(III) and 0.2 g. of zinc chloride in a solution of 13 ml. of benzene and 2.0 ml. of freshly distilled phenylacetaldehyde. After standing at room temperature for 4 hr. the resulting yellow solution was washed with three portions of water, dried over sodium sulfate and evaporated to an oil which crystallized when stirred with petroleum ether. The product was recrystallized once from ethylene bromide and petroleum ether, once from *p*-cymene and three times from xylene yielding 0.34 g. (24%) of white crystals melting at 172.5–173.5° dec.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.15; H, 6.48. Found: C, 70.28; H, 6.39.

Catalytic Dehydrogenation of Dihydrocitrinin.—Oxygen was bubbled slowly through a mixture of 0.10 g. of dihydrocitrinin and 0.05 g. of 30% palladium–charcoal in 1.0 ml. of nitrobenzene. After 23 minutes the solution gave a red color with ferric chloride indicating complete conversion of the dihydro compound. The solution was cooled, diluted to a convenient volume with ether, filtered to remove the catalyst and extracted with 5% sodium bicarbonate solution. Acidification of the aqueous extract with dilute sulfuric acid produced an orange-yellow crystalline precipitate. One recrystallization from hot ethanol yielded 0.05 g. (50%) of lemon-yellow crystals melting at 171.0–171.5° dec. No depression of the melting point was noted when this product was mixed with an authentic sample of citrinin.

The reaction proceeded in the absence of oxygen, but a longer reaction time was required, and the yield was considerably less.

Attempted Catalytic Dehydrogenation of 1-Benzyldihydrocitrinin.—The reaction was carried out using the same quantities and conditions given above for dihydrocitrinin. Heating was continued for 45 minutes before the blue ferric chloride test due to the dihydro compound became negative and a brown color was obtained. No appreciable product could be isolated by extraction of the reaction mixture.

The reaction was repeated using successively higher temperatures. At 150° a reaction time of nine minutes was required. Extraction of the solution yielded 0.02 g. of a yellow crystalline material which after one recrystallization from ethanol melted at 165.0–168.0° dec. A mixture of this product with citrinin melted at 166.0–169.0° dec.

Assay for Antibiotic Activity.—The comparison of the antibiotic activity of the synthetic derivatives to that of citrinin and dihydrocitrinin was made by the agar-streak method of Waksman and Reilly[6] using four organisms, *E. coli*, *S. aureus*, *B. mycoides* and *B. subtilis*. Stock solutions of the compounds to be tested were made up by dissolving the appropriate amount of substances (usually 5.0, 10.0 or 20.0 mg.) in three drops of acetone and three drops of 5% sodium bicarbonate and diluting to a volume of 10.0 ml. In no case did the latter reagents, at a concentration equal to the maximum present in the test cultures, inhibit the growth of control cultures. The stock solutions were used immediately after preparation to avoid decomposition of the sample in the slightly basic solution. A maximum concentration of test substance corresponding to 3,000 dilution units was used. The test cultures were examined after incubation for 20 hr. at 28°. The results for all compounds showing any inhibition of bacterial growth are summarized in Table II.

WILLIAMSTOWN, MASS.

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Ethylenimine Ketones. XII. Stereoisomerism of 1-Cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine. Quinoline Syntheses

BY NORMAN H. CROMWELL AND GERALD D. MERCER

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A *trans* configuration has been assigned to the low melting form of 1-cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine which results from the reaction of 2-nitrochalcone with iodine and cyclohexylamine. Both the *cis* and *trans* forms are obtained in nearly equal amounts from 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone. The assignment of configuration is based upon the diagnostic phenylhydrazine reaction and absorption spectra studies. The catalytic hydrogenation of either the *cis*- or *trans*-ethylenimine ketone to 3-cyclohexylamino-2-phenylquinoline provides a new method of synthesis of such materials not readily available by conventional means. The course of this reaction is considered and the ultraviolet and infrared spectra of several 2-phenylquinolines are discussed.

Several pairs of *cis*- and *trans*-arylaroylethylenimines[1] and one pair of *cis*- and *trans*-alkylaroylethylenimines[2] have been prepared by the reaction of primary amines with α,β-dibromoketones. These isomeric pairs have been separated by fractional recrystallization or by chromatographic means and characterized by chemical and physical methods.

