ment with each other and with the samples dehalogenated with KOH.[14]

Acknowledgment.—The considerable number of microanalyses on which this work is based were done by Mr. Murray E. Taylor assisted by Miss M. Styslinger, and by Mr. Werner Manser, Zürich (carbon and hydrogen, and some of the sulfur and bromine analyses).

SEATTLE, WASHINGTON

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

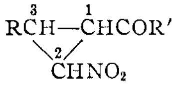
Cyclopropanes. X.[1] The Reaction between Nitrocyclopropyl Ketones and Sodio Malonic Ester

BY LEE IRVIN SMITH AND RALPH E. KELLY[2]

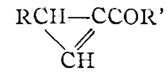
RECEIVED JANUARY 7, 1952

1-Benzoyl-2-nitro-3-phenylcyclopropane I has been subjected to the action of (a) sodio malonic ester and (b) sodium methoxide. Action of the former reagent produced the α-pyrone ester II; action of the latter reagent produced the methyl enol ether VI of the 1,3-diketone VII. Action of sodio malonic ester upon either the enol ether VI or the 1,3-diketone VII failed to produce any α-pyrone; hence, neither of these substances can be a precursor of the α-pyrone formed from I and sodio malonic ester. In an effort to correlate the formation of the pyrone with the mechanism of Smith and Engelhardt (ref. 5), the unsaturated nitro ketone IX has been prepared and subjected to the action of sodio malonic ester. This nitro ketone IX is so constituted that the double bond is α,β- with reference to the nitro group, but is β,γ- with reference to the carbonyl group. Although IX reacts with sodio malonic ester, the products are derived by addition of the reagent to IX acting as an α,β-unsaturated nitro compound, and no α-pyrone is formed. Hence, IX cannot be a precursor of the α-pyrone formed from I. The one remaining compound in the sequence proposed by Smith and Engelhardt which could be the precursor of the α-pyrone is the nitro ketone X which differs from IX in that the double bond is α,β-with reference to both the nitro group and the carbonyl group. A successful synthesis of X was not achieved.

The reaction between nitrocyclopropyl ketones (A) and alkoxides produces, as the first isolable products, enol ethers of 1,3-diketones (B). To account for these products, Kohler and Smith[3] proposed that the initial step in the reaction involved conversion of the nitrocyclopropane, by loss of the elements of nitrous acid, into a cyclopropene (C). The cyclopropene then rearranged into an α,β-acetylenic ketone (D) which, by addition of the solvent alcohol, was converted into (B).



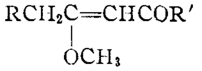
A



C

RCH$_2$C≡CCOR'

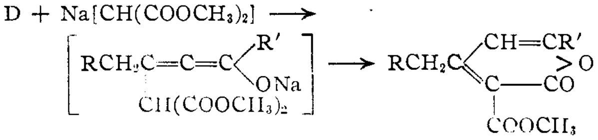
D



$$\begin{array}{l}\mathrm{RCH_2C{=}CHCOR'}\\ \qquad|\\ \qquad\mathrm{OCH_3}\end{array}$$

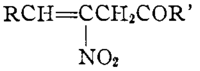
B

Although neither the cyclopropene nor the acetylenic ketone could be isolated, support for the mechanism was obtained when it was found that action of sodio malonic ester upon (A) led to an α-pyrone (E),[3] for it had been shown previously[4] that α,β-acetylenic ketones did in fact react with sodio malonic esters with production of these α-pyrones.



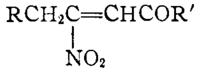
E

In previous papers of this series[5] it has been shown that an acetylenic ketone is not a likely intermediate in the transformation of a nitrocyclopropyl ketone into the enol ether of a 1,3-diketone, and a new mechanism for this transformation was suggested. One of the key intermediates of this mechanism was the β-nitro-β,γ-unsaturated ketone (F), formed from (A) by a "reverse Michael" reaction; by assuming, for (F), reasonable shifts of the double bond and replacement of the nitro group by the anion (OR$^-$) of a base, it was possible to account for the formation of the enol ethers actually isolated when several nitrocyclopropyl ketones reacted with alkoxides. This same intermediate (F) could also be the precursor of the α-pyrones when nitrocyclopropyl ketones react with sodio malonic ester; thus, a shift of the double bond in (F) into the α,β-position (G), followed by replacement of the nitro group by the malonate anion, would lead to (H) and thence to the α-pyrone (E).



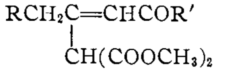
$$\begin{array}{l}\mathrm{RCH{=}CCH_2COR'}\\ \qquad|\\ \qquad\mathrm{NO_2}\end{array}$$

F



$$\begin{array}{l}\mathrm{RCH_2C{=}CHCOR'}\\ \qquad|\\ \qquad\mathrm{NO_2}\end{array}$$

G



$$\begin{array}{l}\mathrm{RCH_2C{=}CHCOR'}\\ \qquad|\\ \qquad\mathrm{CH(COOCH_3)_2}\end{array}$$

H

In order to test these ideas the behavior of 1-benzoyl-2-nitro-3-phenylcyclopropane (I) toward sodio malonic esters and other bases has been examined. This cyclopropane was synthesized according to the method of Kohler and Engelbrecht[6]; the yield in the final cyclization was, however, only 33% as compared with 61% reported by the earlier workers. When the cyclopropane I was subjected to action of excess sodio methyl or ethyl malonate, the respective 3-carbalkoxy-4-benzyl-6-phenyl-α-

---

(1) Paper IX, L. I. Smith and E. R. Rogier, THIS JOURNAL, **73**, 4019 (1951).

