

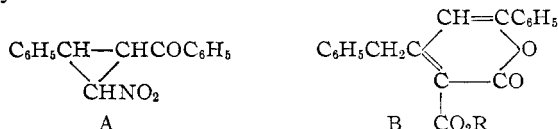
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Cyclopropanes. XV.¹ Action of Sodiomalonic Ester upon Two β -Nitro- α,β -unsaturated KetonesBY LEE IRVIN SMITH AND BOB K. DAVIS²

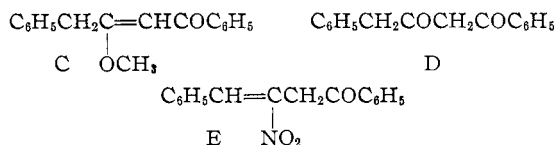
RECEIVED MAY 3, 1954

Two β -nitro- α,β -unsaturated ketones, I and II, have been prepared and subjected to the action of alkaline reagents. From I by action of sodium ethoxide, there was produced in fair yield compound V, the enol ether of 1,3-diketone. Action of sodiomalonic ester upon I produced the pyrone VI, but only in two of many experiments, and then the yield was extremely small. In two other experiments, I behaved toward the enolate as an α,β -unsaturated nitro compound and was converted into VII. The nitro ketone II was obtained in small amounts only, and in one experiment it was converted by action of sodiomalonic ester into the pyrone B, identical with that obtained by action of enolate upon the nitrocyclopropane A. But the yield of B from II was extremely small. It must be concluded that, although nitro ketones of the type of I and II can give rise to α -pyrones by action of sodio malonic ester, these substances are not likely intermediates in the reaction whereby pyrones are produced from nitrocyclopropanes by action of these enolates.

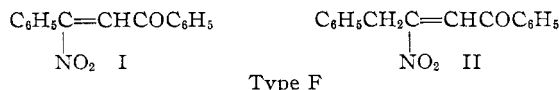
Action of sodiomalonic ester upon secondary nitrocyclopropyl ketones, such as A, produces α -pyrones B.³⁻⁵



All but one of the products derived from A by action of alkali according to the sequence proposed by Smith and Engelhardt,⁶ which could be the precursor of the pyrone, *viz.*, the enol ether C of the 1,3-diketone D, the diketone D itself, and the unsaturated nitro ketone E, have been examined and none of these is converted, by action of sodiomalonic esters, into the α -pyrone B. The one remaining compound in the sequence of Smith and Engelhardt which has not, so far, been examined as a precursor



of the pyrone is the β -nitro- α,β -unsaturated ketone F, isomeric with E. The work described in this paper deals with the synthesis of two compounds of type F—I and II (type F)—and their behavior toward sodio malonic ester and other alkaline reagents. The simpler compound I was investigated first, for although I cannot be derived from a nitrocyclopropyl ketone, it should be converted into a

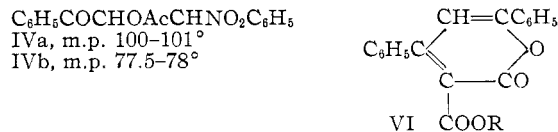
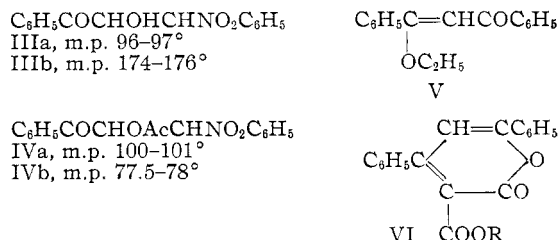


Type F

pyrone by action of sodiomalonic ester. Moreover, in I the position of the double bond is fixed and cannot shift. Compound II can be derived from the cyclopropane A, and theoretically can give rise to the pyrone B, but in II there is the possibility of a

shift of the double bond during a reaction, whereby II would be converted into E.

β -Nitrobenzalacetophenone (I) was synthesized by condensation of phenylglyoxal with phenylnitromethane. When the condensation was carried out at room temperature in dioxane and with *n*-butylamine as the catalyst, I was formed directly, but only slowly and in poor yield (12%) even after eighteen hours. When the condensation was carried out in dry ether, with triethylamine as the catalyst, the first product was a mixture (72%) of the racemic nitroalcohols III. Each of the nitroalcohols gave a single (racemic) acetate IV. Each racemate of the acetate IV, by action of triethylamine in ether, gave both stereo isomers of I; a, m.p. 94–95° and b, m.p. 80–81°. The best over-all yield



of the mixture of isomers of I was 55%, based on phenylnitromethane. Separation of the isomers Ia and Ib was difficult; the higher melting form Ia, present in somewhat larger amount, was fairly easily obtained, however.