To study the sterical and electrical effects of the *o*-nitro group on the β-aryl ring of these ketones and to investigate certain synthetic possibilities, we have now prepared the *cis* and *trans* forms of 1-cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine. A comparable study in the epoxyketone series has been reported.[3]

The reaction of cyclohexylamine with 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone[4] in benzene solution gave an 89% yield of a nearly 50–50 mixture of the *cis* (Ia) and *trans* (Ib) forms of the ethylenimine ketone. These racemic geometrical isomers were separated by column chromatography.[2] The higher-melting *cis* isomer (Ia) in this series was the more strongly absorbed on the alumina. This appears to be a general property of the *cis* forms of the ethylenimine ketones.[2,5]

The low-melting *trans* form (Ib) also was prepared in 64% yield from 2-nitrochalcone,[4] cyclohexylamine and iodine in benzene solution, using a procedure similar to that outlined by Southwick and Christman[6] for a related reaction.

The configurations of Ia and Ib were assigned by methods which have been described previously for analogous compounds.[1–3] The high-melting ethylenimine ketone isomer (Ia) reacted with phenylhydrazine in the presence of acetic acid in an alcohol–chloroform mixture to produce an 85% yield of 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole (II).[3] Under similar conditions the low-melting isomer (Ib) gave what appeared to be, from elemental analysis

(1) (a) N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 1044 (1951); (b) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

(2) N. H. Cromwell and R. J. Mohrbacher, THIS JOURNAL, **75**, 6252 (1953).

(3) N. H. Cromwell and R. A. Setterquist, *ibid.*, **76**, 5752 (1954).

(4) R. Sorge, *Ber.*, **35**, 1065 (1902); W. Dilthey, L. Neuhaus and W. Schommer, *J. prakt. Chem.*, **123**, 235 (1930); I. Tanasescu and A. Georgescu, *ibid.*, **139**, 189 (1934).

(5) N. H. Cromwell, R. P. Cahoy, W. E. Franklin and G. D. Mercer, THIS JOURNAL, **79**, 922 (1957).

(6) P. L. Southwick and D. R. Christman, *ibid.*, **74**, 1886 (1952).

and ultraviolet spectral studies,[1a] see Fig. 1, a mixture of the pyrazole II and 1,3-diphenyl-4-cyclohexylamino-5-(*o*-nitrophenyl)-pyrazoline (III). This mixed material gave a positive Knorr test[7] for pyrazolines.

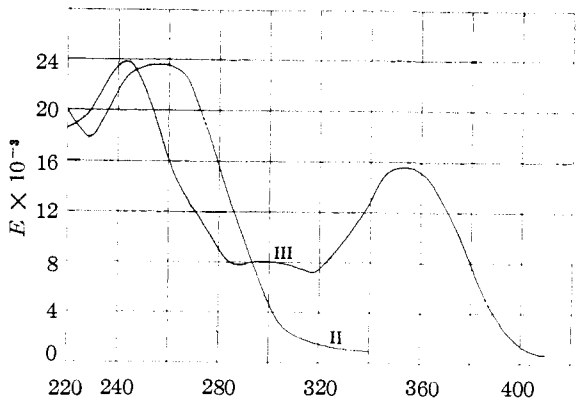


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol of 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole (II) and impure (contaminated with II) 1,3-diphenyl-4-cyclohexylamino-5-(*o*-nitrophenyl)-pyrazoline (III).

Attempts to separate the pyrazoline from the pyrazole by chromatographic adsorption on alumina led to conversion of all of the material to the pyrazole. The pyrazoline readily loses cyclohexylamine to produce the pyrazole, probably because the electron attraction of the *o*-nitro group on the phenyl ring at position-5 of the pyrazoline ring allows the proton to be lost readily from this carbon atom-5.

The aminopyrazolines with an unsubstituted phenyl group in position-5, which have been obtained from other *trans*-ethylenimine ketones,[1] are considerably more stable. The *trans*-arylaroyl ethylenimines are expected to produce aminopyrazolines while the *cis* isomers have been found to give only the pyrazoles.[1,2] The ultraviolet and infrared absorption spectra studies further confirmed the configurations assigned to Ia and Ib; see Absorption Spectra Discussion.

Hydrogenation of the isomeric ethylenimine ketones (Ia and Ib) using W-2 Raney nickel catalyst produced 3-cyclohexylamino-2-phenylquinoline (IV) isolated as its picrate. The isomeric 4-cyclohexylamino-2-phenylquinoline (IX) readily was prepared in good yield from 4-chloro-2-phenylquinoline by reaction with cyclohexylamine.