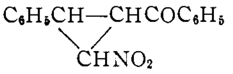
(2) Abstracted from a thesis by Ralph E. Kelly, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, August, 1951. du Pont Fellow, 1950–1951.

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

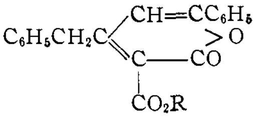
(4) E. P. Kohler, *ibid.*, **44**, 379 (1922).

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

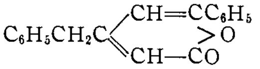
(6) E. P. Kohler and H. F. Engelbrecht, *ibid.*, **41**, 1381 (1919).



I



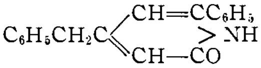
IIa, R = CH_3; b, R = C_2H_5; c, R = *p*-phenylphenacyl
III, R = H



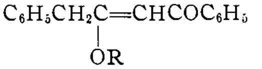
IV

pyrones (IIa) and (IIb) were produced in 33% yields. From the mother liquor, after action of dilute hydrochloric acid, a small amount (16%) of the 1,3-diketone, phenacetylacetophenone (VII), was isolated as the copper enolate. Isolation of this substance from the reaction product was significant, for it indicated that the enol ether VI of the diketone was formed from I in competition with formation of the pyrone II and hence that the pyrone was not derived from the enol ether of the diketone.

Either pyrone ester IIa or IIb could be converted into the pyrone acid III by mild alkaline hydrolysis.[7] This acid was characterized by conversion to a *p*-phenylphenacyl ester (IIc) and by decarboxylation to 4-benzyl-6-phenyl-α-pyrone (IV). Action of methanolic ammonia at room temperature[3] converted the ester IIa into 4-benzyl-6-phenyl-2-pyridone (V) in 47% yield. Neither the carbomethoxy-α-pyrone IIa, nor the pyrone IV gave a solid Diels–Alder adduct when refluxed in xylene with maleic anhydride.



V



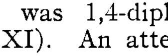
$$C_6H_5CH_2\underset{OR}{C}{=}CHCOC_6H_5$$

VI
a, R = CH_3;
b, R = C_2H_5

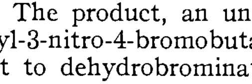
$C_6H_5CH_2COCH_2COC_6H_5$
VII

Since the enol ether VIa, 1,4-diphenyl-3-methoxy-2-butene-1-one, had not been isolated by Kohler and Engelbrecht[6] as a product of the reaction between the cyclopropane I and sodium methoxide, this reaction was repeated, using the procedure of Smith and Engelhardt.[5] The product VIa, obtained in 47% yield, melted at 43° and was converted into the 1,3-diketone VII by action of dilute acid. This diketone gave a copper enolate melting at 196–198°; but since Bulow and Grotowsky[8] reported that this copper enolate melted at 117°, the diketone VII was synthesized from acetophenone and ethyl phenylacetate by action of lithium amide.[9] The copper enolate from the synthetic diketone melted at 200°, alone or when mixed with that obtained from VIa. Ozonolysis of the enol ether VIa produced methyl phenylacetate, identified by conversion to phenylacetic acid, thus locating the double bond in VI as α,β- to the carbonyl group. Action of sodio ethyl malonate in boiling ethanol upon VIa did not produce the α-pyrone IIb; the only reaction was replacement of the methoxyl group by ethoxyl with production of the enol ether VIb. The ethoxy compound was identified by its positive reaction toward 2,4-dinitrophenylhydrazine and toward permanganate in acetone, and its conversion, by action of acid, into the diketone VII in 90% yield. The lack of reactivity of VIa toward sodio malonic ester was surprising, for Basu has reported[10] that enol ethers of β-diketones are converted, by action of cyanoacetamide, into 3-cyano-2-pyridones—a reaction completely analogous to the conversion of enol ether VIa into an α-pyrone by action of sodio malonic ester. In any event, it follows from this result that *the enol ether VIa is not a precursor of the α-pyrone ester IIb* formed when the nitrocyclopropyl ketone I reacts with sodio ethyl malonate. *Nor can the β-diketone VII itself be the precursor of the α-pyrone,* for sodio methyl malonate in boiling ethanol was without action upon VII (88% recovery). This lack of reactivity of the β-diketone was also surprising, for although there are no reports in the literature concerning a reaction between β-diketones and sodio malonic ester, there are several reports[11] that β-diketones react with cyanoacetic ester or cyanoacetamide with production of pyridones.

The remaining compounds in the reaction sequence of Smith and Engelhardt and which could be the precursor of the α-pyrone, are the unsaturated nitro compounds IX and X. Following in general

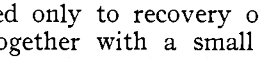


VIII



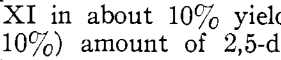
$$C_6H_5CH{=}\underset{NO_2}{C}CH_2COC_6H_5$$

IX



$$C_6H_5CH_2\underset{NO_2}{C}{=}CHCOC_6H_5$$

X



$$C_6H_5CHBr\underset{NO_2}{C}HCH_2COC_6H_5$$

XI

the procedure of Kohler and Engelbrecht[6] the nitrocyclopropyl ketone I was subjected to the action of hydrogen bromide. The product, an unstable solid, was 1,4-diphenyl-3-nitro-4-bromobutane-1-one (XI). An attempt to dehydrobrominate XI by action of methanolic potassium acetate at 0°[12] led only to recovery of XI in about 10% yield, together with a small (10%) amount of 2,5-diphenylfuran[6] (VIII). When the dehydrobromination was carried out at a lower temperature, there resulted in 30% yield a solid, $C_{17}H_{16}O_2$ (XII), melting at 98–98.5°. This material was unsaturated toward permanganate, formed a 2,4-dinitrophenylhydrazone and gave an absorption curve in the ultraviolet with a maximum at 260 mμ, characteristic of α,β-unsaturated ketones. The substance XII was therefore 1,4-diphenyl-4-methoxy-2-butene-1-one and was doubtless formed from XI *via* IX and addition of the elements of methanol to the latter with elimination of the elements of nitrous acid—a reaction for which there are many analogies in the literature.[13] The dehydrobromination of

---

(7) C. L. Bickel, THIS JOURNAL, **72**, 1022 (1950).

