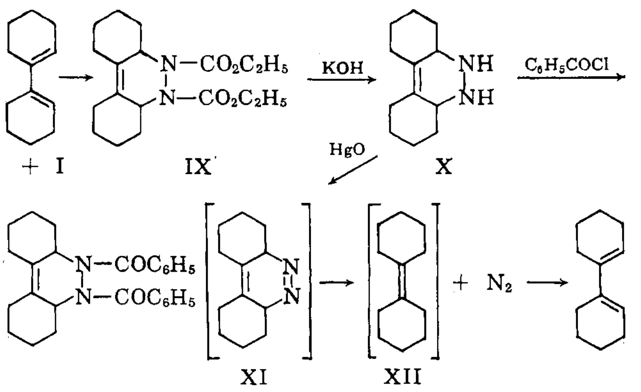


VIII

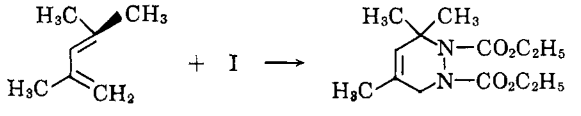
Ethyl azodicarboxylate reacted smoothly at room temperature with the more complex diene, bi(1-cyclohexen-1-yl) to form the Diels–Alder adduct, 1,2-dicarbethoxy-3,4,5,6-bis(tetramethylene)-1,2,3,6-tetrahydropyridazine (IX), in 87% yield. Attempted hydrogenation of IX to the saturated adduct with a variety of catalysts failed and starting IX was reisolated. Other workers[5-7] have found that similar Diels–Alder adducts with this diene also failed to undergo hydrogenation. The failure was attributed to the "blocking effect of the cyclohexane rings on the olefinic linkage. . . .".[5]

The adduct IX was hydrolyzed with potassium hydroxide in refluxing ethylene glycol and gave 66% of the theoretical amount of cyclic hydrazine 3,4,5,6-bis(tetramethylene)-1,2,3,6-tetrahydropyridazine (X). A 78% yield of the dibenzoyl derivative of X was obtained. Oxidation of X was accomplished using yellow mercuric oxide in anhydrous ether. Nitrogen gas was evolved from the oxidation mixture and the only product isolated was the starting diene, bi(1-cyclohexen-1-yl), in 73% yield.

These results indicated that the oxidation of X formed the cyclic unstable azo compound XI, which evolved nitrogen possibly through the biradical XII. However, XII collapsed to the more stable diene by radical shift rather than by closure to the carbocyclic system. Thus, for the synthesis of carbocyclic systems, it appears imperative to use a saturated cyclic hydrazine in the oxidation step.

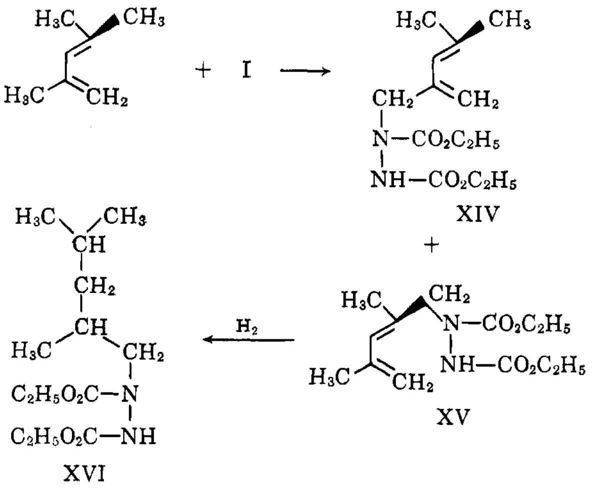


Diels, Blom, and Koll[8] have reported that I, when added to 2,4-dimethyl-1,3-pentadiene, yielded the Diels–Alder adduct, N,N′-dicarbethoxy-3-dimethyl-5-methyltetrahydropyridazine (XIII). Bromine addition to the product furnished resinous material; however, the proposed adduct was not characterized to any further extent.