Colonna and Passerini[8] have prepared 3-arylamino-2-phenylquinolines by applying the Pfitzinger reaction[9] using isatin and ω-arylaminoacetophenones to obtain the 3-arylamino-2-phenyl-4-cinchonic acids, which were readily decarboxylated. Using ω-cyclohexylaminoacetophenone and isatin we obtained a good yield of 3-cyclohexylamino-2-phenyl-4-cinchonic acid (V). This acid was decarboxylated by heating alone to give 3-cyclohexylamino-2-phenylquinoline (IV), the picrate of which was identical with that obtained from the product of the catalytic hydrogenation of Ia and Ib.

When the cinchonic acid (V) was heated with 85% phosphoric acid or concd. sulfuric acid, dealkylation as well as decarboxylation occurred and the known 3-amino-2-phenylquinoline (VI) was produced.

3-Bromo-2-phenylquinoline (VIII) was obtained by a chemical reduction of α-bromo-2-nitrochalcone (VII) which was prepared by dehydrobromination of 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone. Attempts to replace the 3-bromo group in VIII with the cyclohexylamino group were unsuccessful.

The catalytic hydrogenation of 2-nitrochalcone produced 2-phenylquinoline in 82% yield while reduction with hydroiodic acid[10] gave the same compound in 31% yield.

3-(*o*-Nitrophenyl)-propiophenone (X) and 3-(*p*-nitrophenyl)-propiophenone (XI) were prepared by a Friedel–Crafts synthesis employing the acid chlorides of *o*-nitrohydrocinnamic acid and *p*-nitrohydrocinnamic acid. These acids were obtained in good yields from the nitration of hydrocinnamic acid using a procedure similar to that outlined by Buckles and Bellis[11] for the nitration of cinnamaldehyde.

Reduction of 3-(*o*-nitrophenyl)-propiophenone with hydroiodic acid produced a 30% yield of 2-phenylquinoline, but catalytic hydrogenation gave a 40% yield of 1,2,3,4-tetrahydro-2-phenylquinoline, isolated as its hydrochloride XIII.

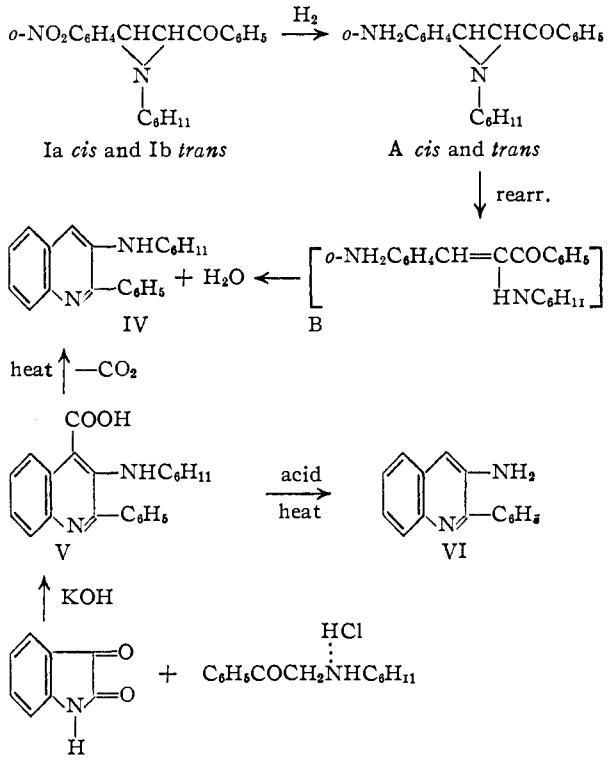
The formation of the 3-cyclohexylamino-2-phenylquinoline from both the *cis*- and *trans*-ethylenimine ketones (Ia and Ib) undoubtedly involves the reduction of the nitro group to the amino group as the first step. The electron-releasing effect of the *o*-amino group would be expected to facilitate a cleavage of the β-carbon-to-nitrogen bond in the ethylenimine ring. This cleavage could lead to a rearrangement of both the *cis* and *trans* forms of the intermediate 1-cyclohexyl-2-(*o*-aminophenyl)-3-benzoylethylenimine (A) to α-cyclohexylamino-2-aminochalcone (B). This latter compound would be expected to undergo a facile ring closure to produce the quinoline IV. A similar mechanism has been suggested[3] to explain the formation of 3-hydroxy-2-phenylquinoline from the catalytic hydrogenation of both *cis*- and *trans*-2-nitrochalcone oxide.

