TABLE VII

KINETICS OF IODINATION OF 4-NITROPHENOL IN WATER AT 50.0°

$(O_2NC_6H_4OH)_0$ = 0.00770 *M*, $(HClO_4)$ = 0.00982 *M*, $(NaClO_4)$ = 0.2902 *M*; 200.0 ml. of reaction mixture titrated with 0.01204 *M* $Na_2S_2O_3$.

Time, sec.	Titer, ml.	Reaction, %	$k_{app} \times 10^2$, l./mole sec.	$0.1/\{k_2[H^+] + k_1K_2\}$, sec.	$k^*[I^-] \times 10^6$, sec.$^{-1}$
$(NaI)_0$ = 0.100 × 10^{-4} *M*, $(I_2)_0$ = 0.0001144 *M*, *B* = 0.950					
0	3.80	0	(15.2)[a]	(47)[a]	(1.45)[a]
120	3.40	10.5	12.1	52	1.87
219	3.19	16.1	10.4	59	1.94
435	2.84	25.2	8.71	67	2.11
687	2.58	32.1	7.35	79	2.10
992	2.24	41.1	6.95	74	2.40
1249	1.95	48.0	6.96	67	2.70
				Av. 66 ± 7	
$(NaI)_0$ = 0.250 × 10^{-4} *M*, $(I_2)_0$ = 0.0001396 *M*, *B* = 0.947					
0	4.64	0	(8.75)[a]	(67)[a]	(2.07)[a]
180	4.15	10.6	8.04	62	2.52
342	3.83	17.5	7.32	65	2.64
575	3.42	26.3	6.90	59	2.96
900	3.05	34.3	6.07	66	2.98
1299	2.65	42.9	5.61	64	3.17
2061	2.10	54.7	5.02	62	3.40
				Av. 63 ± 2	

[a] Value obtained by extrapolation of k_{app} to zero per cent. reaction.

by about an equal percentage for the run at 0.100 × 10^{-4} *M* iodide. On the other hand, attempts to apply eq. 21 to 4-nitrophenol-2,6-d_2 have not been very successful because, in view of the some six-fold larger value of $k_{-1}/k_1k_3K_2$, $1/\{k_2[H^+] + k_1K_2\}$ is obtained as a small difference between large numbers and is therefore highly susceptable to change due to small experimental errors or to the value chosen for $k_{-1}/k_1k_3K_2$.

For mechanism I, which consists of the attack of I^+ or H_2OI^+ upon 4-nitrophenol or 4-nitrophenoxide anion by either a concerted or two-stage mechanism, on the basis of the same simplifying assumptions as used to derive eq. 21, the following integrated rate expression may be derived

$$k^*[I^-] = \frac{Bx}{(B-2)[ArHOH]t} + \frac{B[(I^-)_0 - c]}{(B-2)[ArHOH]t} \times \ln\left(\frac{c+x}{c}\right) \quad (22)$$

where all the symbols are as defined previously. For mechanism I the product k^* $[I^-]$ should be constant during a run and from run to run provided that the hydrogen ion concentration is constant. The failure of this product to remain constant in Table VII provides additional evidence against mechanism I.

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

Diphenylcyclobutadienoquinone. II. Ring Opening Reactions[1]

BY A. T. BLOMQUIST AND EUGENE A. LALANCETTE[2]

RECEIVED AUGUST 3, 1961

The earlier report on the tendency for diphenylcyclobutadienoquinone (I) to undergo ring opening, in ethanol, to give diethyl α,α'-diphenylsuccinate prompted us to examine the behavior of the diketone I in reactions with other nucleophilic reagents. With *o*-phenylenediamine it was found that the reaction with compound I was complex. In only one of the sets of experimental conditions, upon refluxing compound I in ethanol together with sodium acetate, was there formed a product which comprised the combination of one mole of each reactant. This product was shown to be a rearranged quinoxaline, 3-phenylacetyl-2-phenylquinoxaline (III). The oxime of this ketoquinoxaline when subjected to conditions which might be expected to give a typical Beckmann rearrangement cyclized to 2-benzylquino[3,4-b]quinoxaline. Methanolic sodium hydroxide also effected ring opening of the diketone I to give, as isolable products, benzaldehyde and α-keto-β,γ-diphenyl-γ-butyrolactone.

The synthesis and structure of diphenylcyclobutadienoquinone (I) prepared by the sulfuric acid hydrolysis of 1,2-diphenyl-3,3,4,4-tetrafluorocyclobutene has been described[3] together with the observation that opening of the cyclobutene ring of the diketone I occurs in ethanol solution at room temperature to give a mixture of *meso* and *racemic* diethyl α,α'-diphenylsuccinate, probably *via* a bis-phenylketene intermediate. The chemistry of this highly unsaturated compound is now discussed further; in particular, the results of reactions of the diketone I with *o*-phenylenediamine and with sodium hydroxide are presented. With these reagents cleavage of the four-membered ring also occurs.