Reaction of Ia with excess sodium ethoxide produced β -ethoxybenzalacetophenone (V) in fair yield (50%, pure). This enol ether crystallized in colorless plates melting at 80–81°. When the ether V was warmed with dilute hydrochloric acid and then shaken with a saturated aqueous solution of copper acetate, the copper enolate of dibenzoylmethane was obtained quantitatively as a green solid melting at 323–325° dec. in agreement with the value given in the literature.⁸ Thus this β -nitro- α,β -unsaturated ketone I (type F), does react with a base (sodium ethoxide) to give a derivative of a β -diketone.

(1) Paper XIV, Smith and Showell, *J. Org. Chem.*, **17**, 839 (1952).
(2) Abstracted from a thesis by Bob K. Davis, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, January, 1954. General Mills, Inc., Fellow 1952–1953.

(3) E. P. Kohler and L. I. Smith, *THIS JOURNAL*, **44**, 624 (1922).

(4) L. I. Smith and R. E. Kelly, *ibid.*, **74**, 3300 (1952).

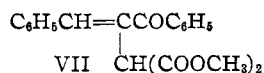
(5) L. I. Smith and R. E. Kelly, *ibid.*, **74**, 3305 (1952).

(6) L. I. Smith and V. A. Englehardt *ibid.*, **71**, 2671, 2676 (1949).

(7) This enol ether V has been reported by Weygand and Hennig, *Ber.*, **59**, 2249 (1946), to exist in two polymorphic forms, melting at 77–78° (needles) and 74–75° (plates). Morton, Hassan and Calloway, *J. Chem. Soc.*, **883** (1934), report three polymorphic forms, melting at 62°, 78° and 81°, respectively. Only the one form of V was obtained from Ia.

(8) Wislicenus, *Ann.*, **308**, 231 (1898); Andre, *Ann. chim. phys.*, [8] **29**, 582 (1913).

Seventeen experiments were conducted upon the reaction between sodiomalonic ester and the two isomers of I. Conditions were varied widely; in each of the experiments there was evidence (warming, color changes) of reaction, and in no experiment was any unchanged I recovered. The products were usually yellow, viscous oils which yielded no solid material, even after chromatographing. Several of these experiments were conducted in the absence of any alcohol, thus excluding formation of an enol ether; all of the oils resulting from the experiments in which alcohol was used were examined for the presence of an enol ether, and in no case was more than a trace found. In two experiments only was the pyrone VI isolated, and then in yields of only 4.1 and 5.6%, respectively. The pyrone VI was identified by comparison with an authentic specimen prepared by action of sodiomalonic ester upon benzoylphenylacetylene.⁹ In two other experiments a solid, $C_{20}H_{18}O_5$, melting at 142–144°, was formed in about 20% yield. This compound was unsaturated, and gave a 2,4-dinitrophenylhydrazone. It was therefore assigned structure VII and thus was formed from I by addition of malonic ester to the α,β -unsaturated nitro system, with subsequent elimination of the elements of nitrous acid.



Formation of the pyrone VI in such small yields, or failure to form it at all, was not caused by any instability of the pyrone VI under the conditions of the experiments, for a blank experiment in which the pyrone was subjected to these conditions for times extending from 15 minutes to 2.5 hours resulted in recovery of the pyrone in 91% yield.

Substitution of magnesiomalonic ester for sodiomalonic ester in the reaction with I produced no better results; there was evidence of a reaction, and no I was recovered, but the product was a viscous yellow oil from which no solid could be isolated. Substitution of sodiocyanoacetic ester for sodiomalonic ester gave similar results. Finally, malonic acid in dimethylformamide in the presence of acetic acid and triethylamine was without any action upon I, even after six hours.

Thus, with reference to the action of bases upon the β -nitro- α,β -unsaturated ketone I, it can be said that action of sodium ethoxide produces the enol ether of dibenzoylmethane, a 1,3-diketone, in fair yield, but that action of sodiomalonic ester produces only very small and non-reproducible yields of the pyrone VI, together with somewhat larger yields, equally non-reproducible, of compound VII. For the most part, the nitroketone I is converted into viscous oils, and none of it can be recovered.

Synthesis of 1,4-diphenyl-3-nitro-2-butene-1-one (II) followed a path analogous to that used for synthesis of I. Condensation of phenylglyoxal with β -phenylnitroethane in the presence of triethylamine led to a mixture of two stereoisomers of the nitro alcohol VIII. The higher melting isomer VIIIA was formed in much the larger amount; the lower melting isomer VIIIB was obtained in amounts too

small for detailed investigation. Action of acetic acid upon VIIIA converted it into the acetate IXa.