An expanded study of these and related methods of synthesis for 3-amino-2-phenylquinolines will be described in a forthcoming paper.

Absorption Spectra Discussion.—The *cis*- and *trans*-ethylenimine ketones Ia and Ib show ultraviolet maxima midway between those of the parent saturated and unsaturated ketones, with the *trans* form exhibiting the stronger absorption. The *trans* form is expected to have a higher degree of three-ring carbonyl hyperconjugation.[1] The 2-nitrochalcone, which is probably the *trans* form, shows a maximum to be expected for the vinyl-benzoyl chromophore. The steric effect of the *o*-nitro group seems to inhibit conjugation sufficiently to exclude maxima to be associated with either the nitrostyryl or ni-

(7) L. Knorr, *Ann.*, **238**, 200 (1887).
(8) M. Colonna and R. Passerini, *Gazz. chim. ital.*, **78**, 778 (1948).
(9) W. Pfitzinger, *J. prakt. Chem.*, **33**, 100 (1886).
(10) A. Janeish, *Ber.*, **56**, 2448 (1923).
(11) R. E. Buckles and M. P. Bellis, *Org. Syntheses*, **33**, 60 (1953).

trocinnamoyl grouping.[12] The ethylenimine ketone Ib showed a carbonyl stretching vibration infrared band at lower frequencies than did Ia, further confirming that the former is undoubtedly the *trans* form, with three-ring carbonyl hyperconjugation making a greater contribution to the ground state than is the case for the *cis* form Ia.



The α-bromo-2-nitrochalcone showed two ultraviolet maxima at 220 and 261 mμ, again indicating that the steric effect of the *o*-nitro group inhibits conjugation and excludes the maxima which might be associated with either the nitrostyryl or nitrocinnamoyl groupings.[12] The relatively high value of 1681 cm.$^{-1}$ for the carbonyl bond stretching frequency in the infrared for this compound VII as compared with the value 1671 cm.$^{-1}$ for 2-nitrochalcone indicates an increase in double bond character for the C=O group in the ground state. This shift may be associated with a decrease in conjugation between the benzoyl and bromovinyl group as well as with the inductive and coulombic field effects of the α-bromo group.[13]

The 2-phenylquinolines show strong ultraviolet absorption between 254 and 265 mμ. In general[14] the 3-amino-2-phenylquinolines absorb at shorter wave lengths and/or lower intensities than the 4-amino-2-phenylquinolines in this range of the spectrum, possibly because of steric crowding between the 2-phenyl group and the space-demanding N-substituted 3-amino groups. In general[14] N-substituted 3-amino-2-phenylquinolines absorb at higher wave lengths above 300 mμ but at lower intensities than the isomeric 4-amino derivatives. The 3-cyclohexylamino-2-phenylquinoline has a third high intensity band at 221 mμ.

All of the 2-phenylquinolines studied showed two moderately strong infrared bands between 1540 and 1620 cm.$^{-1}$. The assignment of bands in this range of the spectrum, where those to be associated with conjugated phenyl, phenyl, C=C, C=N and N—H (B) bending are expected, is difficult and often uncertain.

SUMMARY OF ABSORPTION SPECTRA

Compound	No.	Ultraviolet max.[a] λ, mμ	ε × 10^{-3}	Infrared bands[b] Bond	Wave no.	Approx. % abs.
1-Cyclohexylamino-2-(*o*-nitrophenyl)-(*cis*) 3-benzoylethylenimine (*trans*)	IA	254	17.9	C=O	1687	70
	IB	254	21.5	C=O	1675	64
2-Nitrochalcone (*trans*)[d]	..	262	17.5	C=O	1671	64[c]
					1650	46
α-Bromo (*trans*)	VII	220	13.9	C=O	1681	95[e]
		261	16.7			
3-(*o*-Nitrophenyl)-[d] propiophenone	X	244	15.8	C=O	1690	80
1,3-Diphenyl-5-(*o*-nitrophenyl)-pyrazole	II	257	23.9			
2-Phenylquinoline	..	256	46.7	C=N	1620	15[f]
		322	9.0	C_6H_5	1600	30
3-Bromo	VIII	255	50.8	C=N	1611	20[g]
		323	10.5	C_6H_5	1593	40
3-Amino-	VI	254	34.6	N—H	3480	10[h]
		355	7.4	N—H	3395	14
				C=N	1618	40
				N—H (B)	1545	43
3-Cyclohexylamino-	IV	221	29.0	N—H	3418	20[i]
		258	29.7	C=N	1604	30
		371	5.9	N—H (B)	1560	4
4-Cyclohexylamino-	IX	265	33.6	N—H	3428	50
		332	11.1	C=N	1583	78
				N—H (B)	1555	68
1,2,3,4-Tetrahydro-2-phenylquinoline hydrochloride	XIII	250	12.4			
		300	3.8			