XIII

Levina, *et al.*,[9] have published a report stating that the reaction of I with 2,4-dimethyl-1,3-pentadiene resulted in a mixture of isomers, 1,2-dicarbethoxy-1-[1-(4-methyl-2-methylene-3-pentenyl)]hydrazine (XIV) and 1,2-dicarbethoxy-1-[1-(2,4-dimethyl-2,4-pentadienyl)]hydrazine (XV). Hydrogenation of this mixture purportedly gave rise to a single product, 1,2-dicarbethoxy-1-(2,4-dimethyl-*n*-pentyl)hydrazine (XVI). These Russian workers assumed that the adduct (isomer mixture XIV and XV) arose from radical addition but presented no supporting evidence or definitive structure proof.



Thus, a reinvestigation of this diene system was undertaken in order to clarify the addition of I to 2,4-dimethyl-1,3-pentadiene and to prove rigorously the structure of the product or products.

In this laboratory, when I was mixed with 2,4-dimethyl-1,3-pentadiene in benzene solution, adduct formation took place with an evolution of heat and an 87% yield of purified product was isolated. The infrared spectrum of this product showed bands at 2.90 μ (N–H), and in the carbonyl region at 5.70–5.80 μ (shoulder) and at 5.85 μ. The ultraviolet spectrum of this material exhibited a maximum at 232 mμ (ϵ 6800) which indicated that the product contained 80% of a highly substituted conjugated diene. Gas chromatography showed the product was actually a mixture of two products with the composition of 21.5 and 78.5%,

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(5) N. L. Drake and C. N. Kraebel, *J. Org. Chem.*, **26**, 41 (1961).

(6) F. Bergman, H. Eschinazi, and M. Neeman, *ibid.*, **8**, 185 (1943).

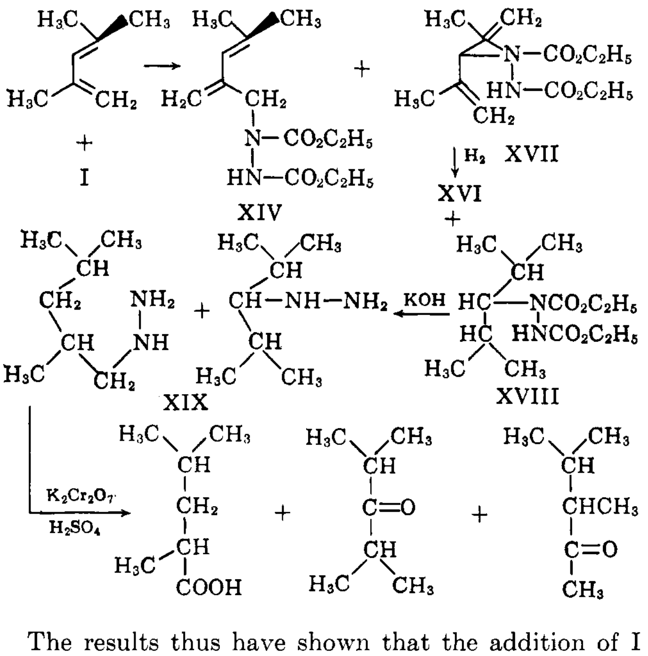
(7) K. Alder, H. Rickert, and E. Windemuth, *Ber.*, **71**, 2451 (1938).

(8) O. Diels, J. H. Blom, and W. Koll, *Ann.*, **443**, 242 (1925).

(9) R. Y. Levina, U. S. Skabarow, and M. H. Kuzmin, *Dokl. Akad. Nauk SSSR*, **131**, 1080 (1962).