(8) C. Bulow and H. Grotowsky, *Ber.*, **34**, 1483 (1901).

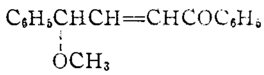
(9) G. R. Zellars and R. Levine, *J. Org. Chem.*, **13**, 162 (1948).

(10) U. Basu, *J. Indian Chem. Soc.*, **7**, 481; **8**, 119, 319 (1930).

(11) (a) J. L. Simonsen and M. Hayak, *J. Chem. Soc.*, 792 (1915); (b) G. Issoglio, *Atti. reale accad. sci. Torino*, **40**, 495 (1905); (c) J. C. Bardhan, *J. Chem. Soc.*, 2223 (1929); (d) U. Basu, *J. Indian U. Chem. Soc.*, **7**, 815 (1930); also ref. 10.

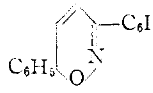
(12) E. P. Kohler and M. S. Rao, THIS JOURNAL, **41**, 1697 (1919).

(13) (a) P. Friedlander and J. Mahly, *Ann.*, **229**, 210 (1885); (b) P. Friedlander and M. Lazarus, *ibid.*, **229**, 233 (1885); (c) B. Flurscheim, *J. prakt. Chem.*, [2] **66**, 16 (1902); (d) K. W. Rosenmunde, *Ber.*, **46**, 1034 (1913); (e) J. Meisenheimer and F. Heim, *ibid*, **38**, 466, (1905); (f) H. Wieland, *Ann.*, **328**, 233 (1903); (g) A. Lambert, C. W. Scaife and S. E. Wilder-Smith, *J. Chem. Soc.*, 1474 (1947).

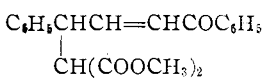


$C_6H_5CH(OCH_3)CH{=}CHCOC_6H_5$

XII

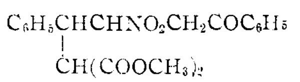


XIII



$C_6H_5CH(CH(COOCH_3)_2)CH{=}CHCOC_6H_5$

XV



$C_6H_5CH(CH(COOCH_3)_2)CHNO_2CH_2COC_6H_5$

XVI

XI was finally achieved by action of pyridine in refluxing chloroform or cyclohexane[14] and IX was formed in 68–70% yields. The analytical values for IX were consistently low when the substance was recrystallized from methanol or ethanol, but when IX was crystallized from cyclohexane it gave proper analytical values. However, action of refluxing methanol or ethanol upon IX for a day was without any perceptible effect other than the slight change in the analytical values. When a base, such as sodium methoxide, was added, there was considerable reaction in the cold, but it was not possible to isolate any pure compounds from the resulting red paste. The nitroketone IX was unsaturated toward permanganate, gave a positive test for the nitro group with alkaline ferrous sulfate, and gave a 2,4-dinitrohydrazone. The ultraviolet absorption spectrum of IX showed maxima at 300 and 243 mμ; the curves for the model compounds, β-methyl-β-nitrostyrene[15] and acetophenone[16] exhibit maxima at 305 and 226 and 243 mμ respectively. The spectrum of IX was therefore roughly the sum of the spectra of the two model compounds. Action of hydroxylamine hydrochloride in pyridine converted IX into a derivative $C_{16}H_{13}NO$ (XIII) which was, however, not a simple oxime of IX. This substance was unsaturated toward permanganate, and reacted with bromine by substitution, and although it was not examined in great detail, its properties agree well with structure XIII, a 1,2,6-oxazine resulting from intramolecular cyclization of the oxime of IX with elimination of the elements of nitrous acid.

The nature of the products resulting from action of sodio methyl malonate upon the nitroketone IX depended upon the temperature at which the reaction was carried out. At room temperature, without cooling—conditions which produced the α-pyrone IIa from the cyclopropane I—only a small amount (10%) of crystalline material could be isolated. This substance XIV, which was not identified, had the composition $C_{20}H_{15}NO_4$, melted at 143.5–144°, slowly reduced permanganate in acetone, and, by action of 2,4-dinitrophenylhydrazine, was converted into a 2,4-dinitrophenylhydrazone melting at 176° identical with those derived from compounds XV and XVI. When the reaction between IX and sodio methyl malonate was carried out at $-5°$, the product was the unsaturated δ-keto ester XV. This substance was unsaturated toward permanganate, gave a 2,4-dinitrophenylhydrazone melting at 178° and identical with those derived from XIV and XVI. The ultraviolet absorption spectrum of XV showed a maximum at 258 mμ characteristic of α,β-unsaturated aryl ketones. When the reaction between IX and sodio methyl malonate was carried out at $-20°$, the product, formed in 65% yield, was the nitroketoester XVI formed by direct addition of the malonic ester to the α,β-unsaturated nitro grouping in IX. The 2,4-dinitrophenylhydrazone derived from XVI was identical with those derived from XIV and XV—thus formation of this derivative from XVI is accompanied by loss of the elements of nitrous acid.

