[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Some Diels–Alder Reactions with 2-Ethoxy-1,3-butadiene

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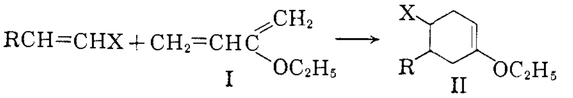
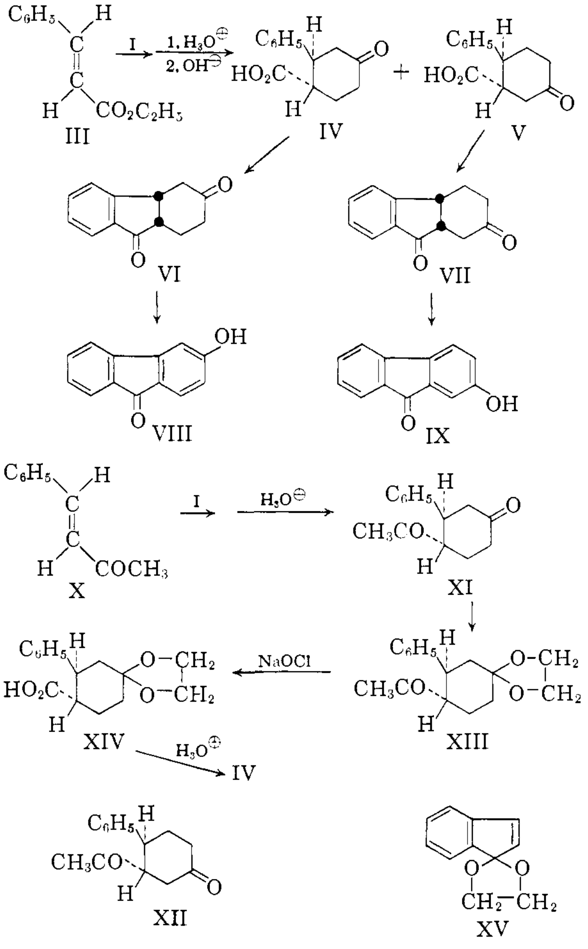
The reaction of 2-ethoxybutadiene with ethyl *trans*-cinnamate yielded, after hydrolysis, *trans*-4-keto-2-phenylcyclohexanecarboxylic acid accompanied by small amounts of *trans*-5-keto-2-phenylcyclohexanecarboxylic acid. Diketones of comparable orientation were obtained from the reaction of *trans*-benzalacetone with 2-ethoxybutadiene. The reaction of indenone ethylene ketal with 2-ethoxybutadiene yielded, after hydrolysis *cis*-hexahydrofluoren-3,9-dione.

We were led to study the structures of the Diels–Alder adducts of 2-ethoxy-1,3-butadiene (I) and certain dieneophiles because of the possible utility of these adducts for the preparation of hexahydrofluorenone derivatives having an oxygen substituent at position 2. Unsymmetrical dienophiles which have been reported to react with 2-alkoxy-1,3-butadienes include acrolein,[3] methyl vinyl ketone,[4] acrylonitrile,[5] methyl acrylate,[6] Δ^2-cyclohexenone[7] and β-nitrostyrene.[8] The adduct isolated in each case corresponded to the structure II in which X is an electron-withdrawing group such as a carbonyl group or a nitro group.



In the present study the reaction of ethyl *trans*-cinnamate (III) with the diene I followed by hydrolysis yielded the isomeric keto acids IV and V, the predominant product being the adduct IV, as would be expected from previous studies. Each of these acids IV and V is presumed to have the indicated *trans* configuration since this configuration is the one expected from the Diels–Alder reaction and, also, the more stable arrangement in which both substituents on the cyclohexanone ring may occupy equatorial positions.