A possible straightforward way in which to transform the diketone I into a diphenylcyclobutadiene derivative[4] would be by its reaction

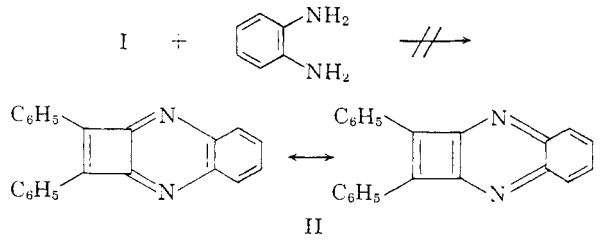
(1) This is the thirteenth publication on the chemistry of small carbon rings. For the preceding paper in this series see A. T. Blomquist and D. J. Connolly, *J. Org. Chem.*, **26**, 2573 (1961). For preliminary communications of portions of this particular investigation see: (a) Abstracts of Papers Presented at the National Meeting of the American Chemical Society in Boston, Mass., April, 1959, p. 54-O; (b) Abstracts of Papers Presented at the Sixteenth National Organic Chemical Symposium of the American Chemical Society, Seattle, Wash., June 15–17, 1959, p. 11.

(2) Support by funds from the Sage Fellowship, Summer, 1957; Procter and Gamble Fellow, Summer, 1958; American Cyanamid Fellow, Summer, 1959; Allied and Chemical and Dye Fellow, 1959–1960.

(3) A. T. Blomquist and Eugene A. LaLancette, *J. Am. Chem. Soc.*, **83**, 1387 (1961).

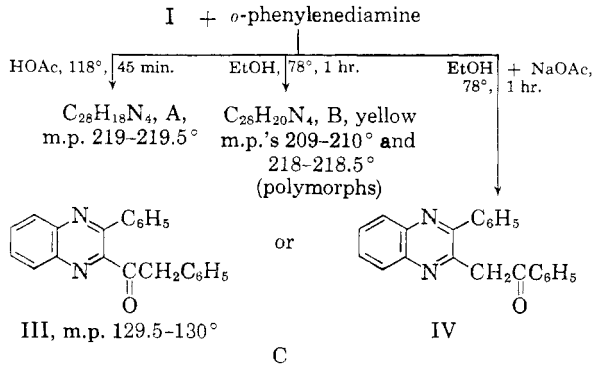
(4) An early envisaged method of transforming compound I into such a derivative was modeled after the photo-chemical work of Schönberg and Mustafa[5] in which it has been shown that addition of

with *o*-phenylenediamine. Although a variety of experimental conditions were tried to effect



II

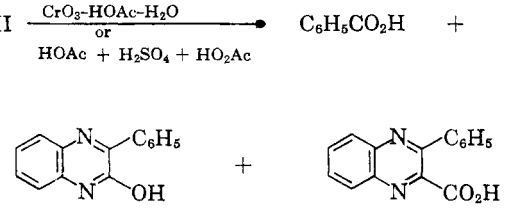
this condensation, in no case was there a product isolated which comprised the condensation of one molecule of the diketone I with one molecule of *o*-phenylenediamine, and the concomitant loss of two molecules of water. All experiments carried out in efforts to prepare compound II as well as the physical properties of the products isolated in these experiments are summarized below.



C

Fuson's[6] general procedure for preparing a quinoxaline gave a product which analyzes for $C_{28}H_{18}N_4$ (A) and which, in ethanol solution, exhibits maxima in the ultraviolet at 246 (ϵ 56,000) and 342 mμ (ϵ 20,000). In a second experiment, upon heating the reagents, I and the diamine, in ethanolic solution, a yellow solid is isolated as two crystalline modifications. Elemental analysis indicates an empirical formula of $C_{28}H_{20}N_4$ (B) and an ethanol solution of this product also has intense ultraviolet absorption: 261 (ϵ 41,800), 353 (ϵ 17,500) and 410 mμ (ϵ 6,000). In both instances apparently two molecules of *o*-phenylenediamine enter into reaction. However, in view of the low yields involved, no further characterization of either product was undertaken. Modification of the experimental conditions used in the second experiment by the addition of sodium acetate, produced a quinoxaline C (88%) which is obviously not the desired product II since the infrared absorption spectrum shows a band at 5.85 μ. This substance has been characterized as 3-phenylacetyl-2-phenylquinoxaline (III).

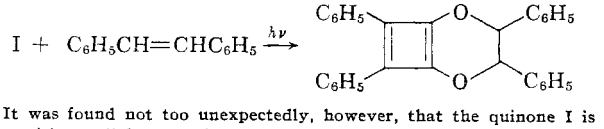
Oxidation of the quinoxaline derivative III with chromic acid gives benzoic acid, 3-phenyl-2-hydroxyquinoxaline[7] and 3-phenylquinoxaline-2-carboxylic acid. The carbon skeleton of compound III is thus that of a 2-phenylquinoxaline with a side chain in the 3-position which has either a phenylacetyl group, as in III, or a phenacyl group, as in IV. That the former structure is the



correct one for the quinoxaline actually obtained is easily determined by examing the n.m.r. proton spectrum of the product, which shows three groups of signals: one signal is observed at 4.43 p.p.m. (downfield from resonance of the methyl hydrogens in an internal sample of tetramethylsilane) which is assigned to the methylene group in the side chain; two sharp signals are found at 7.20 and 7.27 p.p.m. due to resonance of the hydrogens on the two phenyl rings; and an A_2B_2 type multiplet is observed at 7.72 and 8.07 p.p.m. (four hydrogens on the carbocyclic part of the quinoxaline ring).[9] The significant point is that two sharp phenyl signals are observed. This readily rules out the alternative structure IV since in this case the phenyl group[10] conjugated with the carbonyl group would have consisted of a multiplet as observed with acetophenone.