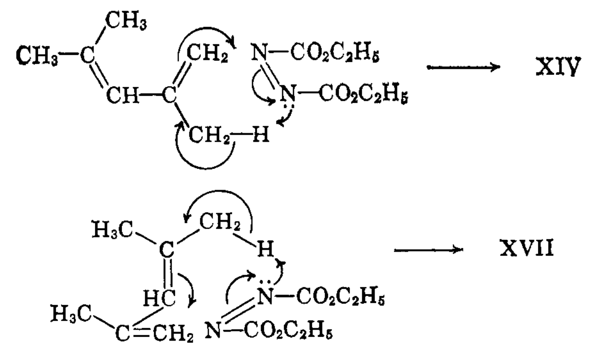
respectively. Assignment of the structures to these products as XIV, the 78.5% component, and 1,2-dicarbethoxy-1-[3-(2,4-dimethyl-1,4-pentadienyl)]hydrazine (XVII), the 21.5% component was made on the basis of the ultraviolet data and the ensuing evidence. The isomer mixture, XIV and XVII, absorbed two molar equivalents of hydrogen to furnish a 90.5% yield of product. Gas chromatography of the latter material showed that the composition was 14% of 1,2-dicarbethoxy-1-[3-(2,4-dimethyl-*n*-pentyl)]hydrazine (XVIII) and 86% of XVI. Hydrolysis of the saturated mixture (XVIII and XVI) with potassium hydroxide in refluxing ethylene glycol furnished an 82.5% yield of the alkyl hydrazine mixture XIX. The mixture was oxidized with potassium dichromate in dilute sulfuric acid solution. From the acidic fraction of the oxidation mixture, 2,4-dimethylpentanoic acid was isolated and characterized as the amide.

The neutral fraction of the oxidation mixture was subjected to gas chromatography. This analysis showed that besides peaks due to ether and water, two other components were present in a ratio of 21.7 to 78.3%. An authentic sample of diisopropyl ketone had the same retention time as the former component. That the latter peak was due to 3,4-dimethyl-2-pentanone was determined from chemical evidence. The neutral fraction gave a positive iodoform test. A semicarbazone derivative was prepared and corresponded to 3,4-dimethyl-2-pentanone. The fact that 3,4-dimethyl-2-pentanone was found in the reaction mixture was consistent with prior observations. Fry[10] has reported that diisopropyl ketone, when subjected to acid conditions, undergoes rearrangement to 3,4-dimethyl-2-pentanone.



The results thus have shown that the addition of I to 2,4-dimethyl-1,3-pentadiene took place by a route other than the Diels–Alder reaction, namely by the cyclic mechanism already postulated.[2] (See col. 2.)

Because of the structural nature of this diene, its reaction with I led to two addition products. The cyclic mechanism proceeded with a shift of the double bond; however, even with the double bond shift, the major product retained conjugation. The high percentage of this product can be easily rationalized on the basis of steric factors.



That the addition of I to 2,4-dimethyl-1,3-pentadiene took place by the cyclic mechanism and not by free-radical addition was substantiated by the fact that when the reaction was carried out in the presence of a free-radical inhibitor, hydroquinone, the course of the reaction remained unchanged. The adduct exhibited the same infrared and ultraviolet spectra as the product which was obtained without the inhibitor. The adducts that formed under both conditions also had identical gas chromatograms.

Experimental[11]

1,2-Dicarbethoxy-7,10-methano-1,2,3,6,7,10-hexahydro-4,5-benzopyridazine (II).—To 8.0 g. (0.068 mole) of 5,6-dimethylenebicyclo[2.2.1]hept-2-ene[12] was added 8.7 g. (0.05 mole) of ethyl azodicarboxylate (I).[13] The slightly yellow crude product was distilled and gave 11.59 g. (80%) of the colorless liquid II, b.p 138–140° (0.26 mm.), $n^{26}\text{D}$ 1.4668, d^{25} 1.1673.

Anal. Calcd. for $C_{15}H_{20}N_2O_4$: C, 61.63; H, 6.90; N, 9.59. Found: C, 61.51; H, 7.10; N, 9.67.

1,2-Dicarbethoxy-7,10-methanodecahydro-4,5-benzopyridazine (III).—The adduct II, (17.0 g., 0.058 mole) was hydrogenated over 0.7 g. of 10% palladium on charcoal in 120 ml. of ethanol at 59 p.s.i. on a Parr apparatus. Two molar equivalents of hydrogen were absorbed. The solution was filtered and the ethanol was removed under vacuum. The residual liquid was distilled and yielded 14.13 g. (82%) of III, b.p. 151° (0.32 mm.), $n^{26}\text{D}$ 1.4930, d^{25} 1.1492.