In order to establish the structures of the keto acids IV and V, they were cyclized in the presence of polyphosphoric acid to form the diketones VI and VII, respectively. Dehydrogenation of the diketones formed the corresponding known hydroxyfluorenones VIII and IX. The intermediate diketones were formed and isolated under conditions which could have permitted equilibration of the *cis* and *trans* isomers. The products isolated have been tentatively assigned the *cis* configuration since the *cis* configuration is believed to be the more stable in the hexahydrofluorenone series.[9]



From the reaction of *trans*-benzalacetone (X) with 2-ethoxy-1,3-butadiene followed by hydrolysis, the diketone XI was isolated. This product is again presumed to have the indicated *trans* configuration for the reasons previously stated. A small amount of an isomeric diketone was isolated from the reaction mixture. This product is presumed to have the structure XII. The structure of the diketone XI was established by converting its monoethylene ketal derivative XIII to the keto acid IV.

We then turned our attention to the reaction of ethoxybutadiene (I) with indenone ethylene ketal (XV), this ketal having been used successfully as a dienophile with butadiene.[9] Consideration of the probable mechanism of the Diels–Alder reaction[10] led us to expect a derivative of the diketone VII as the major product of this reaction. However, after distillation and hydrolysis of the crude adduct, we were able to isolate only the diketone VI.

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(3) A. A. Petrov, *J. Gen. Chem.* (*U.S.S.R.*), **11**, 661 (1941); *Chem. Zentr.*, **113**, **I**, 2766 (1942).

(4) A. A. Petrov, *J. Gen. Chem.* (*U.S.S.R.*), **17**, 538 (1947); *C. A.*, **42**, 881 (1948).

(5) A. A. Petrov and M. G. Vladimirova, *J. Gen. Chem.* (*U.S.S.R.*), **17**, 1543 (1947); *C. A.*, **42**, 2238 (1948).

(6) J. Doucet and P. Rumpf, *Bull. soc. chim. France*, 610 (1954).

(7) I. N. Nazarov and L. D. Bergelson, *J. Gen. Chem.* (*U.S.S.R.*), **2**, 515 (1952).

(8) W. C. Wildman, R. B. Wildman, W. T. Norton and J. B. Fine, THIS JOURNAL, **75**, 1912 (1953).

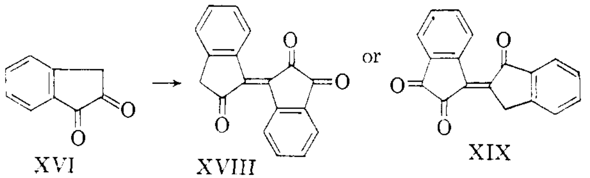
(9) H. O. House, V. Paragamian, R. S. Ro and D. J. Wluka: *ibid.*, **82**, 1457 (1960).

(10) For a discussion and summary of previous work see R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

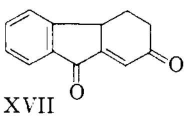
Thus, the orientation observed in the reaction of the styryl ketone X and the ketal XV with ethoxybutadiene (I) is the same. However, we cannot exclude the possibility that the derivative of the expected diketone VII was formed but was not stable to the reaction conditions employed.

As an alternative route to the ketone VII, we explored the condensation of 1,2-indanedione (XVI) with methyl vinyl ketone as a possible preparative method for the enedione XVII. However, the product obtained from this reaction proved to be an aldol condensation product believed to be XVIII or XIX, which was formed readily when the dione XVI was treated with pyridine.

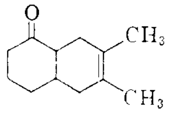
In an effort to increase the yield of Diels–Alder adducts obtained from Δ^2-cyclohexenone without employing a large excess of the unsaturated ketone,[7] we reinvestigated the reaction of Δ^2-cyclohexenone with 2,3-dimethyl-1,3-butadiene.[11] The yields of the adduct XX obtained when two and three equivalents of diene were employed were 31 and 47%, respectively. Attempts to obtain adducts from Δ^2-cyclohexenone and the less reactive dienes 1-phenylbutadiene and 2-methylfuran, were unsuccessful, the unsaturated ketone and the diene (or its dimer) being recovered after reaction periods of 72 hours at 200°.