Thus it has been established that, although the β,γ-unsaturated-β-nitro ketone IX reacts readily with sodio methyl malonate, it behaves in this reaction as an α,β-unsaturated nitro compound and no α-pyrone is found among the products. *Hence the nitroketone IX is not the precursor of the α-pyrone IIb.* There remains, in the reaction sequence of Smith and Engelhardt, only the nitro compound X as a possible precursor of the α-pyrone. Experiments aimed at the synthesis of X or similar compounds are under way.

Experimental Part[17]

1-Benzoyl-2-nitro-3-phenylcyclopropane (I).—The nitrocyclopropane (86.4 g., m.p. 97–98°) was prepared from benzalacetophenone (297 g.) and nitromethane (128 g.).[6,18] The intermediate nitro ketone was converted into the α-bromo compound; no separation of the stereoisomeric α-bromo ketones was made, but the mixture was converted directly to the cyclopropane by action of methanolic potassium acetate.

3-Carbomethoxy-4-benzyl-6-phenyl-α-pyrone (IIa).—Sodium (1.51 g., 0.066 gram atom) was added to a solution of methyl malonate (9.93 g., 0.075 mole) in dry methanol (150 cc.). The flask was equipped with a soxhlet extractor, the cyclopropane I (5 g., 0.02 mole) was placed in the thimble, and the solution was refluxed for one hour. The deep red solution was acidified with acetic acid (3.95 g., 0.066 mole), set aside in a refrigerator, and seeded. The solid was removed, washed with cold methanol, and dried. It weighed 1.95 g. (33%) and melted at 111–113°. The yield of IIa was about the same when dioxane was substituted for methanol as the solvent; the product, however, had a somewhat higher melting point—113–114.5°. When the cyclopropane I was added all at once to the solution of sodio methyl malonate and the mixture was warmed gently until it was homogeneous, then cooled and acidified, IIa was obtained in 16% yield. After removal of this solid, solvent was removed from the filtrate and the residue was refluxed for 10 minutes with methanol (8 cc.) and hydrochloric acid (1.6 cc.). The solution was diluted with water and extracted with ether; the extract was washed with water, evaporated, and the residue was taken up in a little (1 cc.) methanol. Hot, saturated aqueous cupric acetate was added; the copper enolate (0.61 g., 15%) was removed and crystallized from benzene. It melted at 203–204° alone or when mixed with the copper enolate prepared from phenacetylacetophenone VII.

The pyrone IIa gave no color with aqueous–alcoholic ferric chloride, and was recovered unchanged when refluxed with maleic anhydride in toluene. The analytical sample, crystallized three times from methanol, melted at 112°.

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 75.0; H, 5.04. Found: C, 74.8; H, 5.35.

3-Carbethoxy-4-benzyl-6-phenyl-α-pyrone (IIb).—This was prepared as described for IIa above from I (5 g., 0.02 mole), sodium (1.51 g., 0.066 gram atom), ethyl malonate (12 g., 0.075 mole) and dry ethanol (150 cc.). The crude product weighed 3.3 g.; after crystallization from ethanol, it formed long yellow needles (2.1 g., 33%) melting at 122–123°. The analytical sample, recrystallized from ethanol and then from benzene–petroleum ether (b.p., 68–70°), melted at 124.5–125.2°.

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.5; H, 5.43. Found: C, 75.0; H, 5.38.

---

(14) J. L. Bleasdale, Ph.D. Thesis, University of Minnesota, 1950.

(15) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 298 (1945).

(16) E. A. Braude, *Ann. Reports*, **42**, 126 (1945).

(17) Microanalyses by Wm. Cummings, Bob K. Davis, L. Errede, H. Turner and E. Wheeler.

(18) E. P. Kohler, THIS JOURNAL, **38**, 889 (1916).

3-Carboxy-4-benzyl-6-phenyl-α-pyrone (III).—Sodium hydroxide (0.103 *N*, 58 cc., 0.006 mole) was added dropwise (30 minutes) to a solution of the ester IIa (1.87 g., 0.006 mole) in acetone (60 cc., C.P.). The solution was allowed to stand for one hour, then was poured into water and extracted with ether (four 100-cc. portions). The extracts were discarded, the aqueous solution was warmed to expel dissolved ether, then cooled, acidified with dilute hydrochloric acid, and set aside in a refrigerator. The solid (1.4 g., 79%, m.p. 144–145°) was removed and crystallized from methanol, when it formed square, yellow platelets melting at 145.5–147°.

Anal. Calcd. for $C_{19}H_{14}O_4$: C, 74.6; H, 4.61. Found: C, 74.3; H, 4.90.

The *p*-phenylphenacyl ester (IIc), prepared by the method of Shriner and Fuson[19] and crystallized several times from benzene, melted at 195.5–196°.

Anal. Calcd. for $C_{33}H_{24}O_5$: C, 79.2; H, 4.83. Found: C, 78.9; H, 4.82.

4-Benzyl-6-phenyl-α-pyrone (IV).—The acid III (1 g.) was placed in a 25-cc. round-bottomed flask and the flask was immersed in a metal bath at 140°. The temperature was slowly raised to 175°, evolution of gas began and this was complete after five minutes at 175°. The orange-brown, glassy solid was cooled and recrystallized from methanol (20 cc.). The product (0.57 g., 67%) formed yellow needles melting at 130–131.5°. The analytical sample was recrystallized three times from methanol and once from petroleum ether (b.p. 68–70°); it formed pale yellow needles melting at 131–132°.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.4; H, 5.34. Found: C, 82.8; H, 5.48.

