[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

STUDIES ON THE NEF REACTION. I. THE SYNTHESIS OF 6-PHENYL-2- AND 3-CYCLOHEXEN-1-ONES AND 2-PHENYLCYCLOHEXANONES

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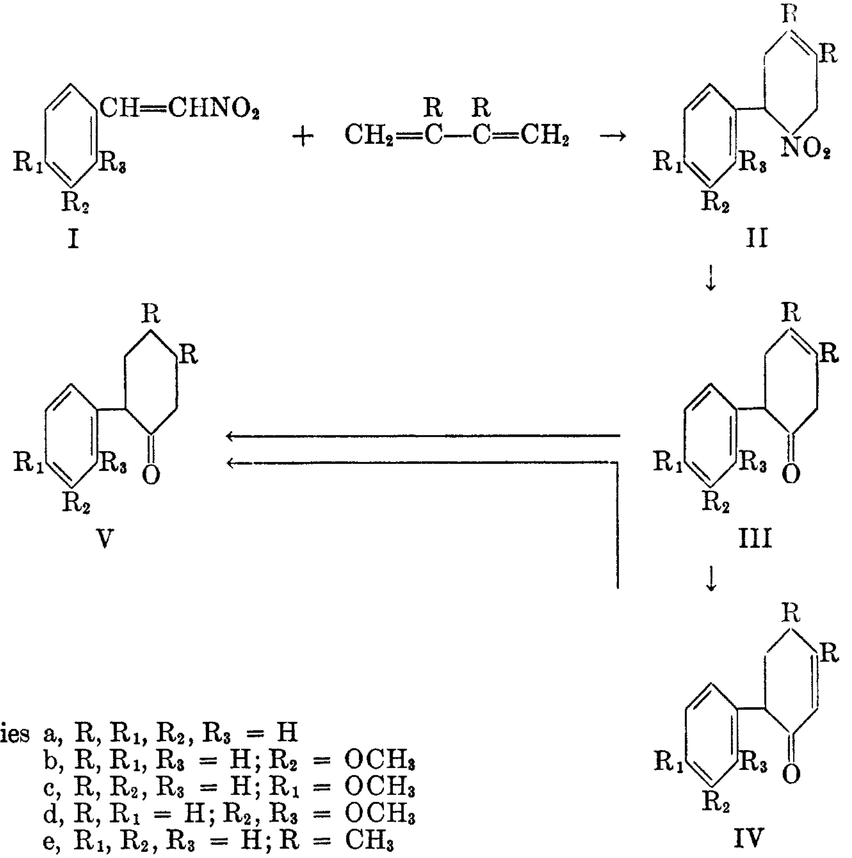
Many syntheses devised for the preparation of resin acids and certain estrogenic hormones and alkaloids employ substituted phenylcyclohexanones as starting materials (1–5). The method of Newman and Farbman (6) has been used to prepare derivatives of 2-phenylcyclohexanone with various substituents on the benzene ring (7), but the yields are less than 52% in each case. This method does not appear to be applicable to the preparation of 2-phenylcyclohexanones with substituents on the cyclohexane ring, since Newman and Booth (8) found that the reaction of phenylmagnesium bromide with 2-chloro-4-methylcyclohexanone gave an inseparable mixture of 4- and 5-methyl-2-phenylcyclohexanones.

This paper describes a synthesis of certain 6-phenyl-2- and 3-cyclohexen-1-ones which on catalytic hydrogenation form 2-phenylcyclohexanones. Three 2-phenylcyclohexanones with substitutents on the benzene ring have been prepared in 70% to 84% over-all yield. The synthesis appears to be much more general than any to date since substituents may be introduced in the first step into known positions on either the aromatic or the alicyclic ring. Various 4-nitro-5-phenylcyclohexenes (II), readily available from the Diels-Alder reaction between a nitroölefin and a diene, serve as basic starting materials. The conversion of these nitro compounds to the corresponding ketones was achieved by the Nef reaction (9, 10).

The reactions of 2-phenylcyclohexanones (V) have been investigated to the extent that various groups have been introduced at carbon atoms 2, 3, and 6 of the cyclohexane ring (1, 2, 4, 5, 7). The number of symmetrical butadienes that may be used to place substituents on the cyclohexane ring by the synthesis discussed in this paper is rather limited. However, the presence of a double bond in III and IV should make possible the introduction of substituents at the previously inaccessible or difficultly approached 4, 5, and 6 positions of the cyclohexane ring in 2-phenylcyclohexanones.

To obtain maximum yields of ketone, it was necessary to prepare the sodium salt of II by treating the nitro compound with two equivalents of sodium ethoxide in ethanol. This ethanolic solution was added slowly to a solution of dilute hydrochloric acid in an organic solvent at 0°. A nitrogen atmosphere was found to produce a higher yield of purer ketone in the simplest case, IIa, and this practice was continued in all the Nef reactions listed. The unconjugated ketones were oils or low-melting solids which could be reduced rapidly and quantitatively to the saturated ketones (V) with palladium-on-carbon catalyst at atmospheric pressure and room temperature. The unconjugated ketones were converted by hydrochloric acid to the conjugated isomers (IV), from which 2-phenylcyclohexanones (V) could be obtained in high yields by reduction.