VIII, R = H: a, m.p. 133–134.5°; b, m.p. 87–88°

IX, R = Ac: a, m.p. 103.5–104°

Action of triethylamine upon IXa produced the nitro ketone II. The ketone II was obtained in two stereoisomeric forms: IIa, m.p. 104°, and IIb, m.p. 52°. The yield of II was small, and was not reproducible. Both isomers of II were unsaturated toward potassium permanganate and gave a positive test for the nitro group with ferrous hydroxide.¹⁰ Both forms of II were different from the isomer E obtained previously by Smith and Kelly, but in one form only. The spectra in the ultraviolet were different for the three compounds IIa, IIb and E. The known form of ketone E was obtained in one experiment in which the acetate IXa was subjected to action of triethylamine. Unfortunately not enough pure IIa or IIb could be obtained for complete proof of structure. However, of the four possible forms of ketones II and E, three have now been prepared and it follows that at least one of these must possess structure II. Although compound E reacted with sodiomalonic ester, the product was not a pyrone.⁴ Only enough of the ketone II was available for one small scale experiment; this was the higher melting isomer IIa. From 79 mg. of IIa there was obtained, by action of sodio malonic ester, about 2 mg. of the pyrone B. The greater part of the product was a red, uncrystallized oil.

The action of sodio malonic ester upon the nitro ketone II is thus similar to the action of the enolate upon the nitro ketone I. Both compounds are converted into α -pyrones, and II thus gives rise to the same α -pyrone (B) which results by action of the enolate upon the nitrocyclopropane (A). But the yield of α -pyrone from A exceeds by many times that from II; this fact indicates that although nitro ketones of type F (I and II) can give rise to α -pyrones by action of sodio malonic ester, such nitro ketones are not likely intermediates in the sequence whereby nitrocyclopropanes are converted into α -pyrones by this reagent.

Experimental Part¹¹

Phenylglyoxal, b.p. 81–83° (4 mm.), was prepared in 67% yield by the method of Riley and Gray.¹²

Phenylnitromethane, b.p. 78–81° (1 mm.), was prepared in 54% yield by the method of Black and Babers.¹³

1,3-Diphenyl-2-hydroxy-3-nitro-1-propanone (IIIa, IIIb).—Triethylamine (2.53 g., 0.025 mole) was added slowly to a cold (0°) solution of phenylnitromethane (68.5 g., 0.5 mole) in dry ether (100 cc.), and this solution was added, dropwise (two hours) and with stirring, to a solution of phenylglyoxal (67 g., 0.5 mole) in dry ether (500 cc.). The solution was stirred for three hours at 0° and for 14 hours at room temperature, after which it was washed with water (three 300-cc. portions) and dried (magnesium sulfate). The solvent was removed under reduced pressure, and the residual solid was crystallized from a mixture of benzene and cyclohexane.

(10) W. M. Hearon and R. G. Gustavson, *Ind. Eng. Chem., Anal. Ed.*, **9**, 352 (1937).

(11) Melting points are uncorrected. Microanalyses by D. Davis, D. Leister, R. Lockwood, O. Runquist, J. Swenson, E. Wheeler and B. Davis.

(12) "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 509.

(13) Reference 12, p. 512.

(9) E. P. Kohler, *THIS JOURNAL*, **44**, 379 (1922).

The product was white, weighed 88.3 g., and melted at 80–160° with effervescence. Concentration of the mother liquors yielded additional solid (10 g.) melting at 60–85°. The solids were combined (98.3 g., 72%) and fractionally crystallized from chloroform. A complete separation of the two isomers of III was not accomplished, but repeated crystallization of the less soluble portion of the mixture from chloroform gave the isomer IIIB as white needles melting at 174–176° with much sublimation. The mother liquors, when concentrated stepwise, yielded solid richer in IIIa; finally, the material remaining after removal of all the solvent, when crystallized from a very small amount of chloroform produced the isomer IIIa melting at 96–97°. The analytical samples were crystallized from cyclohexane, when they melted at 96–97° and 174–176°, respectively.

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83. Found: IIIa, C, 66.43; H, 5.25. IIIB, C, 66.56; H, 5.15.

The absorption spectra in the ultraviolet showed a broad maximum at 247–250 $m\mu$ (both isomers); the extinction coefficient of IIIa (5.13×10^{-5} M in 95% ethanol) was 12,700; that of IIIB (4.17×10^{-5} M in 95% ethanol) was 13,400.

1,3-Diphenyl-2-acetoxy-3-nitro-1-propanone (IVa, IVb).—Each isomer of III gave but one acetate IV; the two acetates were different. A solution of IIIB (1 g., 0.0037 mole, m.p. 174–176°) in dry benzene (20 cc.) containing acetic anhydride (0.4 g., 0.0037 mole) and a drop of sulfuric acid was refluxed for 30 minutes. The cooled solution was washed with water (four 20-cc. portions), dried (magnesium sulfate), and the solvent was removed under reduced pressure. The residual oil (1.2 g.) was dissolved in methanol and the solution was set aside in a refrigerator for 36 hours. The white solid (0.35 g.) melted at 77.0–77.5°; additional material (0.59 g., m.p. 73.5–78°) was obtained by concentration of the filtrate. The combined solid (0.94 g., 81%), when crystallized from petroleum ether (b.p. 60–68°), yielded white needles of IVb melting at 77.5–78°. This acetate was not stable; after standing for a few days, the product became yellow and the odor of acetic acid was observed.