[a] The ultraviolet spectra were determined in the range of 220–450 mμ in 95% ethanol using 10^{-4} molar solutions with a Cary model 11 spectrophotometer. [b] The infrared spectra were determined over the range of 4000–600 cm.$^{-1}$ at 25° using 1.0-mm. matched NaCl cells with a Perkin-Elmer model 21 instrument; the solutions were 6 mg./ml. CCl_4 unless otherwise indicated. [c] Concn. was 12 mg./ml. CS_2. [d] See ref. 3. [e] Concn. was 12 mg./ml. CCl_4. [f] In 0.1-mm. cells. [g] Concn. was 21 mg./ml. CCl_4 in 0.1-mm. cells. [h] Concn. was 37 mg./ml. CCl_4 in 0.1-mm. cells. [i] Concn. was 30 mg./ml. CCl_4 in 0.1-mm. cells.

Acknowledgment.—This work was supported in part by a grant from the National Science Foundation, N.S.F. G-1091.

Experimental

cis- and *trans*-1-Cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimines (Ia and Ib).—To a well-stirred suspension of 50 g. (0.121 mole) of 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone[4] in 150 ml. of dry benzene, cooled to 5°, was added dropwise 36.2 g. (0.376 mole) of cyclohexylamine. The mixture was stirred for 3 hr. and then placed in the refrigerator for 16 hr. The solid cyclohexylamine hydrobromide was removed by filtration and the filtrate concentrated to a thick sirupy residue under vacuum. This residue was taken up in benzene and three successive crops of crystals removed by addition of petroleum ether (b.p. 30–60°); wt. 35.5 g. (89% yield), m.p. 98–120°. This mixed product was separated by column chromatography, using aluminum oxide, into nearly equal amounts of the *cis* isomer Ia, m.p. 130–131°, and the *trans* form Ib, m.p. 114–115°. The total recovery of material was 98% and the *trans* isomer was

(12) See W. B. Black and R. E. Lutz, THIS JOURNAL, **77**, 5134 (1955), who studied the *p*-nitrochalcones.

(13) R. D. Campbell and N. H. Cromwell, *ibid.*, **79**, 3456 (1957).

(14) In a forthcoming article the absorption spectra of a considerable number of N-substituted 3-amino- and 4-amino-2-phenylquinolines will be discussed.

the first to be eluted from the column by the benzene–alcohol mixture.

trans-**1-Cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine (Ib).**—A 11.4-g. (0.045 mole) sample of 2-nitrochalcone[4] and 17.9 g. (0.181 mole) of cyclohexylamine dissolved in 125 ml. of dry benzene was treated with a solution of 11.4 g. (0.045 mole) of iodine in 125 ml. of dry benzene with stirring and external cooling. The product, isolated as before, weighed 10.2 g. (64.6% yield), m.p. 114–115°, identical with Ib described above.

Anal. Calcd. for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99. Found for Ia; C, 72.32; H, 6.56; N, 8.00. For Ib: C, 72.14; H, 6.28; N, 8.18.

Reaction of the Ethylenimine Ketones Ia and Ib with Phenylhydrazine.—The *cis isomer* Ia (2.1 g., 0.006 mole) was dissolved in 25 ml. of a 2:3 alcohol–chloroform mixture and to this solution was added 0.75 g. (0.006 mole) of phenylhydrazine and 0.75 g. (0.012 mole) of glacial acetic acid. The solution was warmed to about 40° for 30 minutes and then allowed to stand at room temperature for 45 hr. The product was isolated by cooling the reaction mixture and recrystallizing the crude product from methanol to yield 2.2 g. (85.7% yield) of 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole (II), m.p. 178–179°, identical with the product previously prepared in this Laboratory.[3]

The *trans* isomer Ib (2.1 g., 0.006 mole) was treated in a similar manner, but without warming, and found to yield after 14 hr., 0.70 g. of 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole.[3] Evaporation of the reaction filtrate produced an additional 1.01 g. of a solid material, m.p. 126–142°. Recrystallization of this product from alcohol gave material melting at 137–147°. Attempts at purification of this mixed product by chromatographic means gave only the pure pyrazole II. The 137–147° melting material gave a positive Knorr[7] pyrazoline test. This mixed product was undoubtedly a mixture of 1,3-diphenyl-4-cyclohexylamino-5-(*o*-nitrophenyl)-pyrazoline (III) and the pyrazole II.