I II III IV V

Series a, $R, R_1, R_2, R_3 = H$
b, $R, R_1, R_3 = H; R_2 = OCH_3$
c, $R, R_2, R_3 = H; R_1 = OCH_3$
d, $R, R_1 = H; R_2, R_3 = OCH_3$
e, $R_1, R_2, R_3 = H; R = CH_3$

1,2-Dimethyl-4-nitro-5-phenylcyclohexene (IIe) was converted to the ketone IIIe in acetone solution in 50% yield. This low yield can be attributed, in part, to the difficulties involved in isolation of the low-melting product. The unconjugated ketone was transformed very readily by acid to a non-crystalline enol. If the Nef reaction mixture was not worked up while still green in color but was allowed to stand overnight at room temperature, a quantitative yield of the enolic oil was obtained. Conversion of the solid ketone IIIe (or the filtrate from its crystallization) to the enolic oil was accomplished by treatment with alcoholic hydrochloric acid for five minutes at room temperature. A 23% yield of conjugated ketone IVe was obtained when this alcoholic acid solution was refluxed overnight. The mother liquor from the initial crystallization of IVe was enolic. The enol gave a deep red ferric chloride test and showed ultraviolet absorption maxima at 236 mμ and 295 mμ. It reacted slowly with 2,4-dinitrophenylhydrazine to give two isomeric derivatives. During the enolization process the double bond appears to have shifted into conjugation. One of these derivatives was identical with that obtained from the solid conjugated ketone IVe, and the other showed an ultraviolet absorption spectrum very similar to those of the 2,4-dinitrophenylhydrazones of IVe and Ie. Reduction of the unconjugated ketone IIIe with 30% palladium-on-carbon proceeded extremely slowly and non-specifically. The ketone group was reduced concurrently with the olefinic bond. The conjugated isomer IVe was reduced normally.

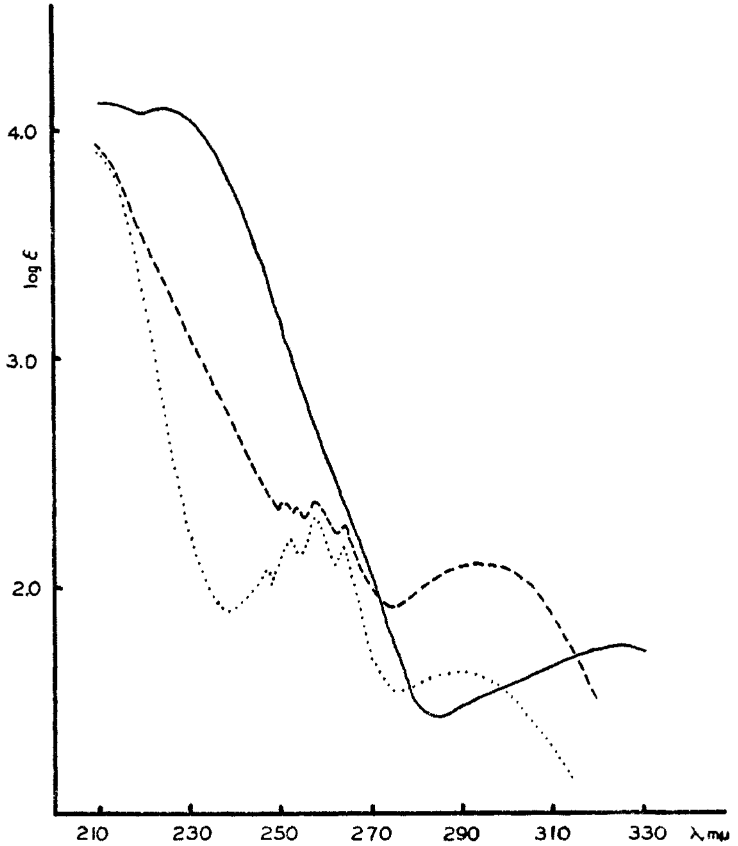
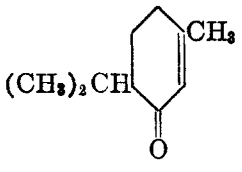


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS IN SERIES a. Dashed line represents β,γ-unsaturated ketone III, solid line represents α,β-unsaturated ketone IV, and dotted line represents saturated ketone V.

No ketonic material could be isolated when the Nef reaction was attempted with 2-phenyl-3-nitrobicyclo[2.2.1]heptene-5 (VI, R = phenyl). Similar results have been recorded by Parham (11). Further studies on the Nef reaction with derivatives of 2-substituted-3-nitrobicyclo[2.2.1]heptene-5 (VI) are in progress.



VII

The ultraviolet absorption spectra of II, III, IV, and V were determined in 95% ethanol. The measurement of all four compounds in each series made it possible to assign definite structures to the isomeric unsaturated ketones. The curves for the unconjugated ketones (III), the saturated phenylcyclohexanones (V), and the nitro compounds (II) were very similar. The conjugated ketones (IVa, b, c, d; solid line, Figs. 1, 2, 3, 4) showed marked maxima in the range 222–225 mμ which is in good agreement with Woodward's calculation (225 mμ) for an α, β-unsaturated ketone with one β-substituent (12). In IVe (solid line, Fig. 5) the maxima at 236 mμ and 321 mμ are identical with those found for piperitone (VII) (13).

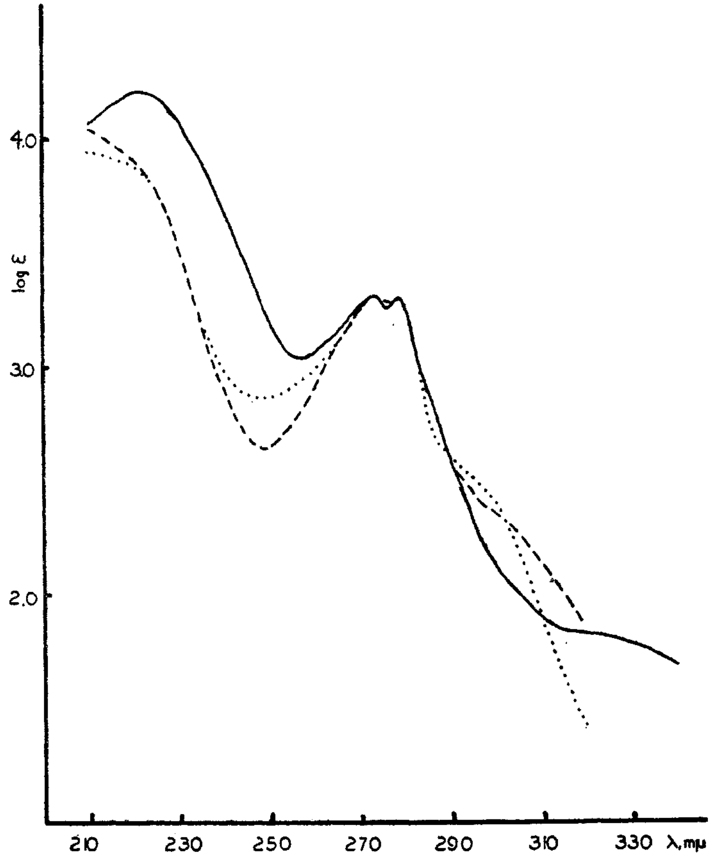


FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS IN SERIES b. Dashed line represents β, γ-unsaturated ketone III, solid line represents α,β-unsaturated ketone IV, and dotted line represents saturated ketone V.