XVI XVIII XIX



XVII



XX

Experimental[12]

Reaction of Ethyl *trans*-Cinnamate with 2-Ethoxy-1.3-butadiene.—A mixture of 10 g. (0.057 mole) of ethyl *trans*-cinnamate, 19.5 g. (0.2 mole) of 2-ethoxybutadiene[13] and several crystals of hydroquinone was heated to 170° in a glass-lined autoclave for 48 hr. Distillation of the resulting mixture through a short-path still afforded 11.22 g. (71.5%) of the crude adduct, b.p. 110–130° (0.35 mm.), which exhibits infrared absorption[14] at 1735 (ester C=O) and 1660 cm.$^{-1}$ (unconjugated enol ether).[15] A solution of the crude adduct in 110 ml. of ethanol containing 5.5 ml. of water and 5.5 ml. of concentrated hydrochloric acid was refluxed for 30 min., cooled, diluted with water and extracted with ether. After the solvents had been removed from the extract, a mixture of the residual oil with a solution of 3.28 g. (0.082 mole) of sodium hydroxide in 35 ml. of water was heated under reflux with stirring for 6 hr. The resulting aqueous solution was decolorized with Norit, acidified and extracted with ether. After the ethereal solution had been dried over magnesium sulfate and concentrated, the residual keto acid mixture, which crystallized on standing, was subjected to a series of fractional recrystallizations from ethyl acetate–hexane mixtures. The higher melting, less soluble ***trans*-5-keto-2-phenylcyclohexanecarboxylic acid** (V) was separated as white prisms, m.p. 192–193.5°. The infrared spectrum[16] has a broad band at 2940 (associated O–H) with bands at 1726 (C=O) and 1680 cm.$^{-1}$ (carboxyl C=O); the ultraviolet spectrum[17] has a series of maxima in the region 230 to 270 mμ with molecular extinction coefficients of less than 1000.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.39; H, 6.76.

The lower melting, more soluble ***trans*-4-keto-2-phenylcyclohexanecarboxylic acid** (**IV**) was separated as white needles, m.p. 146.7–147.5°. The infrared spectrum[16] of this product has broad bands at 3000 (associated O–H) and 1710 cm.$^{-1}$ (C=O of a ketone and a carboxyl group); the ultraviolet spectrum[17] has a series of maxima in the region 240 to 270 mμ with molecular extinction coefficients of less than 1000.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.40; H, 6.53.

In a subsequent experiment a mixture of 26 g. (0.147 mole) of ethyl *trans*-cinnamate, 11.1 g. (0.147 mole) of 2-methoxy-1,3-butadiene[18] in an equal volume of methanol and a few crystals of 2,5-di-*t*-butylhydroquinone was heated to 170° in a glass-lined autoclave for 48 hr. Distillation of the resulting reaction mixture through a short-path still afforded 20.86 g. (52.6%) of the crude adduct, b.p. 82–155° (0.25–0.28 mm.), which was hydrolyzed with acid and then saponified as previously described. The crude acidic product (18.51 g.) was chromatographed on 900 g. of silica gel, fractions being eluted with benzene containing increasing quantities of ether. The combined fractions eluted with 20% ether in benzene were recrystallized from ethyl acetate–hexane mixtures to separate 2.27 g. (7.1%) of *trans*-4-keto-2-phenylcyclohexanecarboxylic acid, m.p. 145.5–146.8°. Attempts to obtain additional quantities of the pure keto acids by repeated chromatography afforded 15 g. of mixtures melting within the range 131–175°. The infrared spectra[16] of these various fractions resembled closely the spectrum of the lower melting *trans*-4-keto-2-phenylcyclohexanecarboxylic acid.

***cis*-Hexahydrofluoren-3,9-dione (VI).**—A mixture of 0.60 g. (0.00275 mole) of *trans*-4-keto-2-phenylcyclohexanecarboxylic acid and 25 g. of polyphosphoric acid was heated to 85° for 1 hr. and then cooled and poured onto ice. After the resulting mixture had been extracted with ether, the ethereal solution was washed with aqueous sodium bicarbonate, dried over magnesium sulfate and concentrated. The residual crude diketone was sublimed at 100° and 0.1–0.2 mm. and the sublimate was recrystallized from an ethyl acetate–hexane mixture. The pure diketone separated as white prisms, m.p. 101.5–103.5°, which exhibit broad infrared absorption[19] at 1708 cm.$^{-1}$ (conj. C=O in a five-membered ring and unconj. C=O) and ultraviolet maxima[17] at 246 mμ (ε 12,300), 288 (2,310) and 293 (2,350).