Two of perhaps the most common chemical methods of determining the structure of unsymmetrical ketones, *i.e.*, the Beckmann rearrangement and the Baeyer–Villiger oxidation, were applied to substantiate the conclusions based on the above

stilbene to benzil, phenanthrene and retenequinone leads to 1,4-dioxins; *i.e.*



It was found not too unexpectedly, however, that the quinone I is sensitive to light. During a 4-day exposure of a benzene solution of I to sunlight it is transformed into a tan solid, which sinters at 310° and has m.p. 318–320° dec.; λ_{max}^{KBr} 5.42(s), 5.52(w) and 5.62(s) μ. This solid, which is perhaps a dimer of I, was not thoroughly studied and as yet no attempt has been made to characterize it.

(5) A. Schönberg and A. Mustafa, *Chem. Revs.*, **40**, 190 (1947).

(6) R. C. Fuson and Q. F. Soper, *J. Org. Chem.*, **9**, 193 (1944).

(7) This compound exists predominantly, if not totally, in the tautomeric amide form. In chloroform solution the infrared spectrum of this substance exhibits no absorption in the 3 μ region. Similar behavior has been reported in the case of other hydroxy heterocyclic systems. For leading references see ref. 8.

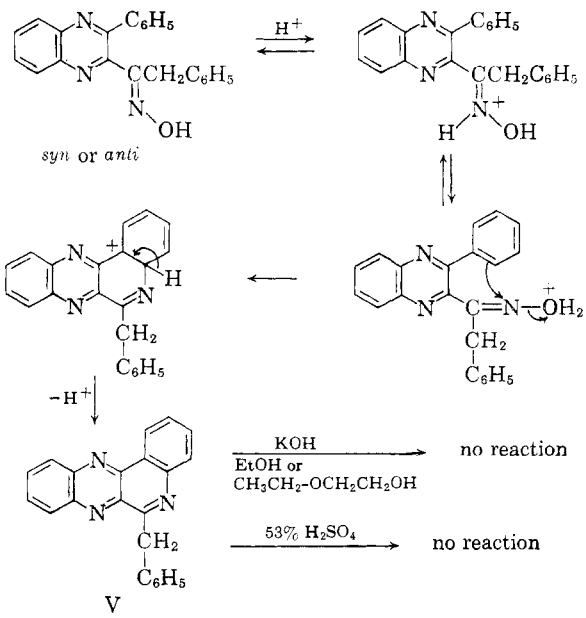
(8) D. J. Brown and S. F. Mason, *J. Chem. Soc.*, 3443 (1956); S. F. Mason, *ibid.*, 4874, 5010 (1957); S. F. Mason, *ibid.*, 674 (1958); 1253 (1959); G. H. W. Cheeseman, *ibid.*, 242 (1960); A. Albert and E. Spinner, *ibid.*, 1221 (1960), and the following three papers; H. E. Baumgarten, W. F. Murdock and J. E. Dirks, *J. Org. Chem.*, **26**, 803 (1961).

(9) This latter assignment has been validated by an examination of model compounds. In both quinoxaline and phenylquinoxaline the same type of multiplet is observed in this region. The same is true of compound V.

(10) An orange compound, m.p. 169–170°, has been assigned structure IV by Lutz and Stuart.[11] Although an aged sample of this substance, kindly supplied by Professor A. H. Blatt of Queens College, possessed the physical constants reported by the original workers, no absorption in the carbonyl region in the infrared is observed below 6 μ (broad λ_{max}^{KBr} 6.30 μ). The spectrum of an ethanolic solution of ths substance is more complex than would be expected for compound IV. The maxima are observed in the ultraviolet and visible regions at 235 (ϵ 24,900), 328 (ϵ 14,000), 428 (ϵ 16,000), 457 (ϵ 14,300) and 483 mμ (ϵ 9100). On this basis, the structural assignment of these workers is questionable.

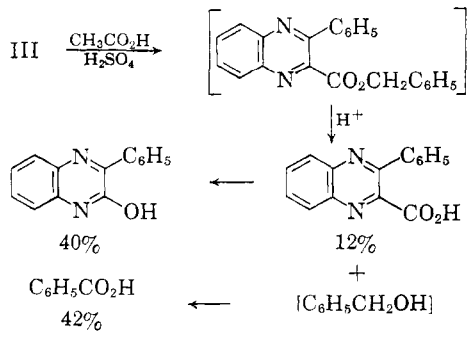
(11) R. E. Lutz and A. H. Stuart, *J. Am. Chem. Soc.*, **58**, 1885 (1936).

interpretation of the n.m.r. data. An attempted Beckmann rearrangement of either the *syn*- or *anti*-oximes of compound III, carried out using the polyphosphoric acid method developed by Horning and Stromberg,[12] gives a red crystalline solid which shows no infrared absorption characteristic of an amide and which has the formula $C_{22}H_{15}N_3$. On the basis of infrared, ultraviolet and n.m.r. spectra (Experimental Part), as well as resistance to attempted basic and acidic hydrolyses, this product is assigned the structure of 2-benzylquino[3,4-b]-quinoxaline (V), which is believed to be a new heterocyclic system. The results of a Baeyer–