The pyrone was recovered unchanged when it was refluxed for seven hours with maleic anhydride in xylene.

4-Benzyl-6-phenyl-2-pyridone (V).—The powdered pyrone ester IIa (2.05 g., 0.006 mole) was added to a saturated solution of ammonia in dry methanol (25 cc.). The flask was tightly stoppered, shaken mechanically for two hours, and then allowed to stand for three hours. Ammonia and methanol were removed in a current of dry air, and the residual solid was crystallized from methanol. The substance weighed 0.96 g. (57%) and melted at 180–185°. Repeated crystallization from chloroform–methanol or from benzene–petroleum ether (b.p. 68–70°) failed to give a better product, so the material was sublimed at 160–170° (0.3 mm.). It then melted at 195–198°.

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.7; H, 5.78; N, 5.36. Found: C, 82.7; H, 5.87; N, 5.73.

The pyridone gave an orange color with aqueous alcoholic ferric chloride.

1,4-Diphenyl-3-methoxy-2-butene-1-one (VIa).—The powdered cyclopropane I (20 g., 0.075 mole) was added all at once to a stirred and cooled (ice–salt-bath) solution of sodium methoxide (from sodium, 6.9 g., and dry methanol, 80 cc.). After two hours, the cooling bath was removed, the solution was allowed to come to room temperature, and was poured into ice-water (100 cc.) and extracted with ether (three 75-cc. portions). The combined ether extracts were washed with aqueous sodium bicarbonate (5%) and water, dried (magnesium sulfate) and the solvent was removed. The residual dark oil gave a distillate (8.82 g., 47%) boiling at 170–174° (0.1 mm.). A solution of this distillate in methanol, when cooled, deposited the methoxy compound as a solid melting at 43°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.39. Found: C, 80.5; H, 6.68.

Ozonolysis.—The enol ether VIa (3 g., 0.012 mole) in ethyl bromide (150 cc.) was subjected to the action of a slight excess of ozonized oxygen (0.043 mole ozone per hour) at the temperature of iced hydrochloric acid. Most of the ethyl bromide was removed under reduced pressure, and the remaining solution was added dropwise to a distilling mixture of water (100 cc.), zinc dust (1.5 g.), a few crystals of hydroquinone, and a few drops of aqueous silver nitrate (5%). Distillation was continued until 50 cc. of water was collected. The distillate was extracted with ether, the extract was dried (magnesium sulfate) filtered and evaporated. The residue, when distilled, gave a neutral liquid (0.7 g., 38%) boiling at 180–195°. This was methyl phenylacetate, identified by hydrolysis to phenylacetic acid, m.p. and mixed m.p., 75–77°.

1,4-Diphenyl-3-ethoxy-2-butene-1-one (VIb).—A solution of VIa (3.82 g., 0.015 mole) in dry ethanol (50 cc.) was added dropwise (30 minutes) to a refluxing solution of sodio ethyl malonate (sodium 1.22 g., 0.053 gram atom; ethyl malonate 9.8 g., 0.06 mole) in dry ethanol (150 cc.). After one hour, the orange solution was acidified with acetic acid (3.2 g., 0.053 mole), filtered, and the solvent was removed from the filtrate under reduced pressure. The residue was poured into water (200 cc.), the mixture was extracted with ether (three 50-cc. portions), the combined extracts were washed with water, dried (magnesium sulfate) and the solvent was removed. Ethyl malonate was removed by distillation and the residue was crystallized from ethanol (20 cc.). It formed light yellow prisms (2.4 g., 60%) melting at 70–73°. The analytical sample, recrystallized from ethanol and then from petroleum ether (b.p. 68–70°) melted at 72.5–73°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.82. Found: C, 80.9; H, 6.91.

No pyrone could be isolated from the above reaction product. The ethoxy compound VIb decolorized permanganate, formed a precipitate with 2,4-dinitrophenylhydrazone, and was converted into the diketone VII (0.79 g., 90%, m.p. and mixed m.p. 52–52.5°) when it (1 g.) was refluxed for one hour with methanol (10 cc.) containing hydrochloric acid (1 cc.).

1,4-Diphenylbutane-1,3-dione (VII) and its Copper Enolate. A.—The methoxy compound VIa (0.3 g., 0.0012 mole) was refluxed with methanol (0.7 cc.) and hydrochloric acid (0.2 cc.) for five minutes. The solution was diluted with ice-water and extracted with ether. The extract was washed with water until neutral, the solvent was removed, and the residue was dissolved in methanol (1 cc.). To this was added a hot saturated aqueous solution (8 cc.) of cupric acetate. The product separated as an oil which crystallized when rubbed. The solid was removed, washed with water and petroleum ether, dried and crystallized from benzene. It formed fine gray-green needles (0.2 g., 30%) melting at 196–198°.

B.—The diketone VII was prepared from acetophenone (24 g., 0.2 mole), ethyl phenylacetate (65.6 g., 0.4 mole) and lithium amide (9.2 g., 0.4 mole) according to the procedure of Zellars and Levine.[9] The crude diketone was purified by way of the copper enolate; the product (9.1 g., 19%) formed heavy yellow prisms melting at 52.5°. The literature gives the m.p. as 54°.[6] From the pure diketone, the copper enolate was prepared and crystallized five times from benzene. It then melted at 200–201°, alone or when mixed with the sample prepared from the enol ether VI.

Anal. Calcd. for $C_{32}H_{26}O_4Cu$: C, 71.4; H, 4.87. Found: C, 71.3; H, 5.02.