The compounds possessing methoxyl substituents on the benzene ring all showed considerable absorption in the 212–230 mμ region. However, it was possible to identify the α, β-unsaturated ketones in each case since their absorption at 220–225 mμ was significantly greater than that of the compounds in which the double bond does not participate in conjugation.

In a recent paper concerning compounds related to morphine, Barltrop (14) utilized 1-(2,3-dimethoxyphenyl)-2-nitrocyclohexane for the preparation of 2-(2,3-dimethoxyphenyl)cyclohexanone (Vd) in 20% over-all yield. The unsaturated nitro compound IId was converted to an unsaturated ketone, m.p. 96–98°.

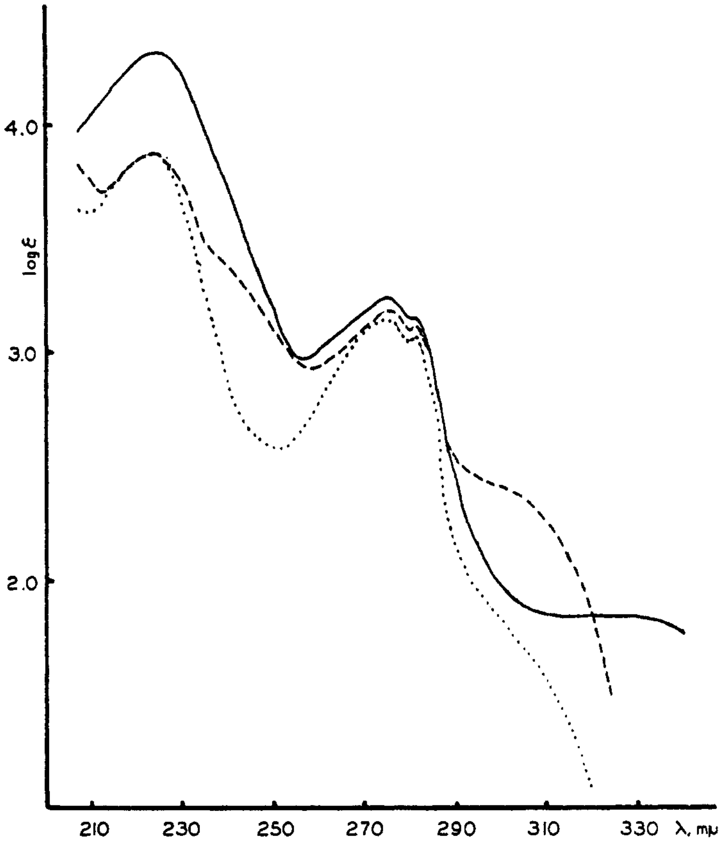


FIG. 3. ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS IN SERIES c. Dashed line represents β, γ-unsaturated ketone III, solid line represents α,β-unsaturated ketone IV, and dotted line represents saturated ketone V.

Barltrop was unable to determine the position of the double bond in this compound by the ultraviolet absorption spectrum. In view of our work, it is evident that this compound is 6-(2,3-dimethoxyphenyl)-3-cyclohexen-1-one (IIId) prepared in this laboratory from Id in 83% over-all yield.

Ultraviolet absorption spectra of the derivatives of the isomeric ketones gave additional evidence for the structures assigned. The 2,4-dinitrophenylhydrazones of 6-phenyl-3-cyclohexen-1-one (IIIa) and 3,4-dimethyl-6-phenyl-3-cyclohexen-

1-one (IIIe) showed ultraviolet absorption maxima in chloroform at 365 mμ which is in agreement with the values found by Braude and Jones (15) for the 2,4-dinitrophenylhydrazones of β, γ-unsaturated ketones or saturated ketones. The 2,4-dinitrophenylhydrazones of the corresponding conjugated isomers (IVa and IVe) showed maxima in chloroform at 382 mμ and 391 mμ, respectively. Braude and Jones (15) found that 2,4-dinitrophenylhydrazones of α, β-unsaturated ketones similar to these possess maxima between 380 mμ and 390 mμ. The 2,4-dinitrophenylhydrazones of the unconjugated ketones and the saturated ketones were yellow, while those of the conjugated ketones were orange or red.

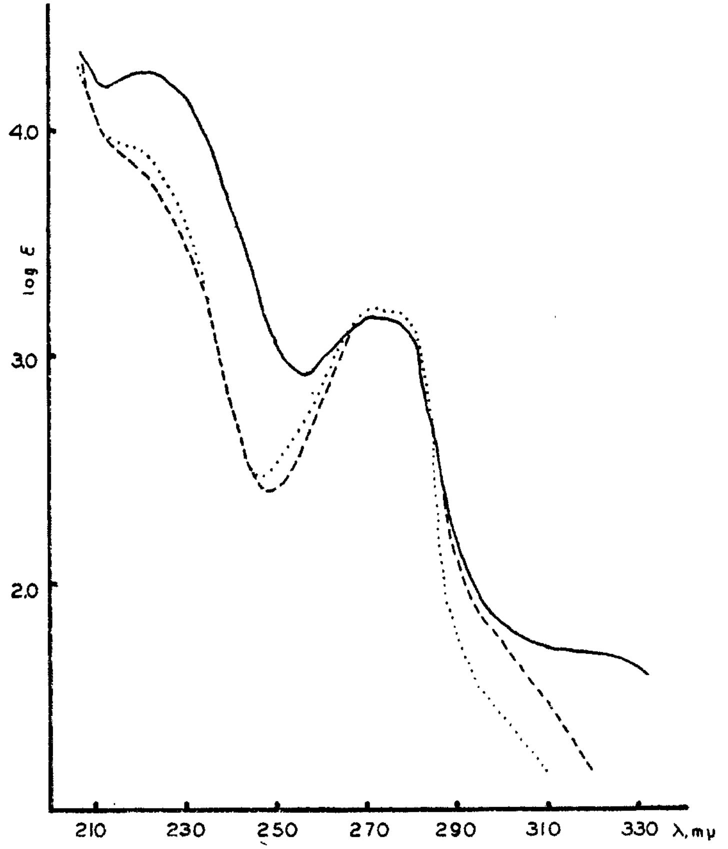


FIG. 4. ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS IN SERIES d. Dashed line represents β, γ-unsaturated ketone III, solid line represents α,β-unsaturated ketone IV, and dotted line represents saturated ketone V.