In a similar manner, IIIa (1 g., m.p. 96–97°) was converted into the acetate IVa (0.62 g., 54%), which after crystallization from petroleum ether (b.p. 60–68°) melted at 100–101°. A mixture of IVa and IIIa melted at 88–98°. This acetate IVa also was not stable, but it decomposed more slowly than did IVb.

Anal. Calcd. for $C_{17}H_{15}O_5N$: N, 4.47. Found: IVa, N, 4.51. IVb, N, 4.41.

A mixture of IIIa and IIIB (79.1 g., 0.292 mole) was dissolved in benzene (250 cc.) containing acetic anhydride (49.7 g., 90%, 0.448 mole) and sulfuric acid (two drops); the solution was refluxed for 45 minutes, washed successively with water (two 100-cc. portions), aqueous sodium bicarbonate (0.2 N, two 100-cc. portions) and water (four 100-cc. portions), and dried (magnesium sulfate). Removal of the solvent under reduced pressure left an orange oil (89.7 g.); this was dissolved in hot methanol (100 cc.) and the solution was cooled. The solid was removed, pressed on a filter, washed with small amounts of cold methanol, and dried in an oven (50°) for several hours. The product weighed 83.4 g. (90%) and melted at 66–95°; the odor of acetic acid was quite pronounced.

β -Nitrobenzalacetophenone (I). **A. From a Mixture of the Acetates IVa and IVb.**—A mixture of the two isomers of IV (83.4 g., 0.266 mole) was dissolved in dry ether (750 cc.) containing triethylamine (26.9 g., 0.266 mole), and the solution was allowed to stand, with occasional shaking, at room temperature for 1.5 hours. The dark orange solution was washed successively with dil. sulfuric acid (5%, two 100-cc. portions), water (three 100-cc. portions), aqueous sodium bicarbonate (0.2 N, two 100-cc. portions) and finally with water (three 100-cc. portions). The solution was dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residual orange oil (70 g.) was crystallized from a mixture of benzene and cyclohexane; the solid (33.8 g.) formed light yellow needles melting at 91–95.5°. The solvent was removed from the filtrate and the residual oil was crystallized from cyclohexane; this resulted in additional yellow solid (24.4 g.) containing two crystalline forms—pale yellow needles and bright yellow plates. The mixture was dissolved in hot cyclohexane and the solution, when cooled and seeded with the yellow plates,

deposited the isomer Ib melting at 80–80.5°. Recrystallization of the light yellow needles (m.p. 91–95.5°) produced isomer Ia as long, pale yellow needles melting at 95–96°. No quantitative separation of the two isomers was made, but the higher melting form Ia was present in somewhat the larger amount. The combined yield of the two isomers was 58.2 g. (86.5%). The analytical sample of Ia, crystallized four times from ethanol, melted at 95–95.5°; that of Ib, crystallized from cyclohexane, melted at 80–80.5°.

Anal. Calcd. for $C_{15}H_{11}O_3N$: C, 71.14; H, 4.37; N, 5.53. Found: (Ia), C, 70.82; H, 4.30; N, 5.68; (Ib), C, 70.70; H, 4.42.

The infrared absorption spectra of the two isomers were different. That of Ib showed a strong absorption from 1500 to 1610 cm^{-1} , with a strong, broad peak from 1540 to 1555 cm^{-1} (nitro group?); somewhat weaker peaks at 1585 and 1605 cm^{-1} ; this spectrum also had a medium peak at 1690 cm^{-1} (conjugated carbonyl group?), and a shoulder on this peak at 1675 to 1685 cm^{-1} . The spectrum of Ia showed a single, sharp, strong peak at 1545 cm^{-1} (nitro group?), a much weaker, but sharp, peak at 1680 cm^{-1} (conjugated carbonyl group?), a peak of about the same intensity at 1620 cm^{-1} ; and a still weaker, but distinct peak at 1665 cm^{-1} . Although the absorptions at 1540 (Ib) and at 1545 cm^{-1} (Ia) were of about equal intensity, the absorption at 1690 cm^{-1} (Ib) was much stronger than that at 1680 cm^{-1} (Ia).

Both Ia and Ib reduced permanganate in acetone; both oxidized ferrous hydroxide.