Anal. Calcd. for $C_{15}H_{24}N_2O_4$: C, 60.79; H, 8.16. Found: C, 60.66; H, 8.28.

7,10-Methanodecahydo-4,5-benzopyridazine (IV).—A solution of 45 g. of potassium hydroxide in 250 ml. of 95% ethanol containing 37.9 g. (0.128 mole) of III was refluxed for 11.5 hr. The precipitated potassium carbonate was filtered from the cooled mixture and the ethanol was removed under vacuum. The residual liquid was distilled and furnished 16.23 g. (84%) of IV, b.p. 122° (6.7 mm.), $n^{27}\text{D}$ 1.5055–1.5100. This material solidified on standing, m.p. 37–40°.

1,2-Dibenzoyl-7,10-methanodecahydro-4,5-benzopyridazine (V).—To 1.55 g. (0.01 mole) of IV in 20 ml. of 10% sodium hydroxide solution, 8 ml. of benzoyl chloride was added slowly with shaking and cooling. After extraction with chloroform, the product was crystallized from hexane. Recrystallization of

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[10] A. Fry, M. Eberhardt, and I. Ookuni, *J. Org. Chem.*, **25**, 1252 (1960).

[11] Boiling points and melting points are uncorrected. Microanalyses were performed by A. Bernhardt, Mülheim, Germany. Spectra of the compounds were measured with a Beckman Model DU ultraviolet spectrophotometer and a Perkin-Elmer Model 137 double beam infrared spectrophotometer. Gas chromatographic analyses were performed on an F & M Scientific Corp. Model 21 B dual heater gas chromatographic apparatus using a 10-ft. long, 0.25-in. diameter Celite-silicone grease column.

[12] Prepared by the method of M. A. P. Bowe, R. G. J. Miller, J. B. Rose, and D. G. M. Wood, *J. Chem. Soc.*, 1541 (1960). The authors wish to acknowledge the gift of a generous quantity of dicyclopentadiene from Union Carbide Olefins Co., which was used in the preparation of the precursor, 5,6-di(chloromethyl)bicyclo[2.2.1]hept-2-ene.

[13] Prepared by the method of N. Rabjohn, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 375.

the resulting solid from ethanol–water yielded 2.96 g. (80%) of V, m.p. 173.5–174.5°.

Anal. Calcd. for $C_{23}H_{24}N_2O_4$: C, 76.64; H, 6.71. Found: C, 76.50; H, 6.74.

7,10-Methano-Δ^2-octahydro-4,5-benzopyridazine (VI).—A solution of 4.4 g. (0.029 mole) of IV in 70 ml. of anhydrous ether was stirred with 20 g. of mercuric oxide (yellow powder) for 18 hr. under a nitrogen atmosphere. The dark solid was filtered and the ether was removed under vacuum. The residual liquid was distilled to give 2.71 g. (63%) of VI, b.p. 124° (7.5 mm.), which solidified on standing, m.p. 52–53°; $\lambda_{\max}^{\mathrm{EtOH}}$ 234–235 mμ (ϵ 2340). Infrared spectrum (chloroform) bands at 2.90 (N–H) and 6.12 μ (C=N).

1,2-Dibenzoyl-7,10-methano-Δ^3-octahydro-4,5-benzopyridazine (VIII).—The cyclic hydrazone VI (0.5 g., 0.0032 mole) in a solution of 20 ml. of benzene and 10 ml. of pyridine to which was added dropwise 1.5 ml. of benzoyl chloride was heated for 1 hr. on a stream bath and the mixture was then poured into water. The benzene layer was separated, washed with sodium carbonate solution and with water, and then dried over anhydrous sodium sulfate. The benzene was concentrated to a small volume and hexane was added. The precipitated white solid, 0.55 g., melted at 177–180°. Recrystallization from ethanol–water gave VIII, m.p. 179–180°. The compound discolored permanganate and also absorbed bromine readily.

Anal. Calcd. for $C_{23}H_{22}N_2O_2$: C, 77.07; H, 6.19; N, 7.82. Found: C, 76.98; H, 6.22; N, 7.78.