The semicarbazones of 6-(2,3-dimethoxyphenyl)-2- and 3-cyclohexen-1-one (IVe and IIIe) were investigated. The unconjugated semicarbazone has a spectrum similar to that of the free unconjugated ketone (IIIe), while the conjugated semicarbazone, in agreement with the findings of Evans and Gillam (16), shows a distinct maximum at 264 mμ, characteristic of semicarbazones of α, β-unsaturated carbonyl compounds.

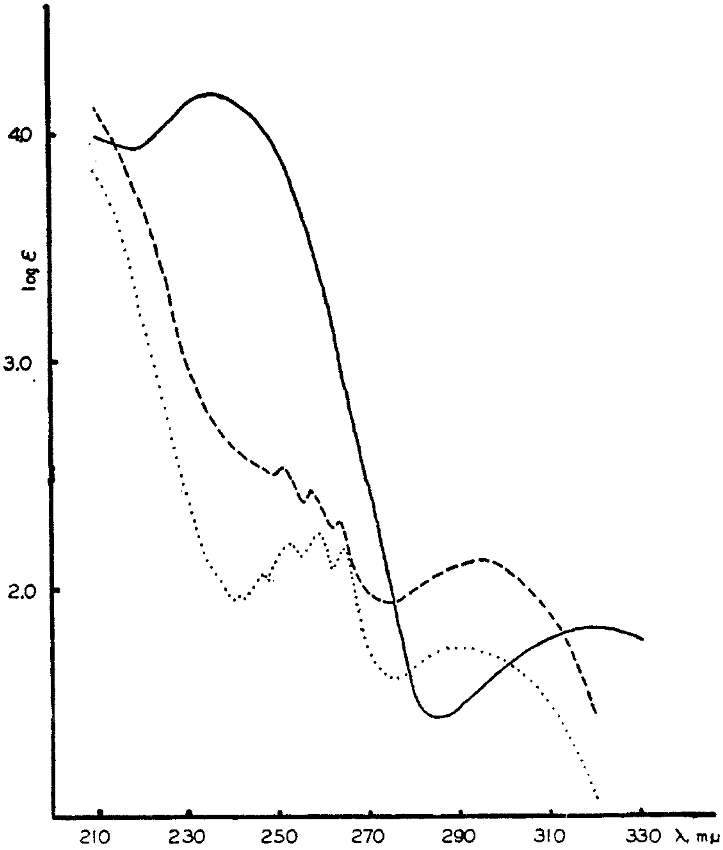


FIG. 5. ULTRAVIOLET ABSORPTION SPECTRA OF COMPOUNDS IN SERIES e. Dashed line represents β, γ-unsaturated ketone III, solid line represents α,β-unsaturated ketone IV, and dotted line represents saturated ketone V.

EXPERIMENTAL[1, 2, 3, 4]

4-NITRO-5-PHENYLCYCLOHEXENES

4-Nitro-5-phenylcyclohexene (IIa). A Pyrex bomb was charged with 10.00 g. (0.067 mole) of β-nitrostyrene, 10.00 g. (0.185 mole) of butadiene, 15 ml. of toluene, and a trace of hydroquinone. The bomb was cooled in a Dry Ice-acetone bath, evacuated to approximately 150 mm. of mercury, and sealed rapidly. The sealed tube was heated at 100° for 48 hours.

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[1] All melting points are corrected. All ultraviolet absorption spectra were determined with a Model DU Beckman spectrophotometer in 1-cm. silica cells.

[2] Analyzed by Tiedcke Laboratory of Microchemistry, Teaneck, N. J.

[3] Analyzed by Clark Microanalytical Laboratory, Urbana, Illinois.

[4] Analyzed by J. F. Alicino, Metuchen, N. J.

The contents of the bomb were concentrated in a stream of nitrogen and recrystallized from methanol to give 11.93 g. (88%) of colorless prisms, m.p. 103–104° [reported (17) 103°].

4-Nitro-5-(3-methoxyphenyl)cyclohexene (IIb). A Pyrex bomb was charged with 3.58 g. (0.020 mole) of *m*-methoxy-β-nitrostyrene (18), 6.00 g. (0.111 mole) of butadiene, 15 ml. of toluene, and a trace of hydroquinone. The tube was sealed in the same manner as IIa and heated at 100° for 4½ days. Concentration of the bomb contents and trituration with methanol gave 4.51 g. (97%) of colorless prisms, m.p. 67–69°. A small portion was recrystallized from methanol for analysis, m.p. 68–68.5°.

Anal.[4] Calc'd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01.
Found: C, 66.81; H, 6.57; N, 5.95.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 273 mμ (log ε 3.26) and 280 mμ (log ε 3.22).

4-Nitro-5-(4-methoxyphenyl)cyclohexene (IIc). A Pyrex bomb was charged with 2.00 g. (0.011 mole) of *p*-methoxy-β-nitrostyrene (19), 10.00 g. (0.185 mole) of butadiene, 15 ml. of toluene, and a trace of hydroquinone. The tube was sealed in the same manner as IIa and heated at 110° for four days. Concentration of the bomb contents and recrystallization from benzene gave 2.11 g. (82%) of colorless prisms, m.p. 75.5–77.5°. A small sample was recrystallized from methanol for analysis, m.p. 76.5–77.5°.