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.92; H, 5.95.

***cis*-Hexahydrofluoren-2,9-dione (VII).**—A mixture of 0.508 g. (0.00233 mole) of *trans*-5-keto-2-phenylcyclohexanecarboxylic acid and 25 g. of polyphosphoric acid was heated to 86° for 75 min. and worked-up as previously described. After sublimation under reduced pressure, the diketone crystallized from an ethyl acetate–hexane mixture as white prisms, m.p. 106–107°. The product exhibits

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(11) P. D. Bartlett and G. F. Woods, This Journal, **62**, 2933 (1940). These authors isolated the adduct of 2,3-dimethyl-1,3-butadiene and Δ^2-cyclohexanone in 20% yield.

(12) All melting points are corrected and all boiling points are uncorrected. The infrared spectra were determined with either a Baird, model B, or a Perkin-Elmer, model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, model 11MS. The gas chromatograms were obtained with a 8 mm. × 215 cm. column packed with Dow Silicone Fluid No. 550 suspended on 50–80 mesh ground firebrick. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(13) This diene, b.p. 91–94°, $n^{27}D$ 1.4354, was prepared by the procedure of E. A. Braude, E. R. H. Jones, F. Sondheimer and J. B. Toogood [*J. Chem. Soc.*, 607 (1949)]. These authors report a boiling point of 94.5–95.5°, $n^{19}D$ 1.4400.

(14) Determined as a solution in carbon tetrachloride.

(15) C. M. Hill, R. Woodberry, D. E. Simmons, M. E. Hill and L. Haynes, This Journal, **80**, 4602 (1958).

(16) Determined as a suspension in a potassium bromide pellet.

(17) Determined as a solution in 95% ethanol.

(18) Prepared by the procedure of I. N. Nazarov, I. V. Torgov, I. I. Zaretskaya, G. P. Verkholetova, S. N. Ananchenko and V. M. Audreev, *Izvest. Akad. Nauk S. S. S. R., Otdel Khim. Nauk*, 78 (1953); *C. A.*, **48**, 3324 (1954).

(19) Determined as a solution in chloroform.

broad infrared absorption[19] at 1713 cm.$^{-1}$ (conj. C=O in a five-membered ring and unconj. C=O) with ultraviolet maxima at 246 mμ (ε 12,500), 288 (2,460) and 293 (2,500).

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.70; H, 6.14.

Dehydrogenation of *cis*-Hexahydrofluoren-3,9-dione (VI).—A mixture of 600 mg. of the diketone, 120 mg. of a 30% palladium-on-carbon catalyst and 5 ml. of *p*-cymene was refluxed for 1 hr. and then cooled and filtered. A solution of the filtrate in ether was extracted with 2 *N* aqueous sodium hydroxide and the resulting alkaline extract was saturated with carbon dioxide and then extracted with ether. After the ethereal extract had been washed with water, dried over sodium sulfate and concentrated, the residue was taken up in boiling xylene. The cold xylene solution deposited 180 mg. (31%) of **3-hydroxyfluorenone** (VIII) as yellow needles melting at 233–234° after undergoing a change in crystalline form at 210–215°. Sublimation of the hydroxy ketone at 140° and 0.07 mm. raised the melting point to 236–237° (lit.[20] 228–229°). The infrared spectrum[16] of the sample exhibits broad absorption at 3150 (associated O–H) as well as a band at 1680 cm.$^{-1}$ (conj. C=O); the ultraviolet spectrum has maxima[17] at 252 (33,200) and 277 mμ (ε 31,400).

Anal. Calcd. for $C_{13}H_8O_2$: C, 79.58; H, 4.11. Found: C, 79.44; H, 3.82.