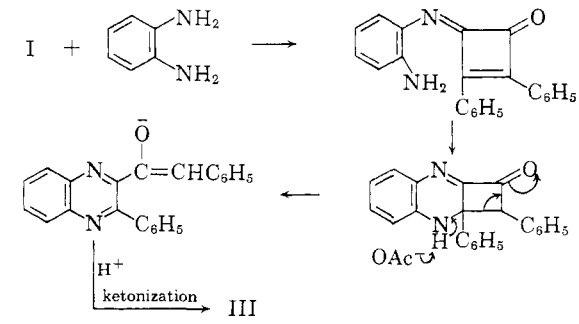


V

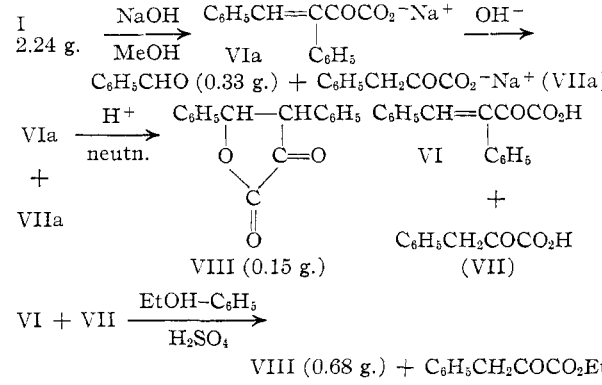
Villiger oxidation of compound III more clearly concurred with the structural assignment concluded from the n.m.r. data. The same three products as were observed in the chromic acid oxidation (*vide ante*) were isolated.[13]

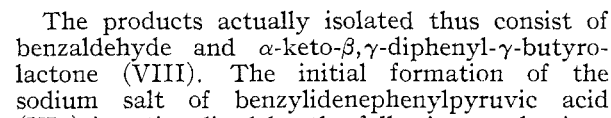


By way of comparison, phenylcyclobutadienoquinone when treated with *o*-phenylenediamine yields phenylacetylquinoxaline,[15] whereas in the case of benzocyclobutadienoquinone 1,4-diazobenzo[b]biphenylene is produced.[16] Thus, in the case of the mono- and diphenyl substituted quinones, it has how been clearly established that cleavage results at the site of the double bond. On the other hand, it would seem from the results obtained with benzocyclobutadienoquinone, that where the π-electrons of the cyclobutene ring are part of an aromatic sextet, a normal reaction can be expected to occur to give stable diazo-biphenylene type analogs.[17]



In order to bear out further the contrast in the chemistry of non-fused *versus* fused cyclobutadienoquinones, ring opening of the diketone I by means of methanolic sodium hydroxide has also been studied. The products obtained together with their mode of formation and method of isolation are given.





The products actually isolated thus consist of benzaldehyde and α-keto-β,γ-diphenyl-γ-butyrolactone (VIII). The initial formation of the sodium salt of benzylidenephenylpyruvic acid (VIa) is rationalized by the following mechanism. Thus, 1,4-addition of hydroxide ion to the α,β-unsaturated ketone followed by abstraction of a proton from the reaction medium produces the intermediate IX which, upon nucleophilic attack and expulsion of hydroxide ion, yields VIa. A

(12) E. Horning and V. L. Stromberg, *J. Am. Chem. Soc.*, **74**, 2680 (1952).

(13) A possible path by which these products originate is shown below. Analogies for the proposed conversion of 3-phenylquinoxaline-2-carboxylic acid to 3-phenyl-2-hydroxyquinoxaline are to be found. Thus, quinoxaline, hydroxyquinoxaline and 2-hydroxyquinoxaline-carboxylic acid can be oxidized with hydrogen peroxide to 1,2-dihydroxyquinoxaline.[14]

(14) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 519 (1948).

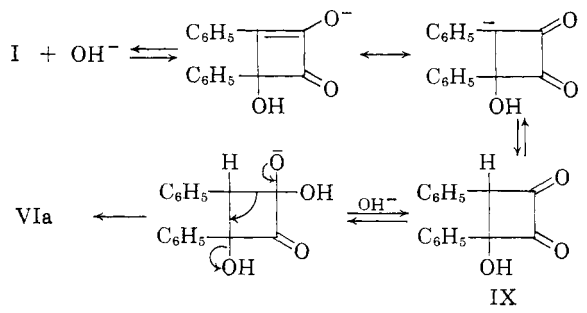
(15) J. D. Roberts, *Rec. Chem. Prog.*, **17**, 103 (1956).

(16) M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **79**, 3606 (1957).

(17) Subsequent to our structure determination of compound III, a reference to a proposed mechanism was found[18] predicting cleavage of the double bond which has now been substantiated. We have modified the mechanism slightly in order to rationalize the need for acetate ion.

(18) J. D. Roberts, Abstracts 14th National Organic Symposium of the American Chemical Society, Purdue Univ., Lafayette, Ind., June, 1955, p. 28; E. J. Smutny, N. C. Caserio and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 1793 (1960).

reverse aldol cleavage of VIa then accounts for the formation of benzaldehyde.



On the basis of the above mechanism, the driving force for the ring-opening of I with base is explained by an examination of the intermediate IX in which the phenyl groups would undoubtedly be *trans*. Thus, the crowding of the bulky phenyl groups in the *cis*-stilbene system of the quinone I is relieved.[19]

The ring opening[16] of benzocyclobutadienoquinone using a 5% solution of sodium hydroxide in aqueous methanol is complete after five hours at 25° and a 94% yield of the sodium salt of phthaldehydic acid is isolated. Skattebøl and Roberts have also studied the ring opening of phenylcyclobutadienoquinone by means of methanolic sodium hydroxide. In this case the products isolated were benzaldehyde and methyl benzylidenepyruvate.[20]

In summary, with both phenylcyclobutadienoquinone and diphenylcyclobutadienoquinone, treatment with hydroxide ion results in cleavage of the 2,3-ring bond whereas the 1,2-bond is cleaved in the case of the fused benzocyclobutadienoquinone.