Anal.[4] Calc'd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01.
Found: C, 66.99; H, 6.57; N, 6.10.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 224 mμ (log ε 4.05), 275 mμ (log ε 3.18), and 282 mμ (log ε 3.10).

4-Nitro-5-(2,3-dimethoxyphenyl)cyclohexene (IId). A Pyrex bomb was charged with 3.50 g. (0.0167 mole) of 2,3-dimethoxy-β-nitrostyrene (20), 8.00 g. (0.148 mole) of butadiene, 15 ml. of toluene, and a trace of hydroquinone. The tube was sealed in the same manner as IIa and heated at 120° for three days. Concentration of the bomb contents gave 4.40 g. (100%) of slightly yellow powder, m.p. 81–82°. A sample was sublimed for analysis, m.p. 81–82°.

Anal.[4] Calc'd for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32.
Found: C, 64.07; H, 6.73; N, 5.07.

The ultraviolet absorption spectrum in 95% ethanol showed a maximum at 273 mμ (log ε 3.21).

1,2-Dimethyl-4-nitro-5-phenylcyclohexene (IIe). A Pyrex bomb was charged with 4.00 g. (0.0268 mole) of β-nitrostyrene, 8.00 g. (0.097 mole) of 2,3-dimethylbutadiene, and a trace of hydroquinone. The tube was sealed in the same manner as IIa and heated at 110° for 24 hours. Concentration of the bomb contents gave 5.35 g. (86%) of colorless prisms, m.p. 93–96°. Recrystallization from methanol gave material melting at 95–96° [reported (17) 96°].

6-PHENYL-3-CYCLOHEXEN-1-ONES

A solution of sodium ethoxide prepared from 20 milligram-atoms of sodium and 15 ml. of ethanol was added to 10 millimoles of the 4-nitro-5-phenylcyclohexene in 40 ml. of ethanol, and allowed to stand, covered by nitrogen, for one hour. This ethanolic solution was added dropwise to a well-stirred solution of 12 ml. (0.144 mole) of concentrated hydrochloric acid, 120 ml. of water, and 100 ml. of ethanol at 0°, in a nitrogen atmosphere. A blue-green color developed immediately. When the addition was completed, the reaction mixture was stirred at 0° for one hour and then at room temperature until the color changed from green to yellow. The reaction mixture was diluted to twice its volume with water and extracted with ether. The ethereal extracts were washed with dilute sodium bicarbonate solution followed by water and were partially concentrated under a jet of nitrogen. The solution was dried over magnesium sulfate, and the ether was removed by evaporation under nitrogen, avoiding heat. With the exception of 6-(3-methoxyphenyl)-3-cyclohexen-1-one, which is an oil, trituration with ethanol or petroleum ether and scratching caused crystallization in every case.

6-Phenyl-3-cyclohexen-1-one (IIIa). One recrystallization from ethanol or sublimation gave a 76% yield of colorless prisms, m.p. 46–48°. On a larger scale, a 78% yield of colorless prisms, m.p. 45–47.5° was obtained using 0.0528 mole of 4-nitro-5-phenylcyclohexene in 85 ml. of ethanol, 0.105 gram-atom of sodium in 50 ml. of ethanol, 0.720 mole of concentrated hydrochloric acid, 200 ml. of water, and 150 ml. of ethanol. A sample was recrystallized from ethanol for analysis, m.p. 48.5–49°.

Anal.[2] Calc'd for $C_{12}H_{12}O$: C, 83.68; H, 7.03.
Found: C, 83.81; H, 7.08.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 251 mμ (log ε 2.36), 254 mμ (log ε 2.33), 258 mμ (log ε 2.36), 264 mμ (log ε 2.26), and 295 mμ (log ε 2.09).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to the method of Birch (21) and recrystallized three times from ether in a Dry Ice-acetone bath to give golden yellow needles, m.p. 149.5°.

Anal.[2] Calc'd for $C_{18}H_{16}N_4O_4$: C, 61.36; H, 4.58; N, 15.90.
Found: C, 61.48; H, 4.51; N, 15.75.

The ultraviolet absorption spectrum in chloroform showed a maximum at 365 mμ (log ε 4.36).

6-(3-Methoxyphenyl)-3-cyclohexen-1-one (IIIb). Evaporative distillation at 120° (0.4 mm.) gave an 87% yield of yellow oil, n_D^{20} 1.6193, which was distilled for analysis, b.p. 130° (0.6 mm.); n_D^{20} 1.6154.

Anal.[4] Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98.
Found: C, 77.04; H, 7.32.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 273 mμ (log ε 3.31) and 279 mμ (log ε 3.30).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to the method of Birch (21) and recrystallized from ethanol-ethyl acetate to give orange-yellow needles, m.p. 145–145.5°.

Anal.[4] Calc'd for $C_{19}H_{18}N_4O_5$: C, 59.68; H, 4.74; N, 14.66.
Found: C, 59.53; H, 5.02; N, 14.85.

6-(4-Methoxyphenyl)-3-cyclohexen-1-one (IIIc). Sublimation at 120–130° (0.2 mm.) gave an 88% yield of colorless prisms, m.p. 52.5–54.5°. After recrystallization from ether-petroleum ether the melting point was 56–57°.

Anal.[4] Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98.
Found: C, 76.93; H, 7.30.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 225–226 mμ (log ε 3.88), 276 mμ (log ε 3.18), and 282 mμ (log ε 3.12).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to the method of Birch (21) and recrystallized three times from ethanol to give yellow needles m.p. 111.5–112.5°.

Anal.[4] Calc'd for $C_{19}H_{18}N_4O_5$: C, 59.68; H, 4.74; N, 14.66.
Found: C, 59.53; H, 4.88; N, 14.67.

6-(2,3-Dimethoxyphenyl)-3-cyclohexen-1-one (IIId). The pale tan solid, 83% yield, m.p. 94–96°, was recrystallized from ethanol to give colorless prisms, m.p. 96–97°.

Anal.[4] Calc'd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.95.
Found: C, 72.54; H, 6.76.

The ultraviolet absorption spectrum in 95% ethanol showed a maximum at 278 mμ (log ε 3.19).