The 2,4-dinitrophenylhydrazones of Ia and Ib were prepared in the usual manner. That of Ib, when crystallized three times from ethyl acetate, was orange-yellow and melted at 210–211°; that from Ia was much more difficult to purify and was pure only after its solution in ethyl acetate was passed through a column of alumina (well washed with ethyl acetate). A red band remained on the column; evaporation of the orange solution passing from the column, and crystallization of the resulting red oil from ethyl acetate-ethanol, produced the derivative of Ia melting at 191–192°.

Anal. Calcd. for $C_{21}H_{15}O_6N_5$: C, 58.20; H, 3.49; N, 16.16. Found: (derivative of Ib) C, 57.95; H, 3.46; N, 15.89. Found: (derivative of Ia) C, 57.49; H, 3.97; N, 16.06.

Action of semicarbazide upon Ia produced a substance which, after crystallization three times from ethanol, melted at 158–162°. The analytical values of this substance corresponded to those required by the expected semicarbazone plus a molecule of water.

Anal. Calcd. for $C_{16}H_{14}O_3N_4 \cdot H_2O$: C, 58.53; H, 4.91; N, 17.07. Found: C, 58.22; H, 4.94; N, 17.01.

B. From the Acetate IVb.—A solution of IVb (0.5 g.) in dry ether (50 cc.) containing triethylamine (0.16 g.) was allowed to stand, with occasional shaking, for 4.5 hours at room temperature. The solution was processed essentially as described under A above; the product, a greenish-yellow oil (0.4 g.) solidified when it was seeded with Ia. Recrystallization of the solid from cyclohexane gave Ia (0.15 g.), melting at 95–96° alone or when mixed with Ia from A. A second crop (0.1 g.) was obtained from the mother liquor; this melted at 54–62.5°. No Ib could be isolated from this (seed of Ib was not available when the experiment was performed) but Ib was undoubtedly present in the mixture.

C. From the Acetate IVa.—A duplicate of experiment B was performed using IVa. The product, a yellow oil (0.41 g.), when crystallized from cyclohexane, gave Ia (0.15 g.) melting at 94–96° alone or when mixed with Ia from A. A second crop (2.26 g.) was obtained from the mother liquor; this was yellow and melted at 50–90°, but at the time, no seed of Ib was available and Ib could not be isolated although it was undoubtedly present.

D. From Phenylglyoxal and Phenylnitromethane Directly.—Phenylnitromethane (13.7 g., 0.1 mole) and *n*-butylamine (1.5 g., 0.02 mole) were dissolved in dry dioxane (25 cc.) and to this solution was added a solution of phenylglyoxal (13.4 g., 0.1 mole) in dioxane. The solution was set aside at room temperature for 18 hours. Removal of the solvent under reduced pressure left a dark red oil (25.9 g.), which was dissolved in ether (100 cc.) and this solution was washed successively with dil. hydrochloric acid (5%, three 30-cc. portions), aqueous sodium hydroxide (5%, three 30-cc. portions) and water (three 50-cc. portions). The solution was dried (magnesium sulfate) and the solvent

was removed under reduced pressure. The residual orange oil (13.5 g.), on standing for several hours, deposited a yellow solid (3 g., 12%) which melted at 85–88°. Crystallization of this material from ethanol yielded Ia, melting at 95–96° alone or when mixed with Ia from A. No other solid material could be isolated.

E. Piperidino Adduct of I.—Piperidine (3 cc.) was added dropwise and with shaking to a cold (5°) solution of phenylglyoxal (3.8 g., 0.028 mole) and phenylnitromethane (3.0 g., 0.022 mole) in dry ethanol (10 cc.) containing acetic acid (2 drops). The solution, on standing overnight at 0–5°, deposited a yellow solid (3.5 g.). This solid, crystallized several times from cyclohexane, formed a pale yellow powder (1.1 g.) which melted at 142.5–144°. The structure was probably $C_6H_5COCH(NC_4H_9)CH(NO_2)C_6H_5$, but it was not investigated further.

Anal. Calcd. for $C_{20}H_{22}O_3N_2$: C, 70.98; H, 6.55; N, 8.28. Found: C, 71.00; H, 6.57; N, 8.58.

β -Ethoxybenzalacetophenone (V).—The nitroketone Ia (1 g., 0.004 mole) was added to a solution of sodium (0.14 g., 0.006 gram atom) in dry ethanol (10 cc.). An orange color developed at once, and a solid was deposited. The dark red mixture was allowed to stand for 70 minutes and was then poured into ice-water (50 cc.) and extracted with ether (three 40-cc. portions). The combined extracts were washed with water, dried (magnesium sulfate), and the solvent was removed under reduced pressure. The residual yellow oil solidified after standing for several hours. The solid (0.63 g., 62%, m.p. 70–76°) was removed and crystallized from cyclohexane, when it formed colorless flat prisms (0.5 g., 50%) melting at 78–80°.⁷

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.36. Found: C, 80.52; H, 5.76.