Hydrogenation of VIII.—The derivative VIII (0.36 g., 0.001 mole) was quantitatively hydrogenated at room temperature and atmospheric pressure over 0.1 g. of 10% palladium-on-charcoal catalyst in 50 ml. of ethanol. One molar equivalent of hydrogen was absorbed. After filtration, the ethanol was evaporated to a small volume and water was added. On cooling, 0.163 g. of a white solid precipitated, m.p. 173.5–174.5°. A mixture melting point with an authentic sample of V was undepressed.

1,2-Dicarbethoxy-3,4,5,6-bis(tetramethylene)-1,2,3,6-tetrahydropyridazine (IX).—One-tenth mole (17.4 g.) of I was added to 19.5 g. (0.12 mole) of bi-(1-cyclohexen-1-yl)[14] dissolved in 30 ml. of benzene. Immediate reaction took place with an evolution of heat. The colorless solution was vacuum concentrated. The residual liquid was distilled and furnished 29.1 g. (87%) of IX, b.p. 167° (0.5 mm.), $n^{26}\mathrm{D}$ 1.5060, which solidified on standing, m.p. 43–44°; lit.[15] b.p. 205–206° (8 mm.), $n^{20}\mathrm{D}$ 1.5080, m.p. 42–43°).

Anal. Calcd. for $C_{18}H_{28}N_2O_4$: C, 64.26; H, 8.39. Found: C, 64.04; H, 8.22.

Attempted Hydrogenation of IX.—A solution of 20.0 g. (0.06 mole) of IX in 130 ml. of 95% ethanol containing 1.0 g. of 10% palladium-on-charcoal catalyst was placed in a Parr hydrogenation apparatus at 59 p.s.i. and shaken for 16 hr. No drop in gage pressure took place. The catalyst was removed by filtration and Raney nickel was added to the solution. Shaking was continued on the Parr apparatus at 61.5 p.s.i. After 46 hr. no hydrogen had been absorbed. The catalyst was filtered from the solution. Vacuum concentration of the solution followed by evaporative distillation gave 14.6 g. of material, $n^{26}\mathrm{D}$ 1.5018. The infrared spectrum of this material was identical with the spectrum of IX.

A similar hydrogenation experiment using rhodium-on-alumina catalyst also failed and starting IX was isolated.

3,4,5,6-Bis(tetramethylene)-1,2,3,6-tetrahydropyridazine (X).—A solution of 37.03 g. (0.11 mole) of IX and 50 g. of potassium hydroxide in 250 ml. of ethylene glycol was refluxed for 13.5 hr. The solution was cooled and 300 ml. of water was added. The resulting solution was extracted with two 200-ml. portions of ether. The combined ether extracts were dried over calcium sulfate, and the ether was removed. The residual liquid was distilled and furnished 14.0 g. (66%) of X, b.p. 110–112° (0.22 mm.), which immediately solidified, m.p. 44–46°; lit.[15] m.p. 45–46°.

The dibenzoyl derivative of X was prepared in 78% yield and melted at 186–188° (from ethanol–water); lit.[15] m.p. 188–189°.

Oxidation of X.—To a solution of X (2.66 g., 0.0139 mole), in 110 ml. of anhydrous ether stirred with a magnetic stirrer was added 8.0 g. of mercuric oxide (yellow powder). Immediate evolution of nitrogen took place and the mercuric oxide darkened. Stirring was continued for 15 hr. after which the solid was filtered and the ether was removed. The crude product, $n^{26}\mathrm{D}$ 1.5330, was distilled and gave 1.63 g. (73%) of bi(1-cyclohexen-1-yl), b.p. 116–117° (5.7 mm.), $n^{26}\mathrm{D}$ 1.5325; lit.[14] b.p. 101–102° (5.5 mm.), $n^{20}\mathrm{D}$ 1.5322. The infrared spectrum of this product was identical with that of authentic bi(1-cyclohexen-1-yl).