The 2,4-dinitrophenylhydrazone could not be isolated in a pure, crystalline state so the *semicarbazone* was prepared according to Shriner and Fuson (22). Four recrystallizations from ethanol gave colorless prisms, m.p. 163.5–164° (dec.).

Anal.[4] Calc'd for $C_{15}H_{19}N_3O_3$: C, 62.26; H, 6.62; N, 14.53.
Found: C, 62.26; H, 6.45; N, 14.62.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 220 mμ (log ε 4.24), 272 mμ (log ε 3.34), and 277 mμ (log ε 3.33).

3,4-Dimethyl-6-phenyl-3-cyclohexen-1-one (IIIe). A solution of sodium ethoxide prepared from 0.876 g. (0.0381 gram-atom) of sodium and 40 ml. of ethanol was added to 4.130 g. (0.0179 mole) of 1,2-dimethyl-4-nitro-5-phenylcyclohexene in 80 ml. of ethanol and allowed to stand, covered by nitrogen, for one hour. This ethanolic solution was added dropwise over 1½ hours to a well-stirred solution of 36 ml. (0.432 mole) of concentrated hydrochloric acid, 500 ml. of water, and 300 ml. of acetone at 0° in a nitrogen atmosphere. When the addition of the sodium salt was half completed, 100 ml. of acetone and 20 ml. of concentrated hydrochloric acid were added. The reaction mixture was stirred at 0° for 1½ hours, allowed to come to room temperature over 3½ hours, and worked up while still green. The yield of the desired ketone was lower when the solution was allowed to stand until it turned yellow. The reaction mixture was diluted with water and extracted with ether. The ethereal extracts were washed with water, concentrated under a jet of nitrogen, and dried over magnesium sulfate. The ether was removed completely by evaporation under nitrogen without heat, leaving a quantitative yield of green oil that crystallized in the refrigerator. The low melting point of this solid prevented isolation of more than 1.80 g. (50%), m.p. 30–32°. Recrystallization from ethanol-water gave colorless prisms, m.p. 34–34.5°.

Anal.[2] Calc'd for $C_{14}H_{16}O$: C, 83.96; H, 8.05.

Found: C, 83.69; H, 8.11.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 251 mμ (log ε 2.52), 257 mμ (log ε 2.42), 264 mμ (log ε 2.28), and 295 mμ (log ε 2.11).

The *2,4-dinitrophenylhydrazone* was prepared according to the method of Birch (21) and recrystallized twice from absolute ethanol to give yellow needles, m.p. 120–121°.

Anal.[2] Calc'd for $C_{20}H_{20}N_4O_4$: C, 63.15; H, 5.30; N, 14.73.

Found: C, 63.17; H, 5.42; N, 14.88.

6-PHENYL-2-CYCLOHEXEN-1-ONES

6-Phenyl-2-cyclohexen-1-one (IVa). A solution of 1.015 g. (0.0059 mole) of 6-phenyl-3-cyclohexen-1-one in 15 ml. of ethanol and 5 ml. of concentrated hydrochloric acid was refluxed for 45 minutes. The reaction mixture was diluted with water and extracted with ether. The ethereal extracts were washed with water until neutral, dried over magnesium sulfate, and concentrated under a jet of nitrogen to give 1.00 g. (98.5%) of colorless prisms, m.p. 60–64°. Sublimation and recrystallization from ethanol-water gave material melting 67.5–68.5°.

Anal.[2] Calc'd for $C_{12}H_{12}O$: C, 83.68; H, 7.03.

Found: C, 83.80; H, 6.98.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 211 mμ (log ε 4.12), 225 mμ (log ε 4.09), and 325 mμ (log ε 1.72).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to Shriner and Fuson (23) and recrystallized four times from absolute ethanol to give orange-red needles, m.p. 162–163°.

Anal.[2] Calc'd for $C_{18}H_{16}N_4O_4$: C, 61.36; H, 4.58; N, 15.90.

Found: C, 61.58; H, 4.66; N, 15.82.

The ultraviolet absorption spectrum in chloroform showed maxima at 256 mμ (log ε 4.20) and 382 mμ (log ε 4.45).

6-(3-Methoxyphenyl)-2-cyclohexen-1-one (IVb). A solution of 2.54 g. (0.0126 mole) of 6-(3-methoxyphenyl)-3-cyclohexen-1-one in 15 ml. of ethanol and 3 ml. of concentrated hydrochloric acid was refluxed for three hours. The reaction mixture was diluted with water and extracted with ether. The ethereal extracts were washed with dilute sodium bicarbonate solution followed by water, dried, concentrated, and distilled to give 2.15 g. (85%) of colorless oil, b.p. 126–130° (0.1 mm.); n_D^{20} 1.6233.

Anal.[4] Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98.

Found: C, 77.27; H, 7.04.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 222 mμ (log ε 4.21), 273 mμ (log ε 3.32), and 280 mμ (log ε 3.29).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to Shriner and Fuson (23) and recrystallized four times from ethanol-ethyl acetate to give orange-red needles, m.p. 156.5–157°.

Anal.[4] Calc'd for $C_{19}H_{18}N_4O_5$: C, 59.68; H, 4.74; N, 14.66.

Found: C, 59.41; H, 4.91; N, 14.99.

6-(4-Methoxyphenyl)-2-cyclohexen-1-one (IVc). A solution of 0.895 g. (0.00443 mole) of 6-(4-methoxyphenyl)-3-cyclohexen-1-one in 15 ml. of ethanol and 3 ml. of concentrated hydrochloric acid was refluxed for two hours, diluted with water, and extracted with ether. The ethereal extracts were washed with dilute sodium bicarbonate solution followed by water, dried, and concentrated to give 0.828 g. (93%) of tan crystals, m.p. 63.5–67.5°. Sublimation at 130° (0.2 mm.) followed by recrystallization from petroleum ether gave colorless needles, m.p. 71.5–72°.

Anal.[4] Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98.