Experimental Part

3-Phenylacetyl-2-phenylquinoxaline (III).—To a hot solution of 1.70 g. (7.26 mmoles) of the diketone I[3] in 42 ml. of 95% ethanol there was added 0.785 g. (7.26 mmoles) of *o*-phenylenediamine and then a hot solution of 2.1 g. of anhydrous sodium acetate in 48 ml. of ethanol. This solution was refluxed 1 hour and allowed to cool to room temperature. The quinoxaline III crystallized and was collected in three crops: (1) 1.38 g., m.p. 129–129.5°; (2) 0.49 g., m.p. 121–123°; (3) 0.18 g., m.p. 120–123°. The compound III had m.p. 129.5–130° after several recrystallizations from ethanol. The ultraviolet spectrum of III, in 95% ethanol solution, showed maxima at, ϵ's in parentheses: 246(30,800), 266 shoulder (18,000) and 331 mμ (7,200).

Anal. Calcd. for $C_{22}H_{16}N_2O$: C, 81.45; H, 4.97; N, 8.64; mol. wt., 324.36. Found: C, 81.35; H, 5.12; N, 8.56; mol. wt. (Rast), 331.

The 2,4-dinitrophenylhydrazone derivative of the quinoxaline III, prepared with the reagent described by Johnson,[21] had m.p. 216–217°.

Anal. Calcd. for $C_{28}H_{20}N_6O_4$: N, 16.66. Found: N, 16.38.

The oxime derivative of the keto-quinoxaline III was prepared. A hot solution of 0.545 g. of compound III, 0.545 g. of hydroxylamine hydrochloride and 1 g. of potassium hydroxide in 11 ml. of 95% ethanol was refluxed 2 hours and poured into 75 ml. of water. After 1 hour an additional 1 g. of potassium hydroxide was added and the small amount of unreacted ketone III separated by filtration. Neutralization of the alkaline filtrate with dilute hydrochloric acid gave 0.530 g. (93%) of the oxime, m.p. 130–131°. After three recrystallizations from benzene–petroleum ether this oxime of III had m.p. 135–136°.

Anal. Calcd. for $C_{22}H_{17}N_3O$: C, 77.84; H, 5.05; N, 12.38. Found: C, 78.09; H, 5.07; N, 12.30.

Two subsequent preparations of the oxime, carried out as described above, gave a low melting form, m.p. 65–67°, of the oxime. This was difficult to crystallize. Preparation of the oxime derivative of the ketone III by the procedure described by Shriner and Fuson[22] also gave the lower melting oxime. The two forms of the oxime had identical infrared spectra. Dissolution of the lower melting oxime in 92% sulfuric acid, followed by pouring the acid solution, after 20 minutes, into water gave the high melting form.

Oxidation of the Quinoxaline III. A. With Chromic Acid.—Compound III (0.806 g.) in a mixture of glacial acetic acid (10 ml.), water (3 ml.) and chloroform (2 ml.) was oxidized by stirring with chromium trioxide (0.606 g.) for 1.75 hr. at 50–55°. Methyl alcohol (5 ml.) was then added to reduce any remaining chromium trioxide, the reaction mixture poured into 100 ml. of water and the product extracted with ether. The ether solution, washed with 5% sodium bicarbonate solution and 5% sodium hydroxide, was finally washed with water. From the dried ether solution, 0.317 g. of unchanged quinoxaline was recovered. Acidification of the bicarbonate extract gave 0.147 g. (80% of one equivalent based on recovered quinoxaline) of benzoic acid together with 0.042 g. (11%) of 3-phenylquinoxaline-2-carboxylic acid which was easily separated from the benzoic acid by virtue of its insolubility in water. Acidification of the sodium hydroxide fraction gave 0.071 g. (21%) of 3-phenyl-2-hydroxyquinoxaline.

In a subsequent run, in which the amount of chromium trioxide was increased, 1 g. of compound III was oxidized with 1.23 g. of chromium trioxide, whereupon 0.35 g. of unchanged quinoxaline was obtained along with 0.225 g. of benzoic acid (61%), 0.075 g. of 3-phenylquinoxaline-2-carboxylic acid (15%) and 0.17 g. (38%) of 3-phenyl-2-hydroxyquinoxaline.