The powdered diketone (5 g., 0.02 mole) was added to a solution of sodio methyl malonate (sodium, 0.65 g., 0.028 mole; methyl malonate, 3.86 g., 0.028 mole) in dry methanol (45 cc.) at room temperature. There was no evidence of any reaction; the solution was then refluxed for 15 minutes (no color change), acidified with acetic acid (1.71 g., 0.028 mole) and set aside in a refrigerator. The solid (4.4 g., 88%) melted at 51–52° alone or when mixed with the diketone VII. No pyrone could be isolated from the reaction product.

1,4-Diphenyl-3-nitro-4-bromobutane-1-one (XI).[6]—The powdered cyclopropane I (25 g., 0.093 mole) was added to a solution of hydrogen bromide in acetic acid (150 cc., saturated at 0°). The flask was stoppered and set aside at room temperature. The light yellow solution slowly deposited a solid; after an hour, the suspension was poured into ice-water (400 cc.), allowed to stand for an hour, and then extracted with chloroform (400 cc.). The extract was dried (magnesium sulfate), and the solvent was removed. The residual solid, formed in quantitative yield, melted at 105° dec. The value given in the literature is 111°.[6]

2,5-Diphenylfuran (VIII).—When the nitro compound XI (12 g., 0.035 mole) was subjected to the action of potassium acetate (5.4 g., 0.055 mole) in methanol (40 cc.) at 0° for 19 hours, according to the procedure of Kohler and Rao[12] there resulted a material (9.1 g.) which, by repeated crystallization from methanol, gave unchanged XI (1.4 g.,

---

[19] R. L. Shriner and R. C. Fuson, "Systematic Identification of Organic Compounds," 3rd Edition, John Wiley and Sons, Inc., New York, N. Y., 1948.

m.p. and mixed m.p. 106–107° dec.) together with the furan VIII (1 g.) melting at 88–88.5°. The value given in the literature is 90°.[6]

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 87.2; H, 5.49. Found: C, 87.2; H, 5.86.

1,4-Diphenyl-4-methoxy-2-butene-1-one (XII).—Potassium acetate (6 g., 0.06 mole) was slowly (five hours) added in five portions to a stirred solution of the nitro compound XI (11.05 g., 0.0325 mole) in dry methanol (100 cc.) at −10°. The solution was stirred for 19 hours at −10 to −20°, then for two hours at 0°, and allowed to come to room temperature. The mixture was poured into ice-water and set aside in a refrigerator. The pasty solid was removed and crystallized from methanol. The product (2.2 g., 25%) when crystallized twice more from methanol melted at 98.2–98.5°. A mixture of XII and XI (m.p. 105°) melted at 84–90°; a mixture of XII and I (m.p. 98°) melted at 80–87°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.39. Found: C, 80.9; H, 6.65.

The substance readily decolorized permanganate, and was recovered unchanged when it was refluxed for 10 minutes with methanol containing hydrochloric acid. The 2,4-dinitrophenylhydrazone crystallized from ethyl acetate or ethyl acetate–methanol in fine orange needles melting at 154.5–155°.

Anal. Calcd. for $C_{23}H_{20}N_4O_5$: C, 63.9; H, 4.66. Found: C, 64.0; H, 4.60.

The ultraviolet absorption spectra of XII (c 8.7 × 10^{-5} mole/l.) and of the 2,4-dinitrophenylhydrazone (c 5.0 × 10^{-5} mole/l.) in ethanol were determined.[20]

1,4-Diphenyl-3-nitro-3-butene-1-one (IX). A.—Pyridine (15.8 g., 0.2 mole, dried over potassium hydroxide) was added to the chloroform solution of XI (prepared as described above; theoretical amount of XI, 32.5 g., 0.093 mole), and the mixture was refluxed for 17 hours. A small amount of bromine vapor appeared in the condenser. The cooled solution was washed with water, dried (magnesium sulfate), and the solvent was removed. The residual brown solid was crystallized from methanol (60 cc.). The stout yellow needles (17.1 g., 68%) melted at 92–92.5°; after another crystallization from methanol, the product melted at 92.5–93°. The product was not pure; but when crystallized from cyclohexane, it melted at 93–94° and gave the proper analytical values.

Anal. Calcd. for $C_{16}H_{13}NO_3$: C, 71.9; H, 4.91; N, 5.24. Found (sample from methanol): C, 71.3; H, 5.28; N, 5.07. Found (sample from cyclohexane): C, 72.1; H, 4.91.

B.—The powdered nitro ketone XI (12.58 g., 0.036) was added to a solution of pyridine (7.9 g., 0.1 mole) in cyclohexane (300 cc.) at room temperature. The solution was allowed to stand at room temperature for three hours, then was refluxed for 14 hours. Pyridine hydrobromide was removed by filtration and the filtrate was cooled. The solid (6.62 g., 68%, m.p. 92–94°) was removed, washed with cold methanol and then with water, and dried. The mother liquor was washed successively with dilute hydrochloric acid, aqueous sodium bicarbonate (5%), and water, dried (magnesium sulfate), concentrated under reduced pressure to a volume of 10 cc., and cooled. The solid weighed 0.21 g. (2%) and melted at 88–92°. The total yield of IX was 70%. The substance reduced permanganate, gave a positive test for the nitro group with alkaline ferrous sulfate; and was recovered unchanged after it has been refluxed for 24 hours with either methanol or ethanol. The 2,4-dinitrophenylhydrazone, crystallized from ethyl acetate-methanol, melted at 191–192°.

Anal. Calcd. for $C_{22}H_{17}N_5O_6$: C, 59.1; H, 3.85; N, 15.7. Found: C, 59.3; H, 3.65; N, 15.4.