Anal. Calcd. for $C_{27}H_{22}N_4O_2$: C, 73.61; H, 6.41; N, 12.72. Found: C, 73.29; H, 5.46; N, 12.33.

2-Phenyl-3-cyclohexylaminoquinoline (IV) from Ethylenimine Ketones Ia and Ib. (a) **From the *trans* isomer Ib.**—A 4.1-g. sample of Ib was dissolved in 20 ml. of ethyl acetate and shaken under 45 lb./in.^{2} of hydrogen in the presence of 0.50 g. of W-2 Raney nickel catalyst for 2 hr. Filtration and evaporation left an oil which could not be crystallized from ethanol. Treatment of the ethanol solution of the oil with picric acid produced 3.1 g. (50% yield) of the picrate of 2-phenyl-3-cyclohexylaminoquinoline, m.p. 203–205°, identical with the authentic compound described below.

b. **From the *cis* Isomer Ia.**—In a similar experiment, using 30 ml. of ethanol as solvent, after 3 hr. of hydrogenation 3.5 g. of Ia produced 2.69 g. (56% yield) of the picrate, m.p. 203–205°, identical with the one obtained in (a).

ω-Cyclohexylaminoacetophenone Hydrochloride.[15]—To 88.5 g. (0.894 mole) of cyclohexylamine in 200 ml. of ethyl ether and 132 ml. of dry benzene, held to 14°, slowly was added 88 g. (0.443 mole) of ω-bromoacetophenone dissolved in 160 ml. of ethyl ether and 55 ml. of dry benzene. The reaction mixture was stirred an additional hour. The by-product cyclohexylamine hydrobromide was removed and the product isolated as the hydrochloride by passing dry hydrogen chloride gas into the solution; wt. 60 g. (54% yield), m.p. 250–252° dec., recrystallized from abs. ethanol.

Anal. Calcd. for $C_{14}H_{20}NOCl$: Cl, 13.97. Found: Cl, 13.98.

3-Cyclohexylamino-2-phenyl-4-cinchonic Acid (V).—A solution of 25 g. (0.171 mole) of isatin in aqueous potassium hydroxide (400 g. in 500 ml. of water) was added to a hot solution of 43.5 g. (0.171 mole) of ω-cyclohexylaminoacetophenone hydrochloride in 800 ml. of 95% ethanol. The mixture was heated under reflux for 5 hr. and then 800 ml. of solvent removed by distillation. The residual solution was cooled to precipitate the potassium salt which was removed by filtration and converted to the yellow colored acid in hot water, acidified with glacial acetic acid. This product was recrystallized from 95% ethanol to give 38 g. (64% yield) of 3-cyclohexylamino-2-phenyl-4-cinchonic acid (V), m.p. 198–200° dec.

(15) This compound was first prepared in this Laboratory by E. A. Nielsen, M.S. thesis, 1950, Univ. of Nebraska.

Anal. Calcd. for $C_{22}H_{22}N_2O_2$: C, 76.27; H, 6.40; N, 8.08. Found: C, 76.43; H, 6.53; N, 7.87.

3-Cyclohexylamino-2-phenylquinoline (IV).—A 6.92-g. sample of the cinchonic acid V was heated at its melting point (200°) for 30 minutes and then distilled under vacuum (pot temp. 240°, 300 μ pressure). A pale yellow oil (IV) was collected, 3.2 g. (51% yield). The spectra of this material was determined without further purification. A sample of this oil was treated with the picric acid to produce the 3-cyclohexylamino-2-phenylquinoline picrate, m.p. 204–205°, in a 95% yield.

Anal. Calcd. for $C_{27}H_{25}N_5O_7$: C, 61.01; H, 4.74; N, 13.18. Found: C, 61.36; H, 4.83; N, 13.47.