All oxidation products were compared with authentic samples. In all cases no depression in m.p. was observed upon admixture with authentic samples. In addition, the infrared spectra were also found to be identical with those of the known compounds. Authentic 3-phenylquinoxaline-2-carboxylic acid was prepared, according to a report of Wahl,[23] from the condensation of α-oximinobenzoylacetic ester and *o*-phenylenediamine followed by alkaline hydrolysis, whereas 3-phenyl-2-hydroxyquinoxaline was prepared from the reaction of benzoylformic acid[24] and *o*-phenylenediamine following the procedure described by Buraczewski and Marchlewski.[25]

B. Baeyer–Villiger Oxidation.—The quinoxaline III (0.529 g., 1.63 mmoles) dissolved in glacial acetic acid (6 ml.) was treated with concentrated sulfuric acid (0.65 ml.) and 40% peracetic acid (Becco Chemical). After standing in the dark for 6 days, the reaction mixture was poured into 200 ml. of an ice–water mixture and excess solid sodium bicarbonate added to neutralize the solution. Filtration of the brown solid gave 146 mg. (40.4%) of 3-phenyl-2-hydroxyquinoxaline as determined by m.p., mixed m.p. and infrared comparison. The aqueous sodium bicarbonate solution was acidified and extracted with ether. The orange-red ether extract was then separated into neutral and acidic fractions by washing with a 5% sodium bicarbonate solution, water and drying over anhydrous magnesium

(19) The cyclization of VIa, presumably *via* the free acid VI, occurred with extreme ease. Part of the VIa cyclized even under the mild conditions of neutralization.

(20) L. Skattelbøl and J. D. Roberts, *J. Am. Chem. Soc.*, **80**, 4085 (1958). These workers proposed a benzilic acid type rearrangement involving ring contraction to a cyclopropene derivative followed by ring opening to the sodium salt of benzylidene pyruvic acid. Reverse Aldol cleavage of this salt accounted for the presence of benzaldehyde. In accord with this mechanism, it was found that when the reaction was carried out with sodium deuteroxide, α-deuteriobenzaldehyde is observed. This is equally explained, however, on the basis of the mechanism proposed (*vide ante*) involving 1,4-addition of hydroxide ion.

(21) G. D. Johnson, *J. Am. Chem. Soc.*, **73**, 5888 (1951).

(22) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3d ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 202.

(23) M. A. Wahl, *Bull. soc. chim.* [4] **1**, 461 (1907).

(24) H. Gilman, Ed., "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 244.

(25) J. Buraczewski and L. Marchlewski, *Ber.*, **34**, 4009 (1901).

sulfate. The 5% bicarbonate extract was then acidified, extracted with ether and this ether solution also dried. Evaporation of the ether from the neutral solution gave 56 mg. of a brown oil (strong absorption from 5.7–6.1 μ in the infrared). The acidic fraction gave, after removal of ether and acetic acid (air jet for 2 days), a residue comprising 84 mg. (42.2%) of benzoic acid and 40 mg. (12.3%) of 3-phenylquinoxaline-2-carboxylic acid, separated by extracting the benzoic acid with petroleum ether (30–60°).

2-Phenylquinoxaline for N.m.r. Model.—3-Phenylquinoxaline-2-carboxylic acid was decarboxylated by heating in a sublimation apparatus to 130° (0.6 mm.). As isolated, it had a m.p. of 71–73°. Upon recrystallizing from dilute ethanol, pure product was obtained, m.p. 76–77° (reported[26] m.p. 78°). In methanolic solution maxima are observed in the ultraviolet (Beckman DK) at 261 mμ (ϵ 27,800) and 333 mμ (ϵ 12,700). The reported[27] maxima are 263 mμ (ϵ 28,000) and 335 mμ (ϵ 12,000).

Reaction of the Oxime of Compound III with Polyphosphoric Acid.—The polyphosphoric acid method developed by Horning and Stromberg[12] for Beckmann rearrangements was used.

A solution of 7.5 g. of phosphorus pentaoxide and 7.5 g. of 85% phosphoric acid was added to 0.4 g. of the oxime of III (either the low or high melting form could be used) in a 50-ml. beaker. The reaction mixture was heated to 100° within 3 min. and kept between 100–105° with manual stirring for 10 min. The crimson reaction mixture was then poured into 75 ml. of water and the red solid which precipitated was collected, taken up in ether, washed with sodium bicarbonate, water and concentrated sodium chloride solution. From the dried, filtered ether solution, 246 mg. (65%) of a red crystalline product, V, was collected in two or three crops (m.p. 221–222° and 218–220°). After two recrystallizations from 95% ethanol, an analytical sample, m.p. 223–223.5°, was obtained. The following maxima are observed in 95% ethanolic solution (Beckman DK instrument): 222 mμ (shoulder, ϵ 38,000), 243 mμ (ϵ 52,500), 320 mμ (ϵ 39,000), 370 mμ (ϵ 5,600), 390 mμ (ϵ 5,300) and 470 mμ (ϵ 3,000).

At a frequency of 60 Mc./sec., the proton n.m.r. spectrum was found to be consistent with structure V.

Anal. Calcd. for $C_{22}H_{15}N_3$: C, 82.21; H, 4.71; N, 13.07; mol. wt., 321.26. Found: C, 82.30; H, 4.90; N, 12.89; mol. wt., 305 (Rast).

Stability of Compound V to Base. A.—Compound V (180 mg.) was refluxed with 14 ml. of a 15% potassium hydroxide solution in 95% ethanol for 20 hr. More ethanol (10 ml.) was then added and the solution again heated for 3 more hr. After removal of the solvent with an air jet, water was added and the unchanged starting material collected by filtration; 161 mg., m.p. 221–222°. B.-Compound V (100 mg.) was heated at reflux with 10 g. of potassium hydroxide in 50 ml. of ethoxyethanol and 5 ml. of water for 24 hr. After a similar work-up as described above, again essentially all of the product was recovered unchanged, m.p. 219–220°.