A small amount of V (0.08 g.) was dissolved in ethanol (1 cc.) containing hydrochloric acid (15%, 4 drops), and the solution was heated on the steam-bath for five minutes. Water (20 cc.) was added, and the solution was extracted with ether (two 10-cc. portions). The combined extracts were washed with water (three 10-cc. portions) and then shaken with saturated aqueous cupric acetate (10 cc.). The light green solid (0.8 g., 100%) melted at 323–325° dec.⁸

Methyl 4,6-Diphenyl-2-pyrone-3-carboxylate (VI).—A warm solution of sodio methyl malonate (sodium, 0.28 g., 0.012 gram atom; methyl malonate, 3.96 g., 0.03 mole) in methanol (5 cc.) was added dropwise (ten minutes) to a warm solution of I (95°, 2.53 g., 0.01 mole) in methanol (10 cc.). Heat was evolved; the red solution was allowed to cool to room temperature (15 minutes) and then was poured into ice-water (30 cc.). The yellow flocculent solid (0.17 g., 5.6%) melted at 132–135° alone or when mixed with authentic VI.⁹ The aqueous filtrate was acidified with acetic acid (0.8 g., 0.013 mole), extracted with ether (three 50-cc. portions), and dried (magnesium sulfate). Removal of the solvent under reduced pressure left a viscous yellow oil (2.0 g.) from which no solid material could be obtained. Repetition of the above experiment, but with addition of the solution of I to the solution of the enolate, led to isolation of VI (0.05 g., 4.1% melting at 128–132° alone or when mixed with authentic VI.⁹ The rest of the product was an uncrystallizable oil.

A solution of methyl malonate (2.6 g., 0.02 mole) in methanolic sodium methoxide (13 cc., 1 M) was added to a suspension of VI (2.0 g.) in methanol (25 cc.). The red suspension was warmed gently until solution was complete. Portions (about 10 cc.) were removed at intervals and added to acetic acid (0.21 g.). From the cooled solution, solid VI was isolated; dilution of the filtrate with water and extraction with ether produced more VI. Five portions were taken; the time interval was 15 to 150 minutes; the total VI recovered was 1.82 g. (91%). Thus, the very low yields of VI obtained from I were not caused by destruction of VI by the alkaline reagents.

Methyl 2-Carbomethoxy-3-benzoyl-4-phenyl-3-butenate (VII).—A warm solution of I (95°, 1.0 g., 0.004 mole) in methanol (10 cc.) was added dropwise (30 minutes) to a warm (steam-bath) solution of sodium (0.11 g., 0.005 gram atom) in methyl malonate (4.1 g., 0.03 mole). The mixture was heated on the steam-bath for one hour; water (80 cc.) was added and the mixture was extracted with ether (three 50-cc. portions) (Ether A). The aqueous layer was acidified with acetic acid (0.3 g.) and again extracted with

ether (two 50-cc. portions) (Ether B). The combined extracts B were washed with water (two 50-cc. portions), dried (magnesium sulfate), and the solvent was removed under reduced pressure. The viscous residual oil could not be crystallized. The combined extracts A were washed with water (two 100-cc. portions), dried (magnesium sulfate), and the solvent was removed under reduced pressure. The residual orange oil (1.24 g.) deposited colorless needles of VII (0.3 g., 22%) melting at 142–144°. In a duplicate of this experiment, except that the time of heating was twelve hours, VII was obtained in 20% yield. The analytical samples, crystallized from cyclohexane, melted at 145–146°.

Anal. Calcd. for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36. Found: C, 70.63; H, 5.01.

The substance reduced permanganate in acetone, and gave a precipitate with 2,4-dinitrophenylhydrazine. The oil (0.9 g.) remaining after removal of VII was separated into five parts by chromatography, but no solid material could be obtained from any of the fractions.

The four experiments described above, two leading to VI and two leading to VII, were the only ones out of 17 performed which led to any solid material. Time, temperature, solvent, relative amounts of reagents and base—all were varied, but only viscous yellow oils resulted. When triethylamine acetate was used as the catalyst, there was no reaction between I and malonic ester—practically all of the I used was recovered unchanged. Substitutions of magnesium malonic ester for sodiomalonic ester in reaction with I produced no better results; only a viscous yellow oil resulted. Action of sodiocyanoacetic ester upon I likewise produced nothing but a dark red oil.