Found: C, 77.06; H, 7.22.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 224–5 mμ (log ε 4.32), 275 mμ (log ε 3.23), and 282 mμ (log ε 3.16).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to Shriner and Fuson (23) and recrystallized four times from ethanol to give orange-red needles, m.p. 137.5–138.5°.

Anal.[4] Calc'd for $C_{19}H_{18}N_4O_5$: C, 59.68; H, 4.74; N, 14.66.

Found: C, 59.59; H, 4.84; N, 14.75.

6-(2,3-Dimethoxyphenyl)-2-cyclohexen-1-one (IVd). A solution of 0.660 g. (0.00284 mole) of 6-(2,3-dimethoxyphenyl)-3-cyclohexen-1-one in 10 ml. of ethanol and 2 ml. of concentrated hydrochloric acid was refluxed for two hours, diluted with water, and extracted with ether. The ethereal extract was washed with dilute sodium bicarbonate solution followed by water, dried, and concentrated to give an oil that solidified. Recrystallization from ethyl acetate-petroleum ether gave 0.550 g. (83%) of colorless solid, m.p. 56.5–58.5°, which was sublimed at 120° (0.06 mm.) and recrystallized from ethyl acetate-petroleum ether to give stout prisms, m.p. 58–59.5°.

Anal.[4] Calc'd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.95.

Found: C, 72.39; H, 7.14.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 222 mμ (log ε 4.25) and 273 mμ (log ε 3.17).

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to Shriner and Fuson (23) and recrystallized four times from ethanol-ethyl acetate to give pale orange prisms, m.p. 140.5–141°.

Anal.[4] Calc'd for $C_{20}H_{21}N_4O_6$: C, 58.10; H, 5.12; N, 13.55.

Found: C, 58.48; H, 5.13; N, 13.69.

The *semicarbazone* was prepared according to Shriner and Fuson (22) and recrystallized three times from ethanol to give colorless prisms, m.p. 195–196° (dec.).

Anal.[4] Calc'd for $C_{15}H_{19}N_3O_3$: C, 62.26; H, 6.62; N, 14.53.

Found: C, 62.32; H, 6.67; N, 14.51.

The ultraviolet absorption spectrum in 95% ethanol showed a maximum at 264 mμ (log ε 4.27).

3,4-Dimethyl-6-phenyl-2-cyclohexen-1-one (IVe). A solution of 1.758 g. (0.0088 mole) of 3,4-dimethyl-6-phenyl-3-cyclohexen-1-one in 10 ml. of ethanol and 5 ml. of concentrated hydrochloric acid was refluxed for eight hours. After the addition of 5 ml. of ethanol and 5 ml. of concentrated hydrochloric acid, the solution was refluxed for 18 hours, diluted with water, and extracted with ether. The ethereal extracts were washed with water, dried, and concentrated to give 1.64 g. (94%) of yellow oil which on trituration with petroleum ether gave 0.70 g. of pale yellow solid, m.p. 47–57°. Recrystallization from ethanol gave 0.407 g. (23%) of colorless prisms, m.p. 57–61°. A sample was further recrystallized from ethanol for analysis, m.p. 59.5–61.5°.

Anal.[4] Calc'd for $C_{14}H_{16}O$: C, 83.96; H, 8.05.

Found: C, 84.21; H, 8.08.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 236 mμ (log ε 4.17) and 321 mμ (log ε 1.82).

The *2,4-dinitrophenylhydrazone* was prepared according to Shriner and Fuson (23) and recrystallized three times from absolute ethanol to give orange needles, m.p. 144.5–145.5°.

Anal.[2] Calc'd for $C_{20}H_{20}N_4O_4$: C, 63.15; H, 5.30; N, 14.73.
Found: C, 63.04; H, 5.43; N, 14.94.

The ultraviolet absorption spectrum in chloroform showed maxima at 257.5 mμ (log ε 4.24), and 391–392 mμ (log ε 4.48).

The enolic oil was prepared by treating 3.0 g. of oily filtrate from the crystallization of 3,4-dimethyl-6-phenyl-3-cyclohexen-1-one (IIIe) with 5 ml. of concentrated hydrochloric acid and 10 ml. of ethanol. The reaction mixture was allowed to stand at room temperature for five minutes and then was poured into water and extracted with ether. The ethereal extracts were dried and distilled to give an orange-yellow oil, b.p. 135–139° (0.2 mm.), which on redistillation gave a pale yellow oil, b.p. 122–125° (0.1 mm.); n_D^{20} 1.5732.

Anal.[4] Calc'd for $C_{14}H_{16}O$: C, 83.96; H, 8.05.
Found: C, 83.99; H, 8.05.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 232 mμ (log ε 4.03) and 295–296 mμ (log ε 3.15).

A mixture of *2,4-dinitrophenylhydrazones* formed very slowly when the method of Birch (21) was used. Six recrystallizations from ethanol gave orange needles, m.p. 175.5–176°.

Anal.[4] Calc'd for $C_{20}H_{20}N_4O_4$: C, 63.15; H, 5.30; N, 14.73.
Found: C, 63.42; H, 5.35; N, 14.76.

The ultraviolet absorption spectrum in chloroform showed maxima at 260 mμ (log ε 4.20) and 385 mμ (log ε 4.48).

From the combined filtrates of recrystallization of the above 2,4-dinitrophenylhydrazone (m.p. 175.5–176°), a *2,4-dinitrophenylhydrazone* of greater solubility was recovered by adding 1 ml. of concentrated hydrochloric acid and concentrating the ethanolic solution. An orange solid precipitated and was recrystallized four times from absolute ethanol to give orange needles, m.p. 142.5–144°. The melting point of a mixture with the 2,4-dinitrophenylhydrazone prepared from crystalline 3,4-dimethyl-6-phenyl-2-cyclohexen-1-one was not depressed.

2-PHENYLCYCLOHEXANONES

A sample of 3–5 millimoles of the ketone to be reduced was mixed with 50 mg. of 30% palladium-on-carbon (24) and 10 ml. of ethanol and hydrogenated at room temperature and atmospheric pressure. The theoretical amount of hydrogen was absorbed in every case. The catalyst was removed by filtration. The ethanolic solution was evaporated under a jet of nitrogen to give the desired product, which was a solid in every case except for 2-(3-methoxyphenyl)cyclohexanone, an oil.