Stability of Compound V to Acid.—Compound V (161 mg.) was heated at reflux with 15 ml. of 53% sulfuric acid for 35 min. and then poured into 200 ml. of an ice–water mixture. Unchanged starting material (134 mg.), m.p. 219–220°, was thus obtained.

Quinoxaline "A":—Fuson's method[28] of preparing quinoxalines was used. Diphenylcyclobutadienoquinone (2.25 g., 9.6 mmoles) in 33 g. of glacial acetic acid was heated at reflux temperature with 1.04 g. (9.6 mmoles) of *o*-phenylenediamine for 40 min. Water and ether were then added and the two phases separated. The aqueous phase was extracted with ether and the ether layers combined. The organic phase was then washed with water, saturated sodium bicarbonate, more water and finally with a saturated solution of sodium chloride. After drying the solution over anhydrous magnesium sulfate, filtering and evaporating the ether solution to dryness, the residue was dissolved in benzene and carefully chromatographed on a column (27 mm. × 62 cm.) of alumina (Merck 71607). The product was eluted with benzene and, after recrystallizing from ethanol, there was obtained 284 mg. (7%) of a solid, m.p. 215.5 217°. A further recrystallization from ethanol gave white crystals, m.p. 219–219.5°. The ultraviolet spectrum in 95% ethanol (Beckman DK instrument) exhibits the maxima at 246 mμ (ϵ 56,000) and 342 mμ (ϵ 20,000).

Anal. Calcd. for $C_{28}H_{18}N_4$: C, 81.93; H, 4.42; N, 13.65; mol. wt., 410.46. Found: C, 82.06; H, 4.49; N, 13.81; mol. wt., 373 (Rast).

Quinoxaline "B":—Diphenylcyclobutadienoquinone (750 mg., 3.2 mmoles) was heated at reflux temperature with 346 mg. (3.2 mmoles) of *o*-phenylenediamine in 95% ethanol (39 ml.) for 60 min. Some of the ethanol was removed and, upon crystallization, 284 mg. (22% based on quinone) of a yellow solid, m.p. 193–203°, collected in two crops. Three more crops (212 mg.) of less pure product were then collected, the infrared spectrum of which showed the presence of compound III as a contaminant.

By recrystallizing the combined first two drops either from chloroform–petroleum ether (30–60°) or from 95% ethanol, a bright yellow crystalline solid, m.p. 209–210°, 218–218.5° (polymorphs), was obtained. The following maxima are obtained in 95% ethanol in the ultraviolet (Beckman DK instrument): 261 mμ (ϵ 41,800), 353 mμ (ϵ 17,500) and 410 mμ (ϵ 6,000).

Anal. Calcd. for $C_{28}H_{20}N_4$: C, 81.53; H, 4.89; N, 13.58; mol. wt., 412.47. Found: C, 81.75; H, 5.08; N, 13.35; mol. wt., 419 (Rast).

In an attempt to improve the above yield, the experiment was repeated using two moles of *o*-phenylenediamine per mole of quinone: a solution of 495 mg. of quinone and 450 mg. of *o*-phenylenediamine in 25 ml. of 95% ethanol was heated at reflux temperature for 60 min. The ethanolic solution was concentrated and allowed to deposit 0.3 g. (44% based on quinone) of compound III followed by 0.1 g. of an orange solid, m.p. 180–183°, which was shown by infrared analysis to consist mainly of quinoxaline "B" along with some compound III.

Ring Opening of I with Base.—The diketone I (2.24 g.) was refluxed for 8.5 hr. with 100 ml. of 0.5 *N* methanolic sodium hydroxide and then allowed to stand at room temperature overnight. Most of the methanol was removed *in vacuo* at room temperature using a 12-inch Vigreux column. Water (55 ml.) was then added along with ether (50 ml.). The ether phase was separated and the water phase extracted with ether (2 × 50 ml.). The combined ether layers were then washed with water (until no longer basic to litmus) and finally with a saturated solution of sodium chloride. Upon removal of the ether after drying with anhydrous magnesium sulfate, 0.33 g. of a light yellow oil was obtained. The infrared spectrum of this oil was in every respect identical with that of an authentic sample of benzaldehyde. In addition it formed a 2,4-dinitrophenylhydrazone derivative whose m.p., mixed m.p. and infrared spectrum were identical with that of an authentic sample.

The light yellow aqueous phase from the initial reaction mixture was acidified with dilute sulfuric acid to congo red at which point a yellow oily layer was observed suspended in the acid solution. The acid solution then was extracted with ether and the ether solution washed with a 5% solution of sodium bicarbonate (3 × 25 ml.). From this ether solution which had been extracted with alkali there was obtained 0.15 g. of impure VIII. The bicarbonate layer from the above was acidified and extracted with ether and the ether solution dried overnight over anhydrous magnesium sulfate. Filtration and evaporation of this ether extract gave a semi-solid residue which was refluxed for 24 hr. with a 5:1 mixture of anhydrous ethanol in benzene containing a small amount of concentrated sulfuric acid. After concentrating this solution to *ca.* 35 ml., ether (65 ml.) was added, the solution washed with a saturated solution of sodium bicarbonate (20 ml.) and dried (magnesium sulfate). Filtration, removal of the ether and trituration of the residue with *n*-pentane caused some crystallization to take place almost immediately and the residual oil phase crystallized when the whole was placed in a refrigerator overnight. Compound VIII (0.68 g.), m.p. 204–206°, was thus collected in two crops. Recrystallization from aqueous ethanol yielded pure lactone of m.p. 212–213°. No de-

(26) Heilbron, "Dictionary of Organic Compounds," Vol. IV revised ed., Oxford University Press, New York, N. Y., 1953, p. 173.