Reaction of 2,4-Dimethyl-1,3-pentadiene with I.—One-tenth mole (17.4 g.) of I and 12.5 g. (0.13 mole) of 2,4-dimethyl-1,3-pentadiene[16] were mixed in 30 ml. of benzene. Immediate reaction occurred with an evolution of heat. The colorless solution was vacuum concentrated to yield a thick viscous liquid. Purification by evaporative distillation yielded 22.1 g. (82%) of XIV and XVII, b.p. 132° (0.06 mm.), $n^{26}\mathrm{D}$ 1.4742, d^{25} 1.0653[17]; infrared spectrum ($CHCl_3$) bands at 2.90 (N–H), 5.70–5.80 (shoulder), and 5.85 μ (C=O). The ultraviolet spectrum of the product exhibited $\lambda_{\max}^{\mathrm{EtOH}}$ 232 mμ (ϵ 6800) and indicated that 80% of conjugated diene was present.[18]

Gas chromatography of the product gave two peaks with the composition 21.5 and 78.5%, respectively, as determined by the peak area method.[19]

Anal. Calcd. for $C_{13}H_{22}N_2O_4$: C, 57.76; H, 8.20. Found: C, 57.57; H, 8.02.

Addition of I to 2,4-Dimethyl-1,3-pentadiene under Nonradical Conditions.—To a solution of 6.25 g. (0.065 mole) of 2,4-dimethyl-1,3-pentadiene in 20 ml. of benzene containing 0.1 g. of hydroquinone, which was kept under a nitrogen atmosphere, 8.7 g. (0.05 mole) of I was added in one lot. Immediate reaction took place with an evolution of heat. The colorless solution was extracted twice with two 25-ml. portions of 5% sodium hydroxide solution and once with water. The benzene, after drying over anhydrous sodium sulfate, was vacuum concentrated. The residual liquid was distilled evaporatively and gave 10.46 g. (75%) of product, $n^{26}\mathrm{D}$ 1.4740. The infrared spectrum of this liquid was identical with that of authentic adduct. The ultraviolet spectrum exhibited $\lambda_{\max}^{\mathrm{EtOH}}$ 232 mμ (ϵ 6600) and indicated that 77% of conjugated diene was present.

Gas chromatography showed this product to have the following composition: 27% of product with retention time of 13 min.; 73% of product with retention time of 18.3 min.[20]

Hydrogenation of XIV and XVII.—The addition product, mixture XIV and XVII, (18.43 g., 0.068 mole) was hydrogenated over 1.0 g. of 10% palladium-on-charcoal catalyst in 130 ml. of ethanol at 59.1 p.s.i. on a Parr apparatus. Two molar equivalents of hydrogen were absorbed. The catalyst was removed by filtration and the ethanol was removed under vacuum. Purification of the clear, viscous liquid by evaporative distillation yielded 16.85 g. (90.5%) of XVI and XVIII, b.p. 163° (0.04 mm.), $n^{26}\mathrm{D}$ 1.4450, d^{22} 1.0205; lit.[9] b.p. 169–170° (10 mm.), $n^{20}\mathrm{D}$ 1.4530, d^{20} 1.0207. Gas chromatography of the product gave two peaks with the composition of 14 and 86%, respectively, as determined by the peak area method.[21]

Anal. Calcd. for $C_{13}H_{26}N_2O_4$: C, 56.91; H, 9.55. Found: C, 56.87; H, 9.44.

Hydrolysis of XVI and XVIII.—A solution of 38.5 g. (0.14 mole) of mixture XVI and XVIII in 250 ml. of ethylene glycol containing 60 g. of potassium hydroxide was refluxed for 15 hr. The mixture was cooled and 400 ml. of water was added. The resulting solution was extracted with three 300-ml. portions of ether. The combined ether extracts were dried over calcium sulfate, and the ether was removed. The residual liquid distilled and yielded 15.03 g. (82.5%) of the alkyl hydrazine mixture XIX, b.p. 94–104° (18 mm.), $n^{26}\mathrm{D}$ 1.4458; lit[9] b.p. 84–85° (25 mm.), $n^{20}\mathrm{D}$ 1.4550.

Oxidation of XIX.—To a solution of 50.0 g. (0.17 mole) of potassium dichromate dissolved in 300 ml. of 15% sulfuric acid

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[14] Prepared by the method of E. E. Gruber and R. Adams, *J. Am. Chem. Soc.*, **57**, 2555 (1935).