The ultraviolet spectra of IX (c 5.0 × 10^{-5} mole/l.) and of the 2,4-dinitrophenylhydrazone (c 4.31 × 10^{-5} mole/l.) in ethanol were determined.[20] The nitro ketone IX (3.95 g., 0.015) was added, all at once, to a stirred solution of sodium (0.69 g., 0.03 gram atom) in methanol (40 cc.) at 0°. The temperature rapidly (10 minutes) rose to 24°; after 30 minutes, the solution was acidified with acetic acid (1.8 g.), poured into water and extracted with ether. The extract was washed with aqueous sodium bicarbonate, then with water, dried (magnesium sulfate) and the solvent was removed. No solid could be obtained from the residual red, pasty oil.

3,6-Diphenyl-1,2,6-oxazine (XIII).—A solution of IX (1 g.) and hydroxylamine hydrochloride (1 g.) in pyridine (5 cc.) and dry ethanol (5 cc.) was refluxed for two hours. The solvents were removed in a current of dry air; the residue solidified when triturated with cold water (5 cc.). The product, crystallized from methanol, melted at 213–214° and was white, but it developed a slight pink color on standing.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.7; H, 5.57; N, 5.95. Found: C, 81.3; H, 5.92; N, 5.72.

The oxazine decolorized permanganate and reacted with bromine in chloroform with evolution of hydrogen bromide.

Action of Sodio Methyl Malonate upon IX. A. Without External Cooling; Compound XIV.—The powdered nitro ketone IX (3 g., 0.011 mole) was added, all at once and at room temperature to a stirred solution of sodio methyl malonate (prepared by addition of sodium, 0.64 g., 0.028 gram atom, to a solution of methyl malonate, 4.44 g., 0.033 mole, in dry methanol, 50 cc.). Within eight minutes, the solid dissolved, a red color developed, and the temperature rose to 33°. When the temperature began to fall, the solution was heated to the boiling point and then set aside. After 30 minutes, the solution was cooled (10°), acidified with acetic acid (1.96 g., 0.033 mole), allowed to stand for an hour, and the methanol was removed under reduced pressure. The residue was dissolved in ether (100 cc.), the solution was washed free of acid, dried (magnesium sulfate) and ether was removed. The residual oil was dissolved in methanol (15 cc.) and the solution was cooled. The product (0.35 g.) was removed and recrystallized from methanol, when it formed fine white needles melting at 143.5–144°. The substance slowly decolorized permanganate and gave the same 2,4-dinitrophenylhydrazone as that obtained from XV and XVI. Although the substance appeared to be pure and no other compound could be obtained from it by repeated crystallization, nevertheless the analytical values corresponded to those required by $C_{20}H_{15}NO_4$—a composition impossible for any simple derivative formed by action of sodio methyl malonate upon IX.

Anal. Calcd. for $C_{20}H_{15}NO_4$: C, 72.1; H, 4.50; N, 4.20. Found: C, 71.8, 72.0; H, 4.54, 4.66; N, 4.37, 4.54.

The 2,4-dinitrophenylhydrazone crystallized from ethanol, formed fine orange needles melting at 175.5–176.5°.

Anal. Calcd. for $C_{27}H_{24}N_4O_8$: C, 60.9; H, 4.54; N, 10.52. Found: C, 61.2; H, 4.77; N, 10.63.

B. At −5°. Methyl 2-Carbomethoxy-3-phenyl-5-benzoyl-4-pentenoate (XV).—A solution of sodio methyl malonate (prepared by addition of sodium, 0.43 g., 0.02 mole, to a solution of methyl malonate, 4.96 g., 0.038 mole, in dry methanol, 50 cc.) was added dropwise (one hour) to a stirred and cooled (−5°) suspension of powdered IX (5 g., 0.02 mole) in dry methanol (100 cc.). Stirring was continued for an additional hour at −5° and then the solution was acidified with acetic acid (1.1 g., 0.02 mole). After removal of most of the solvent in a current of air, the solution was cooled and the product (1.5 g., 30%) was removed and crystallized first from methanol and then from petroleum ether (b.p. 68-70°). It then melted at 109.8–110.2°.

Anal. Calcd. for $C_{21}H_{20}O_5$: C, 71.6; H, 5.72. Found: C, 71.6; H, 5.83.

The substance was unsaturated toward permanganate and gave the same 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 177–178° as that obtained from XIV and XVI.

Anal. Calcd. for $C_{27}H_{24}N_4O_8$: C, 60.9; H, 4.54; N, 10.52. Found: C, 61.0; H, 4.75; N, 10.2.

The ultraviolet absorption spectra of XV (c = 6.28 × 10^{-5} mole/l.) and of the 2,4-dinitrophenylhydrazone (c = 3.77 × 10^{-5} mole/l.) in ethanol were determined.[20]

C. At −20°. Methyl 2-Carbomethoxy-3-phenyl-4-nitro-5-benzoylpentanoate (XVI).—The experiment described in B above was repeated, but at −20° and 30 minutes for the addition. The solid IX dissolved only slowly and the mixture was stirred for two hours at −20°, when most of the solid had dissolved. The temperature was allowed to rise to 0° and was held there for two hours, after which acetic acid (1.1 g., 0.02 mole) was added and the mixture was set aside in a refrigerator. The solid (3.8 g., 65%, m.p. 147.5–150°) was removed and crystallized several times from meth-

---

[20] The complete curves may be found in the Ph.D. thesis of Ralph E. Kelly, ref. 2.

anol and from benzene–petroleum ether (b.p. 68–70°) when it formed clear white prisms melting at 169.5–171.5°.

Anal. Calcd. for $C_{21}H_{21}NO_7$: C, 63.2; H, 5.30; N, 3.51. Found: C, 63.1; H, 5.46; N, 3.41.