A suspension of 200 mg. of the phenol in 200 ml. of ether containing 2 ml. of methanol was treated an ethereal solution of diazomethane prepared from 400 mg. of N-nitroso-N-methylurea. After the mixture had been allowed to stand for 1 hr., the unchanged diazomethane was removed by the addition of acetic acid. The resulting solution was concentrated, washed successively with 2 *N* aqueous sodium hydroxide and water and then dried over sodium sulfate and concentrated. The **3-methoxyfluorenone**, after elution from a column of Merck acid-washed alumina with a benzene–ether mixture, crystallized from methanol as yellow needles, m.p. 97.5–98° (lit.[20] 96–97°; 2-methoxyfluorenone is reported[21] to melt at 77–78°), yield 30 mg. (14%). The 3-hydroxyfluorenone, m.p. 231–233°, recovered from the alkaline extract amount to 96 mg. (48% recovery). The methoxy ketone exhibits infrared absorption[16] at 1705 cm.$^{-1}$ (conj. C=O in a five-membered ring) with ultraviolet maxima[17] at 253 mμ (ε 39,200), 275 (36,800), 298 (5,300), 331 (3,680) and 339 (3,680).

A solution of 54 mg. of the hydroxy ketone and 0.5 ml. of acetic anhydride in 1 ml. of pyridine was heated on a steam-bath for 50 min. and then concentrated under reduced pressure. After the residual product had been partially purified by elution from a Merck acid-washed alumina column with a benzene–ether mixture, the pure **3-acetoxyfluorenone** crystallized from methanol as pale yellow needles, m.p. 116–117.5° (lit.[20] 115°), yield 40 mg. (61%). The infrared spectrum[16] of the acetoxy ketone has bands at 1760 (C=O of a phenyl ester) and 1715 cm.$^{-1}$ (conj. C=O in a five-membered ring).

Dehydrogenation of *cis*-Hexahydrofluoren-2,9-dione (VII).—A sample of the crude diketone obtained by the cyclization of *trans*-5-keto-2-phenylcyclohexanecarboxylic acid was dehydrogenated with a 30% palladium-on-carbon catalyst in boiling *p*-cymene as previously described. The crude phenolic product crystallized from xylene as red prisms, m.p. 205–208°. This product was shown to be identical with an authentic sample of 2-hydroxyfluorenone by a mixed melting point determination and by the identity of the infrared spectra of the two samples.

An ethanol solution of 2-nitrofluorenone[22] was hydrogenated in the presence of a platinum catalyst to form **2-aminofluorenone** which crystallized from ethanol as violet crystals, m.p. 157.5–158.5° (lit.[23] 160.5°), yield 35%. Diazotization of this amino ketone as previously described[22,24] followed by recrystallization of the crude product from xylene afforded the pure **2-hydroxyfluorenone** (IX) as red-violet prisms, m.p. 209–211° (lit.[22] 210–211°). The hydroxy ketone exhibits infrared absorption[16] at 3260 (broad, associated O–H) and 1690 cm.$^{-1}$ (conj. C=O) with ultraviolet maxima at 267 mμ (ε 64,000), 298 (4,170) and 310 (3,150).

Reaction of Indenone Ethylene Ketal (XV) with 2-Ethoxy-1,3-butadiene (I).—A solution of 10.5 g. (0.06 mole) of the ketal, 26 g. (0.27 mole) of 2-ethoxybutadiene and a few crystals of hydroquinone in 20 ml. of benzene was heated to 180° in a glass-lined autoclave for 15 hr. Distillation of the crude reaction mixture afforded 6 g. (37%) of the crude **ethylene ketal of 2-ethoxy-1,1a,4,4a-tetrahydrofluorenone**, b.p. 170° (1.4 mm.), which exhibits infrared absorption at 1665 cm.$^{-1}$ (unconjugated enol ether).[15] A solution of 2 g. (0.0073 mole) of the crude adduct, 1 ml. of water and 2 ml. of concentrated hydrochloric acid in 20 ml. of ethanol was refluxed for 2 hr. and then diluted with water, neutralized with sodium bicarbonate and extracted with ether. After the ethereal extract had been dried over magnesium sulfate and concentrated, crystallization of the residue from an ethyl acetate–hexane mixture afforded 1 g. (68%) of ***cis*-hexahydrofluoren-3,9-dione** (VI), m.p. 97–99°. Recrystallization raised the melting point of the diketone to 101–102°. The product was shown to be identical with the sample previously described by a mixed melting-point determination and by comparison of the infrared and ultraviolet spectra of the two samples.