β -Phenylethyl iodide, 140.3 g., b.p. 122–123° (13 mm.), was prepared in 60% yield essentially as described by Vogel,¹⁴ although the procedure was modified somewhat in accordance with the procedures of Hartman, Byers and Dickey, and of King.¹⁵

β -Phenylnitroethane, 17.2 g., b.p. 136–138° (16 mm.), n_D^{20} 1.5251, was prepared in 52% yield according to the method of Borsche and Barthenheier.¹⁶

1,4-Diphenyl-2-hydroxy-3-nitro-1-butanone (VIII).—Triethylamine (3.6 g., 0.036 mole) was added dropwise (15 minutes) to a cooled (ice-salt-bath) solution of β -phenylnitroethane (108 g., 0.72 mole) in dry ether (25 cc.), and this cold orange solution was then added dropwise (1.5 hours) and with stirring to a cold (ice-salt-bath) solution of phenylglyoxal (96.2 g., 0.72 mole) in dry ether (100 cc.). Cooling and stirring were continued for about two hours (until the mixture solidified); thereafter the mixture was allowed to stand at 0–5° for two hours. The solid (136 g., m.p. 130–133.5°) was collected and washed on the filter with cold ether. This was crude VIIa. Solvent was removed under reduced pressure from the combined filtrate and washings; additional solid (m.p. 109–125°) was removed, and acetic acid (2.25 g., 0.036 mole) and ether (75 cc.) were added to the filtrate. This solution was washed with water (four 75-cc. portions), dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residual oil (57 g.), when set aside in a refrigerator for three weeks, deposited 1.9 g. of solid melting at 135°. This was removed and the filtrate was diluted with a small amount of benzene-petroleum ether and again set aside in the refrigerator for three weeks. The solid (3.2 g., m.p. 130–133°) was removed (filtrate A) combined with the other solids, and the whole was recrystallized from cyclohexane. The product, VIIa, was white, melted at 134–135°, and weighed 97.5 g. (47.5%). The analytical sample, crystallized three times from cyclohexane, melted at 133–134.5°.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.59; H, 5.49; N, 4.72.

A portion of the filtrate A above was dissolved in benzene-petroleum ether (1:2, b.p. 60–68°) and the solution was poured through a column of activated silica gel (70 g.). The column was eluted successively with the mixed solvent (4 l.), a 1:1 mixture (2 l.), a 2:1 mixture (6 l.), 2:1 benzene-chloroform (500 cc.), chloroform (1 l.), 1:1 chloroform-ethanol (700 cc.) and finally ethanol. From the 2:1 ben-

(14) British Patent 565,452, Nov. 10, 1944.

(15) "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 322, 399.

(16) Borsche and Barthenheier, *Ann.*, **553**, 250 (1942).

zene-petroleum ether eluate there was isolated 1.1 g. of solid melting at 84–87° (VIIIb). The analytical sample, crystallized twice from cyclohexane, melted at 87–88°.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.07; H, 5.54; N, 5.00.

The other eluates yielded only benzoic acid, small amounts of VIIa and oils. The ultraviolet spectra of the two isomers were very similar: that of VIIa (4.03×10^{-5} M in 95% ethanol) showed a maximum at 249 m μ , ϵ 12,900; that of VIIb (4.17×10^{-5} M in 95% ethanol) showed a maximum at 248 m μ , ϵ 13,000.

1,4-Diphenyl-2-acetoxy-3-nitro-1-butanone (IXa).—Only the higher melting form VIIa was converted into the acetate, for insufficient VIIIb was obtained for investigation. A solution of VIIa (10 g., 0.035 mole) in dry benzene (150 cc.) containing acetic anhydride (4.0 g., 0.035 mole) and sulfuric acid (one drop) was warmed on the steam-bath for 30 minutes. The cooled solution was poured into water (150 cc.), the organic layer was removed, washed with water (three 100-cc. portions), dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residual oil, when crystallized from methanol, yielded white plates of IXa (11 g., 96%) melting at 103–104°. The analytical sample, crystallized twice from methanol, melted at 103.5–104°. The ultraviolet absorption spectrum of IXa (4.63×10^{-5} M in 95% ethanol) showed a broad maximum at 247–250 m μ , ϵ 11,400.

Anal. Calcd. for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.24; N, 4.28. Found: C, 66.28; H, 5.61; N, 4.38.

1,4-Diphenyl-3-nitro-2-butene-1-one (II).—The acetoxy compound IXa (1 g.) and lithium chloride (3 equiv.) were suspended in ether (225 cc.) containing triethylamine (1 equiv.), and the mixture was allowed to stand at room temperature for six hours with occasional shaking. The mixture was washed twice with hydrochloric acid (5%), then with water, and dried (magnesium sulfate). The solvent was removed under reduced pressure; the residual oil, fractionally crystallized from cyclohexane, yielded IIa (0.08 g.), IIb (0.1 g.), a mixture of IIa and IXa (0.5 g.) and a yellow oil (0.3 g.). The experiment described here was one of a series of nineteen such experiments in which the amount and nature of the base, time, temperature, solvent, and order of mixing the reagents were all varied. Only when trimethylamine was used was any IIa or IIb produced; always there was recovered some IXa, which was extremely difficult to separate from II. Once seed of IIa and IIb were available, isolation of these from the reaction product was facilitated, although it was never easy or clean-cut; however, when the reactions were continued until all of the IXa was consumed, the products were oils from which no solids could be isolated.