[15] Y. S. Skabarow, M. G. Kuzmin, and R. Y. Levina, *Zh. Obshch. Khim.*, **30**, 2473 (1960).

[16] Purchased from Aldrich Chemical Co., Milwaukee, Wis.

[17] Levina, *et al.*, in ref. 9 reported for the adduct (XIV and XVII); b.p. 172–175° (10 mm.), $n^{20}\mathrm{D}$ 1.4760, d^{20} 1.0637. Diels, *et al.*, in ref. 8 reported b.p. 136° (0.5 mm.).

[18] The diene, 2,4-dimethyl-1,3-pentadiene, exhibits $\lambda_{\max}^{\mathrm{EtOH}}$ 232 mμ (ϵ = 8500): J. C. Lunt and F. Sondheimer, *J. Chem. Soc.*, 2957 (1950).

[19] Retention times of the peaks were 13.2 and 19.0 min., respectively. Flow rate of helium was 45 ml. per min. with the column temperature of 220° and the detector temperature of 275°.

[20] Flow rate of helium was 45.5 ml. per min. with the column temperature of 230° and the detector temperature of 268°.

[21] Retention times of the peaks were 13.5 and 15.8 min., respectively. Flow rate of helium was 46 ml. per min. with the detector temperature of 265° and the column temperature of 224°.

solution and stirred with a magnetic stirrer, 15.3 g. (0.117 mole) of XIX was added dropwise. After the addition was completed, the reaction mixture was stirred for 2 hr. and allowed to come to room temperature. The mixture was extracted two times with 200 ml. of ether. The combined ether extracts were washed twice with 200-ml. portions of 5% sodium hydroxide solution and once with water. The ether phase was dried over calcium sulfate. Removal of the ether on a steam bath gave 4.92 g. of crude neutral liquid with a ketonic odor. The infrared spectrum confirmed the presence of a ketone. Gas chromatography of this material showed four peaks. The first two peaks, which were off scale, corresponded to ether and water. The third peak had a retention time of 9.11 min. and the fourth peak had a retention time of 10.64 min.[22] The ratio of the third to fourth peak was 21.7 to 78.3%. An authentic sample of diisopropyl ketone[23] had a retention time of 9.11 min. under the same conditions. This material gave a positive iodoform test. A semicarbazone derivative was prepared, m.p. 111–113°.[24]

The basic extract was acidified and extracted with two 200-ml. portions of ether. The ether was dried over calcium sulfate and then evaporated. The crude residual liquid amounted to 2.5 g. The infrared spectrum of this liquid indicated that a carboxylic acid was present. The amide was prepared from the crude liquid and gave 1.23 g. of 2,4-dimethylpentanoic acid amide, m.p. 88–90° (from petroleum ether); lit.[25] m.p. 90°.

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[22] Flow rate of helium was 45.5 ml. per min., with detector temperature of 128° and column temperature of 105°.

[23] Purchased from Eastman Kodak Co.

[24] Reported for 3,4-dimethyl-2-pentanone semicarbazone, m.p. 112°: J. Colonge and K. Mostafar, *Bull. soc. chim. France*, 335 (1939).

[25] M. W. Burrows and W. H. Bentley, *J. Chem. Soc.*, **65**, 512 (1895).

The Reduction of Acid Adducts of Isoquinoline Reissert Compounds[1]

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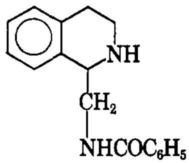
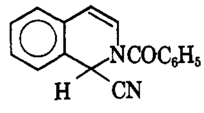
2-Benzoyl-1,2-dihydroisoquinaldonitrile (isoquinoline Reissert compound) forms adducts with hydrobromic or perchloric acid. Reduction of these adducts either by sodium borohydride or by catalytic hydrogenation affords 2-benzyl-1,2,3,4-tetrahydroisoquinaldamide. The structure of the reduction product is established by an alternative synthesis. A preparation of 2-benzoyl-1,2,3,4-tetrahydroisoquinaldonitrile (dihydroisoquinoline Reissert compound) and the perchlorate salt is described. Whereas isoquinoline Reissert compound yields benzaldehyde on hydrolysis, the dihydro derivative gives only benzoic acid.