1,2-Indandione (XVI).—To a cold (0°) solution of 145 g. (1.1 moles) of 1-indanone and 134 g. (1.3 moles) of *n*-butyl nitrite in 400 ml. of methanol was added, dropwise and with stirring and external cooling, 10 ml. of concentrated hydrochloric acid. After the addition was complete, the mixture was stirred for 1 hr. and then allowed to stand overnight at room temperature. The crude **2-oximinoindanone** which separated was collected on a filter and washed with water, m.p. 205–208° dec. (lit.[25] 218–220° dec., yield 117 g. (66%)). The melting point of the oximino ketone was raised to 215–220° dec. by washing the product with aqueous methanol. The product exhibits infrared absorption[16] at 3200 (associated O–H), 1720 (conj. C=O in a five-membered ring) and 1650 cm.$^{-1}$ (C=N) with an ultraviolet maximum[17] at 273 mμ (ε 16,800). Reaction of 60 g. (0.37 mole) of the crude oximino ketone with 250 g. of 40% aqueous formaldehyde and 100 ml. of concentrated hydrochloric acid for 2 hr. at room temperature yielded 50 g. (90%) of **1,2-indandione**, m.p. 114–116° (lit.[26] 95–115°), which was collected on a filter and washed with water. The diketone exhibits infrared absorption[16] at 1765 (C=O in a five-membered ring) and 1705 cm.$^{-1}$ (conj. C=O in a five-membered ring) with ultraviolet maxima[17] at 249 (11,900) and 292 mμ (ε 3,170).

Self-condensation of 1,2-Indandione (XVI).—A solution of 200 mg. (0.0014 mole) of the diketone in 2 ml. of pyridine was heated on a steam-bath for 2 hr. and then diluted with ether and extracted with dilute, aqueous sulfuric acid. During this extraction the crude product separated and was collected on a filter. Recrystallization from a methanol–ethyl acetate mixture afforded 120 mg. (65%) of **3-[2(or 1)-keto-1(or 2)-indanylidene]-1,2-indandione (XVIII or XIX)**, m.p. 270–276° dec. An additional recrystallization from a methanol–chloroform mixture raised the decomposition point of the triketone to 289–292°. The product exhibits infrared absorption[19] at 1748 (C=O in a five-membered ring) with a shoulder at 1700 (conj. C=O in a five-membered ring) and at 1644 cm.$^{-1}$ (conj. C=C exocyclic to a five-membered ring) and ultraviolet maxima at 253 (17,300) and 329 mμ (ε 11,600).

Anal. Calcd. for $C_{18}H_{10}O_3$: C, 78.82; H, 3.68. Found: C, 78.51; H, 3.70.

This same product was obtained in several attempts to condense 1,2-indandione with methyl vinyl ketone in the presence of pyridine or pyridine–benzene mixtures.

6,7-Dimethyl-Δ^6-octal-1-one (XX).—A mixture of 10 g. (0.104 mole) of Δ^2-cyclohexenone,[27] 25.5 g. (0.312 mole) of 2,3-dimethylbutadiene and a few crystals of hydroquinone was heated to 200° in a glass-lined autoclave for 72 hr. Distillation of the resulting mixture afforded 18.4 g. of

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(20) G. Errera and G. La Spada, *Gazz. chim. ital.*, **35**, **II**, 539 (1905).

(21) A. Werner and A. Grob, *Ann.*, **322**, 168 (1902).

(22) O. Diels, *Ber.*, **34**, 1758 (1901).

(23) G. W. Gray, J. B. Hartley and A. Ibbotson, *J. Chem. Soc.*, 2686 (1955).