The analytical sample of IIa, crystallized from cyclohexane, melted at 104–104.5°. The analytical sample of IIb,

crystallized (Dry Ice bath) first from ether and then from petroleum ether (b.p. 60–68°), melted at 53.5–54°.

Anal. Calcd. for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: IIa, C, 71.77; H, 5.18; N, 5.11. Found: IIb, C, 71.26; H, 5.14; N, 5.42.

Both IIa and IIb decolorized an acetone solution of potassium permanganate; both compounds oxidized ferrous hydroxide. The ultraviolet spectra of the two compounds were different. That of IIa (5.85×10^{-5} M in 95% ethanol) showed a maximum at 243 m μ , ϵ 22,500; that of IIb (5.02×10^{-5} M in 95% ethanol) showed a maximum at 245–250 m μ , ϵ 13,000.

In one experiment the β , γ -isomer (E) of II was produced from IXa. A solution of IXa (1 g.) in cyclohexane (100 cc.) was refluxed while a solution of triethylamine (1 equiv.) in cyclohexane (50 cc.) was slowly (2.5 hours) added. The reaction mixture, processed as above, yielded 0.3 g. of E, m.p. and mixed m.p. 98°. A mixture of E and IIa melted at 90–98°.

Ethyl 4-Benzyl-6-phenyl-2-pyrone-3-carboxylate (B).—A solution of sodioethyl malonate (from sodium, 0.024 g., and ethyl malonate, 0.189 g.) in dry ethanol (4 cc.) was refluxed through a small Soxhlet apparatus, the cup of which contained IIa (0.08 g.). After all the IIa had dissolved, the dark orange solution was refluxed for one hour, then cooled, acidified with acetic acid (0.062 g.), and allowed to stand for four hours at 5°. The white solid (0.05 g., inorganic) was removed; the filtrate was diluted with water (4 drops), seeded with a tiny crystal of B, and allowed to stand for 12 hours at 5°. As no crystallization occurred, the solvent was removed under reduced pressure, the residual oil (0.02 g.) was taken up in a little ether, and this solution was poured onto a column (1 \times 20 cm.) of activated alumina which had been thoroughly washed with ethyl acetate and then with petroleum ether (b.p. 60–68°). The column was developed and eluted successively with mixtures of ether-petroleum ether (b.p. 60–68°) as follows: 1:9 mixture, 50 cc., 25 cc., 25 cc.; 1:4 mixture, 25 cc., 25 cc., 50 cc.; 3:7 mixture, 25 cc., 25 cc., 50 cc. These nine fractions were followed by two of ether alone (50 cc. each). No definite bands were observed on the column; each of the fractions (except the last), upon removal of the solvent, left a small amount of viscous oil. Each of these ten oils was dissolved in a drop or two of methanol; the solution of the second fraction, when cooled, deposited a yellow solid (2 mg.) which melted at 123–126°. A mixture of this substance with authentic B (m.p. 128–129°), melted at 123–128°. None of the other solutions yielded any solid material. The solution of the third fraction was saturated with dry ammonia, but no solid (pyridone) could be isolated; the only product was a dark red gum.

MINNEAPOLIS 14, MINNESOTA

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

The Rupe Rearrangement of 2,6-Dimethyl-2-carbethoxy-1-(phenylethynyl)-cyclohexanol (II) and 2,6-Dimethyl-2-carbethoxy-1-(3-isopropylphenylethynyl)-cyclohexanol (III)

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RECEIVED APRIL 26, 1954

The Rupe rearrangement of the acetylenic carbinols II and III has been studied, and chemical and spectral evidence for the course of the reaction has been obtained. The principal products from these reactions are cyclic lactones to which the configurations shown in formulas VIIa and VIIb, and XIIa and XIIb, have been tentatively assigned. The synthesis of *m*-isopropylphenylacetylene is described.

Our interest in developing a synthetic method, subject to steric control, for 1-carboxy-12-alkylotetrahydrophenanthrenes, has prompted us to investigate the Rupe rearrangement of the acetylenic car-

(1) From the Ph.D. Thesis of Edward L. Wheeler, University of Minnesota (1953).

(2) Parke, Davis Fellow (1952–1953). Part of this work was sponsored by the Greater University Fund of the University of Minnesota.

binols II and III. The results of this investigation constitute the subject of this report.

The acetylenic alcohols II and III were prepared in 50 and 56% yields, respectively, by the reaction of the Grignard reagent, prepared from the corresponding phenylacetylene, with 2,6-dimethyl-2-carbethoxycyclohexanone (I).