(27) F. Bohlman, *Ber.*, **84**, 860 (1951).

(28) C. Erlenmeyer Jr., and N. Knight, *Ber.*, **27**, 2222 (1894).

pression in m.p. was observed upon admixture with an authentic sample of m.p. 212–213° (reported[28] m.p. 206°). The infrared spectra also proved to be identical.

Upon removal of the *n*-pentane from the above mother liquor, a sweet smelling oily residue remained which failed to crystallize.

[CONTRIBUTION FROM NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, URBANA, ILL.]

An Investigation into the Importance of Heterogeneity as a Directive Influence in the Alkylation of Sodium 4-*t*-Butyl-2,6-dimethylphenoxide[1] with Benzyl Chloride

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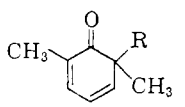
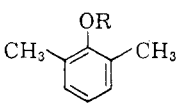
Sodium 4-*t*-butyl-2,6-dimethylphenoxide (I) has been found to undergo alkylation both on the oxygen atom and at an *ortho*-position to give 6-benzyl-4-*t*-butyl-2,6-dimethyl-2,4-cyclohexadienone (II) which, unlike similar dienones previously prepared, does not dimerize readily. The ratio of carbon to oxygen alkylation varies from a value of 1.4 in a heterogeneous experiment in toluene to about 0.17 in a homogeneous solution containing 16% of tetrahydrofuran. In the more polar media (containing 5.6 or 16% tetrahydrofuran) the alkylation follows second-order kinetics for the first 70% reaction. In the less polar media (0.84 and 1.3% tetrahydrofuran) which show light scattering the rate "constants" drift downward throughout the reaction. The effect of added tetrahydrofuran or inclusion of a quaternary ammonium salt is to accelerate the oxygen alkylation much more than the carbon alkylation. A heterogeneous reaction of tetramethylammonium 4-*t*-butyl-2,6-dimethylphenoxide with benzyl chloride in toluene containing 1.3% of tetrahydrofuran gives 70% of benzyl 4-*t*-butyl-2,6-dimethylphenyl ether (III) (oxygen alkylation) and approximately 0.5% of dienone II (carbon alkylation). A change in the amount of undissolved sodium salt (I) by a factor of about 10 fails to change appreciably the ratio of carbon to oxygen attack by benzyl chloride (in toluene). It is concluded that in these reactions, at least, heterogeneity *per se* has no significant effect on the ratio of carbon to oxygen alkylation.

Previous studies[3,4] of the alkylation of salts of *o*-substituted phenols have shown that the reaction provides a direct method of synthesis of cyclohexadienones. For example, sodium 2,6-dimethylphenoxide was shown to react with allyl halides, benzyl halides and methyl iodide to give mixtures of dienone A and ether B. Certain properties of these dienones made reliable quantitative

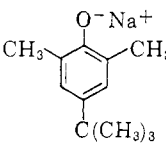


A

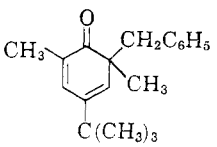


B

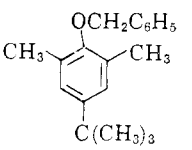
studies of their formation difficult, however. Thus, the dienones A derived from allylic halides undergo the Claisen rearrangement at temperatures only slightly above room temperature[5] and all of these dienones form dimers by a Diels–Alder reaction rather readily even at room temperature. For this reason, in the present work the reaction of benzyl chloride with the sodium salt (I) of 4-*t*-butyl-2,6-dimethylphenol was chosen for study since the derived dienone II might be expected to dimerize much less readily owing to steric strain introduced into the dimer by the presence of the *t*-butyl groups. The sodium salt I was prepared in analytical purity. An authentic sample of the dienone II



I



II



III

was prepared by treatment of a suspension of the sodium salt I with benzyl chloride in toluene. Extensive chromatography was required to remove all traces of the $-OCH_2-$ absorption characteristic of III from the n.m.r. spectrum of II. As had been hoped, there was no evidence of dimerization of the dienone II even after several months at room temperature. Authentic ether III was prepared by the benzylation of the salt I in methanol. It had been supposed that the formation of dienone II plus ether III could be followed by titration of the liberated chloride ion, the dienone II determined quantitatively from the ultraviolet spectrum of the reaction mixture, and the ether III then determined by difference. It was found, however, that unless reaction mixtures were extracted with Claisen alkali, the ultraviolet spectroscopic determination of the dienone II gave values which were sometimes too high due to absorption in the dienone region by an oxidation product from the sodium salt I. This impurity was removable by the alkaline extraction, but it was generally more satisfactory to use infrared spectroscopy to determine dienone and ether directly.

The alkylation with benzyl chloride of the sodium salt I was examined in toluene (heterogeneous) and in toluene containing amounts of tetrahydrofuran varying from 0.75% to about 16%. Addition of 0.0024 mole of sodium salt I to 50 ml. of toluene gives a mixture which is clearly heterogeneous. When the toluene contains 0.84% of tetrahydrofuran, there is no visible precipitate, but the solution appears cloudy and on centrifugation some solid settles. Examination of the extent

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(2) National Science Foundation Fellow, 1959–1960.

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