(24) R. Patrizietti, *Anales asoc. quim. Argentina*, **22**, 24 (1934); *C. A.*, **28**, 7256 (1934).

(25) F. S. Kipping, *J. Chem. Soc.*, **65**, 480 (1894). In our hands the nitrosation procedure described was definitely superior to the procedure reported by Kipping.

(26) W. H. Perkin, Jr., W. M. Roberts and R. Robinson, *ibid.*, **101**, 232 (1912).

(27) Prepared by the procedure of H. Born, R. Pappo and J. Szmuszkovicz, *J. Chem. Soc.*, 1779 (1953).

forerun, boiling up to 72° (0.27 mm.), and 8.65 g. (46.8%) of crude adduct, b.p. 72–110° (0.17–0.3 mm.), which crystallized on standing. The gas chromatogram of the forerun indicated the presence of unchanged cyclohexenone and the dimer of 2,3-dimethylbutadiene. Redistillation of the forerun through an 18-in. spinning band column separated the diene dimer, 4-isopropenyl-1,2,4-trimethylcyclohexene, b.p. 110–112° (45 mm.), n^{25}D 1.4784 (lit.[28] b.p. 85° (15 mm.), n^{23}D 1.4804), which exhibits infrared absorption[14] at 1635 (C=C) and 895 cm.$^{-1}$ (C=CH_2) and only end absorption in the ultraviolet.[17] Recrystallization of the crude octalone from ethanol afforded 5.44 g. (29.4%) of the pure adduct, m.p. 61.5–62.5° (lit.[11] 62°), which exhibits infrared absorption[14] at 1712 cm.$^{-1}$ (C=O) and only end absorption in the ultraviolet.[17] In a comparable experiment in which only two equivalents of diene was employed, the yield of crude adduct was 31%. *Anal.* Calcd. for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.82; H, 10.20.

Reaction of *trans*-Benzalacetone with 2-Ethoxy-1,3-butadiene.—A mixture of 177 g. (1.21 moles) of *trans*-benzalacetone, 118 g. (1.21 moles) of 2-ethoxybutadiene and a few crystals of 2,5-di-*t*-butylhydroquinone was heated to 180° in an autocalve for 48 hr. Distillation of the resulting mixture afforded 150 g. (51%) of crude adduct, b.p. 92–165° (0.68–0.85 mm.), which exhibits infrared absorption[14] at 1710 (C=O) and 1662 cm.$^{-1}$ (enol ether).[15] A solution of the adduct in a mixture of 200 ml. of ethanol, 100 ml. of concentrated hydrochloric acid and 50 ml. of water was refluxed for 2 hr., cooled, neutralized with dilute, aqueous sodium hydroxide and extracted with ether. After the ethereal solution had been dried over magnesium sulfate and concentrated, distillation of the residue afforded 64.5 g. of crude diketone, as a liquid, b.p. 150° (0.65 mm.). A solution of the crude product in an ether–hexane mixture deposited 41 g. (17% based on the starting benzalacetone) of ***trans*-4-acetyl-3-phenylcyclohexanone (XI)**, as white needles, m.p. 73.3–75°. Sublimation at 0.1–0.2 mm. afforded the pure diketone, m.p. 75–75.5°, which exhibits infrared absorption[14] at 1717 cm.$^{-1}$ (C=O) with a series of ultraviolet maxima[17] in the region 250–270 mμ with molecular extinction coefficients of less than 300.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.79; H, 7.38.

A series of fractional crystallizations of the mother liquors from hexane–benzene mixtures and, finally, from hexane separated a small amount of ***trans*-3-acetyl-4-phenylcyclohexane (XII)** as white needles, m.p. 107.5–109.5°. This diketone exhibits infrared absorption[19] at 1710 cm.$^{-1}$ with a shoulder at 1720 cm.$^{-1}$ (C=O) and a series of low intensity ultraviolet maxima[17] (ε 177 to 264) in the region 250–270 mμ.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.51; H, 7.41.