2-Phenylcyclohexanone (Va). Prepared in yields of 100% and 99% from 6-phenyl-3-cyclohexen-1-one and 6-phenyl-2-cyclohexen-1-one, respectively; m.p. 56.5–57.5°. Recrystallization from petroleum ether gave colorless prisms, m.p. 57–58° [reported (7) 59.5–60°]. The melting point of a mixture with an authentic sample of 2-phenylcyclohexanone prepared by oxidation of 2-phenylcyclohexanol (7) was not depressed.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 247 mμ (log ε 2.06), 252 mμ (log ε 2.20), 258 mμ (log ε 2.29), 264 mμ (log ε 2.18), and 291 mμ (log ε 1.61).

2-(3-Methoxyphenyl)cyclohexanone (Vb). Prepared as a colorless oil in yields of 100% and 98% from 6-(3-methoxyphenyl)-3-cyclohexen-1-one and 6-(3-methoxyphenyl)-2-cyclohexen-1-one, respectively; b.p. 136–138° (0.6 mm.); n_D^{20} 1.5496.

Anal.[4] Calc'd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90.
Found: C, 76.25; H, 7.96.
Found: C, 76.29; H, 7.98.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 273 mμ (log ε 3.33) and 279 mμ (log ε 3.30).

The *oxime* of each sample of 2-(3-methoxyphenyl)cyclohexanone was prepared according to the method of Shriner and Fuson (25) and recrystallized four times from methanol to give colorless needles, m.p. 128–129° [reported (7) 129.5–130°]. The melting point of a mixture of the two derivatives was not depressed.

The *2,4-dinitrophenylhydrazone* of each sample of 2-(3-methoxyphenyl)cyclohexanone was prepared according to Shriner and Fuson (23) and recrystallized three times from ethanol to give orange-yellow needles, m.p. 124–125° [reported (7) 124–125°]. The melting point of a mixture of the two derivatives was not depressed.

2-(4-Methoxyphenyl)cyclohexanone (Vc). Prepared in yields of 100% and 99% from 6-(4-methoxyphenyl)-3-cyclohexen-1-one and 6-(4-methoxyphenyl)-2-cyclohexen-1-one, respectively; m.p. 85.5–86.5°. Two recrystallizations from petroleum ether gave colorless prisms, m.p. 87–87.5° [reported (7) 89–89.2°]. The melting point of a mixture of the two samples was not depressed. The ultraviolet absorption spectrum in 95% ethanol showed maxima at 224 mμ (log ε 3.89), 275 mμ (log ε 3.14), and 282 mμ (log ε 3.07).

The *oxime* and the *2,4-dinitrophenylhydrazone* were prepared according to Shriner and Fuson (25, 23). The oxime was recrystallized four times from methanol to give colorless needles, m.p. 165–166° [reported (7) 166–167°]. The 2,4-dinitrophenylhydrazone was recrystallized three times from ethanol to give yellow needles, m.p. 144.5–145° [reported (7) 144–145°].

2-(2,3-Dimethoxyphenyl)cyclohexanone (Vd). Prepared as a colorless oil in yields of 98% and 92% from 6-(2,3-dimethoxyphenyl)-3-cyclohexen-1-one and 6-(2,3-dimethoxyphenyl)-2-cyclohexen-1-one, respectively. Trituration with ethanol in a Dry Ice-acetone bath gave colorless prisms that were recrystallized from ethyl acetate-petroleum ether, m.p. 70.5–71.5° [reported (26) 70–71°; (27) 67–68.5°]. The melting point of a mixture of the two samples was not depressed.

Anal.[4] Calc'd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74.
Found: C, 71.64; H, 7.96.

The ultraviolet absorption spectrum in 95% ethanol showed a maximum at 273 mμ (log ε 3.20).

The *oxime* and *2,4-dinitrophenylhydrazone* were prepared according to Shriner and Fuson (25, 23). The oxime was recrystallized three times from ethanol, m.p. 136.5–138.5° [reported (26) 139–140°; (27) 137–138°]. The 2,4-dinitrophenylhydrazone was recrystallized three times from ethanol, m.p. 124.5–125.5° [reported (26) 125–127°; (27) 123–124°].

4,5-Dimethyl-2-phenylcyclohexanone (Ve). Prepared in 42% yield, m.p. 66.5–70.5°, from 3,4-dimethyl-6-phenyl-2-cyclohexen-1-one. Recrystallization from ethanol-water gave colorless prisms, m.p. 73–74°.

Anal.[3] Calc'd for $C_{14}H_{18}O$: C, 83.12; H, 8.97.
Found: C, 83.25; H, 8.77.

The ultraviolet absorption spectrum in 95% ethanol showed maxima at 241–242 mμ (log ε 1.96), 247 mμ (log ε 2.06), 252 mμ (log ε 2.19), 258 mμ (log ε 2.28), 264 mμ (log ε 2.17), and 292–293 mμ (log ε 1.73).

The *2,4-dinitrophenylhydrazone* was prepared according to Birch (21) and recrystallized three times from absolute ethanol to give yellow needles, m.p. 141.5–142.5°.

Anal.[4] Calc'd for $C_{20}H_{22}N_4O_4$: C, 62.81; H, 5.80; N, 14.65.
Found: C, 63.14; H, 5.99; N, 14.64.

The oily mother liquor from the hydrogenation was converted, according to Shriner and Fuson (23), to a mixture of 2,4-dinitrophenylhydrazones from which no derivative except the one reported above (m.p. 141.5–142.5°) could be isolated in a pure state.

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SUMMARY

The preparation of a series of 6-phenyl-3-cyclohexen-1-ones from 4-nitro-5-phenylcyclohexenes by the Nef reaction is described. The unconjugated ketones can be isomerized by hydrochloric acid to the corresponding 6-phenyl-2-cyclohexen-1-ones. Both unsaturated ketones are converted to derivatives of 2-phenylcyclohexanone in high yield by catalytic hydrogenation. The ultraviolet absorption spectra of representative compounds are given.

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