The 2,4-dinitrophenylhydrazone of XVI was identical with those derived from XIV and XV and melted at 177.5–178°, alone or when mixed with these. An attempt was made to prepare a semicarbazone of XVI, but the product of this reaction was XV, m.p. and mixed m.p. 108.5–110°. Action of potassium acetate (2 g., 0.02 mole) in methano (50 cc.) upon XVI (1 g.) converted it into XV. The solution was refluxed for one hour, then poured into water, and extracted with ether (four 50-cc. portions). The combined extracts were dried (magnesium sulfate), the solvent was removed, and the residue was crystallized from petroleum ether (100 cc., b.p. 68–70°). It weighed 0.57 g. (65%) and melted at 107–108°, alone or when mixed with XV.

MINNEAPOLIS 14, MINNESOTA

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

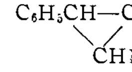
Cyclopropanes. XI.[1] Pyrones from Nitrocyclopropyl Ketones

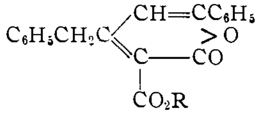
BY LEE IRVIN SMITH AND RALPH E. KELLY[2]

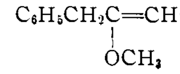
RECEIVED JANUARY 7, 1952

Three nitrocyclopropyl ketones, of two different types—I and II having no hydrogen atoms attached in the 3-position, and III having none in the 1-position—have been subjected to the action of sodio malonic esters. All three of the cyclopropanes were converted into α-pyrone esters by action of this reagent. The reaction of II, which differs from I only in that it is a methyl ketone instead of a phenyl ketone, was complicated because of the presence of the aliphatic ketone group. Because of this, II gave more products than did I or III, and the yield of pyrone from II was low. This pyrone ester V was therefore synthesized *via* an independent sequence of reactions, starting with isopropylacetylene. Formation of pyrone esters from cyclopropanes I and II is consistent with the assumption that an acetylenic ketone is involved as an intermediate, but formation of such a pyrone ester from cyclopropane III cannot be reconciled with this assumption, unless the further assumption is made that the intermediate β,γ-acetylenic ketone XVIII would add malonic ester in one direction only. There is, *a priori*, no reason for assuming that this would be the case.

In the previous paper[1] the action of sodio malonic esters upon the nitrocyclopropyl ketone A was examined; it was shown that the product was the α-pyrone ester B. Moreover, all but one of the products derived from A by action of alkali according to the sequence proposed by Smith and Engelhardt[3]—the enol ether C of the 1,3-diketone D, the diketone D itself, and the unsaturated nitro ketone E—were examined, and none of these was converted, by action of sodio malonic esters, into the α-pyrone B.


A

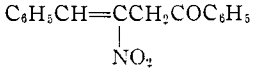

B


$$C_6H_5CH_2\underset{\displaystyle OCH_3}{C}{=}CHCOC_6H_5$$

C

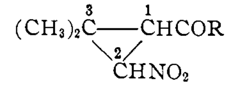
$C_6H_5CH_2COCH_2COC_6H_5$

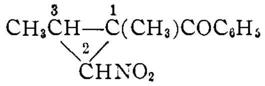
D


$$C_6H_5CH{=}\underset{\displaystyle NO_2}{C}CH_2COC_6H_5$$

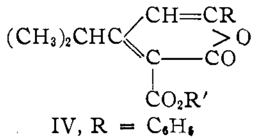
E

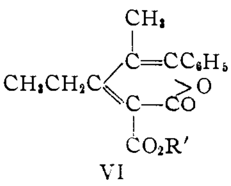
The number of nitrocyclopropyl ketones examined in the earlier work[1,4] was small, and moreover they were all of the same type as A, in which each of the carbon atoms of the ring held one hydrogen atom. Because this conversion of nitrocyclopropanes into pyrones is an important reaction which must be taken into account in formulating any comprehensive mechanism for the reaction between nitrocyclopropyl ketones and bases, the study has been extended to include nitrocyclopropyl ketones differing from A in the location of the hydrogen atoms attached to the ring. Three nitrocyclopropyl ketones—I, II, III—were selected for the study. These are of two types: I and II possess no hydrogen atom on the number 3 carbon atom of the ring, but have one on each of the other two carbon atoms; III has no hydrogen atom on the number 1 carbon atom of the ring, but has one on each of the other two carbon atoms. I differs from II only in the nature of the acyl group; in one case this is benzoyl, and in the other case, acetyl. The latter compound was included in the study so that the series under examination would comprise not only aromatic, but at least one purely aliphatic, nitrocyclopropyl ketone.

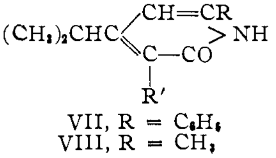

I, R = C_6H_5
II, R = CH_3


II

The nitrocyclopropyl ketones I, II and III, when subjected to the action of sodio malonic ester, were converted into the α-pyrone esters IV, V and VI, respectively.


IV, R = C_6H_5
V, R = CH_3


VI


VII, R = C_6H_5
VIII, R = CH_3

---

(1) Paper X, L. I. Smith and R. E. Kelly, THIS JOURNAL, **74**, 3300 (1952).

(2) Abstracted from a thesis by Ralph E. Kelly, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, August, 1951. du Pont Fellow, 1950–1951.

(3) L. I. Smith and V. A. Engelhardt, THIS JOURNAL, **71**, 2671, 2676 (1949).

(4) E. P. Kohler and L. I. Smith, *ibid.*, **44**, 624 (1922).