The Monoethylene Ketal of *trans*-4-Acetyl-3-phenylcyclohexanone (XIII).—A solution of 37 g. (0.171 mole) of the diketone, 12.4 g. (0.2 mole) of ethylene glycol and 0.1 g. of *p*-toluenesulfonic acid in 400 ml. of benzene was refluxed for 5 hr., the water (3 ml. or 98%) being separated as formed. After the benzene solution had been washed with aqueous sodium bicarbonate and concentrated, distillation of the residue afforded 43.49 g. (88%) of the monoketal as a colorless liquid, b.p. 135–140° (0.2–0.25 mm.), n^{25}D 1.5321. The monoketal exhibits infrared absorption[14] at 1717 (C=O) and 1090 and 1127 cm.$^{-1}$ (ketal C–O) with a series of low intensity ultraviolet maxima[17] (ε 167 to 255) in the region 250–270 mμ.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.69; H, 7.86.

The Ethylene Ketal of *trans*-4-Keto-2-phenylcyclohexanecarboxylic Acid (XIV).—To a solution of 10.15 g. (0.039 mole) of the monoketal XIII in 200 ml. of dioxane was added, dropwise and with stirring, 21.5 g. (0.15 mole) of a 5.25% solution of sodium hypochlorite in water. After the mixture had been stirred for 2 hr. with no external heating, it was heated to 60° for 1 hr. and then cooled. After the reaction mixture had been made distinctly basic by the addition of aqueous sodium hydroxide and diluted with water, it was extracted with ether. The ethereal extract was washed with aqueous sodium hydroxide, dried over magnesium sulfate and concentrated to leave 6.62 g. (65% recovery) of the crude, unchanged diketone monoketal, n^{25}D 1.5220. The combined aqueous, alkaline solutions were acidified and extracted with ether. After the ethereal extract had been dried and concentrated, several recrystallizations of the residue from ethyl acetate–hexane mixtures afforded 1.68 g. (16.5%) of the crude keto acid ethylene ketal as white plates melting in the range 120–130°. An additional recrystallization afforded the pure ketal, m.p. 129.5–130.5°. The product exhibits infrared absorption[14] at 2950 (broad, associated OH), at 1710 (carboxyl C=O) and at 1093 and 1128 cm.$^{-1}$ (ketal C–O) with a series of low intensity (ε 94 to 210) ultraviolet maxima[17] in the region 240–270 mμ.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.66; H, 6.88.

A solution of 0.49 g. (0.00187 mole) of the keto acid ethylene ketal in a mixture of 5 ml. of ethanol, 4 ml. of concentrated hydrochloric acid and 4 ml. of water was refluxed for 70 min. and then diluted with water and made alkaline by the addition of aqueous sodium hydroxide. After the resulting mixture had been extracted with ether and then acidified, an additional extraction with ether separated the crude ***trans*-4-keto-2-phenylcyclohexanecarboxylic acid** which crystallized from an ethyl acetate–hexane mixture as white needles, m.p. 144.5–145.5°, yield 0.096 g. (24%). The product was shown to be identical with the sample previously described both by a mixed melting point determination and by comparison of the infrared spectra of the two samples.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

1-Hydroxypyrrolizidine and Related Compounds

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A new method for preparation of certain pyrrolizidine derivatives is described. 1-Oxo-3H-1,2-dihydropyrrolo[1,2-a]pyrrole (Ia) is reduced with sodium borohydride to the corresponding alcohol which is reduced further with hydrogen and rhodium-on-alumina catalyst to 1-hydroxypyrrolizidine or is reduced in one step to 1-hydroxypyrrolizidine with hydrogen and rhodium catalyst. It was converted to 1-chloropyrrolizidine which was reduced with Raney nickel to pyrrolizidine. The hydroxypyrrolizidine was resolved.

The alkanolamine moieties of Senecio alkaloids, the substituted pyrrolizidine bases, have been subjected to intensive study in the last two decades.[1] Synthetic methods leading to the preparation of the pyrrolizidine nucleus may be divided as follows: the methods involving (a) intramolecular alkylation of an amino group,[2] (b) intramolecular cyclodehydration of an amino alcohol,[3] (c) ring

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