1-Benzamidomethyl-1,2,3,4-tetrahydroisoquinoline (**1**) which was of interest to us in connection with another synthetic problem was prepared earlier by Rupe and Frey by drastic reduction of 2-benzoyl-1,2-dihydroisoquinaldonitrile (**2**, isoquinoline Reissert compound).[2,3] Attempts to hydrogenate **2** under milder conditions than Rupe's method failed to yield any discrete reduction products.[4] The recent isolation of a hydrobromide salt (**3**, $X^- = Br^-$) of isoquinoline Reissert compound suggested that this derivative might be more easily reduced to **1**.[5] In addition to the hydrobromide, a perchlorate salt (**3**, $X^- = ClO_4^-$) of the Reissert compound was prepared. Platinum-catalyzed hydrogenation of **3** ($X^- = ClO_4^-$) at three atmospheres pressure afforded a reduced salt that was converted to the corresponding base, $C_{17}H_{18}N_2O$, formed by the uptake of three moles of hydrogen. The same basic product was obtained unexpectedly on treatment of either salt **3** with sodium borohydride. Although the reduced base was isomeric with Rupe's compound **1**, the failure of our derivative to form an N-nitroso or an acetyl derivative or to yield benzoic acid on hydrolysis excluded **1** and the unrearranged structure **4** from consideration. The first real clue to the structure **5** of the reduction product was obtained when the sulfuric acid-catalyzed hydrolysis mixture was made alkaline; a strong odor of ammonia was observed. A second hydrolysis product ($C_{17}H_{17}NO_2$) proved to be 2-benzyl-1,2,3,4-tetrahydroisoquinaldinic acid (**6**).



1



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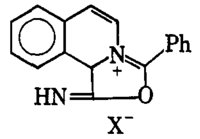

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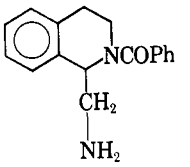

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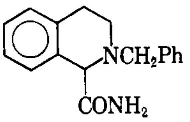

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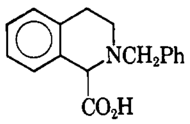

6

Confirmation of structure **5** for the reduced base was obtained by an alternative synthesis (Chart I). The Reissert compound **2** was degraded to isoquinaldamide (**7**), and **7** was hydrogenated in acidic solution to form 1,2,3,4-tetrahydroisoquinaldamide (**8**). A reaction between the reduced amide **8** and benzyl chloride at reflux temperature produced the chloride salt **9** that was converted directly to 2-benzyl-1,2,3,4-tetrahydroisoquinaldamide (**5**). The product from this reaction sequence proved identical by infrared spectra and melting point determinations with the reduction product from the salt.

Further support for **5** as the correct structure of the reduced base was adduced from the n.m.r. spectrum.[6] The salient feature in the spectrum was the unsplit band at τ 5.83 due to a single proton. This can be

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[1] (a) We gratefully acknowledge grants in support of this work from the Tennessee Heart Association and the National Institutes of Health (NB-03329); (b) presented in part at the 14th Southeastern Regional Meeting of the American Chemical Society, Gatlinburg, Tenn., November 1-3, 1962.

[2] H. Rupe and W. Frey, *Helv. Chim. Acta*, **22**, 673 (1922).

[3] A. Reissert, *Ber.*, **38**, 1603 (1905); W. E. McEwen and R. L. Cobb, *Chem. Rev.*, **55**, 511 (1955).

[4] W. E. McEwen, R. H. Terss, and I. W. Elliott, *J. Am. Chem. Soc.*, **74**, 3605 (1952).

[5] J. W. Davis, *J. Org. Chem.*, **25**, 376 (1960). Davis referred to **3** as a "Reissert imine"; in this paper the same compounds are called Reissert salts or acid adducts.

[6] The n.m.r. measurements were run in deuteriochloroform with tetramethylsilane as internal reference. We thank Dr. Harold Boaz of the Eli Lilly Research Laboratories, Indianapolis, Ind., for this information.