3-Amino-2-phenylquinoline (VI).—When 3-cyclohexylamino-2-phenyl-4-cinchonic acid (V) was heated with 85% phosphoric acid or concd. sulfuric acid at 200°, a gas was evolved. Isolation of the product upon dilution with water and basification with sodium hydroxide produced a solid (VI) which was recrystallized from 95% ethanol; m.p. 118–119°. This product V was identical with an authentic sample of 3-amino-2-phenylquinoline,[16] m.p. 118–119°.

Anal. Calcd. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 82.13; H, 5.68; N, 12.34.

α-Bromo-2-nitrochalcone (VII).—To 31 g. (0.075 mole) of 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone,[4] suspended in 300 ml. of abs. ethanol, was added 7.5 g. (0.0754 mole) of freshly fused potassium acetate. The reaction mixture was refluxed for 2 hr. after which the solid potassium bromide was removed by filtration. Cooling the filtrate gave 22.3 g. (93% yield) of the product (VII), m.p. 85–86°.

Anal. Calcd. for $C_{15}H_{10}NO_3Br$: C, 54.24; H, 3.03; Br, 24.06; N, 4.22. Found: C, 54.39; H, 3.15; Br, 23.81; N, 4.26.

Attempts to use sodium acetate in place of potassium acetate gave a mixture of the α-bromo-2-nitrochalcone and 2-nitrochalcone, indicating that debromination as well as dehydrobromination was taking place.

3-Bromo-2-phenylquinoline (VIII).—To a solution of 3.22 g. (0.01 mole) of the bromo ketone VII dissolved in 50 ml. of 50% ethanol–water, was added 50 ml. of hydrobromic acid (29%) and 18 g. of stannous chloride dihydrate. The mixture was warmed for 2 hr., made basic with sodium hydroxide and extracted with ether to produce 0.82 g. (30% yield) of 3-bromo-2-phenylquinoline, m.p. 85–86°, corresponding to that reported by John[17]; mixed m.p. with starting material, 60–65°.

Treatment of a sample of 3-bromo-2-phenylquinoline with cyclohexylamine in a sealed tube by the procedure used for the preparation of the 4-position isomer IX resulted in the recovery of the starting material.

4-Cyclohexylamino-2-phenylquinoline (IX).—A 1.2-g. sample of 4-chloro-2-phenylquinoline was heated in a sealed tube[17] at 200° for 10 hr. with 0.90 g. (an excess) of cyclohexylamine. The product was recrystallized from 95% ethanol; 1.35 g. (89% yield), m.p. 128–129°.

Anal. Calcd. for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.27. Found: C, 83.26; H, 7.43; N, 9.12.

3-(*o*-Nitrophenyl)-propiophenone (X) and 2-(*p*-Nitrophenyl)-propiophenone (XI).—*o*-Nitro- and *p*-nitrohydrocinnamic acid were prepared by the nitration of hydrocinnamic acid using the procedure described by Buckles and Bellis[11] for cinnamaldehyde. The *o*- and *p*-isomers were obtained in an over-all yield of 69%; 64% of the product was the *o*-isomer. They were separated by fractional crystallization from hot water and alcohol; *o*-isomer, m.p. 111–112°[18]; *p*-isomer, m.p. 161–163°.[18]

o-Nitrohydrocinnamoyl chloride was prepared by treating 14.3 g. of the acid with thionyl chloride. A Friedel-Crafts reaction was carried out with the crude acid chloride and benzene, using aluminum chloride as the catalyst. Hydrolysis of the product complex gave 12.2 g. (66% yield) of 3-(*o*-nitrophenyl)-propiophenone; recrystallized from benzene and petroleum ether, m.p. 58–59°; Janeish[10] reported m.p. 68–69°.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13. Found: C, 70.60; H, 5.12.

(16) Prepared in this Laboratory by Dr. H. E. Baumgarten by the reduction of 3-nitro-2-phenylquinoline.

(17) H. John, *J. prakt. Chem.*, **118**, 303 (1927); **131**, 350 (1932).

(18) F. Konek and E. Pacsu, *Ber.*, **51**, 855 (1918).

Using the above procedure, 35 g. of *p*-nitrohydrocinnamic acid produced 31.1 g. (69% yield) of 3-(*p*-nitrophenyl)-propiophenone, m.p. 94–96°.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13. Found: C, 70.73; H, 5.24.

2-Bromo-3-(*p*-nitrophenyl)-propiophenone (XII).—A 25.5-g. sample of 3-(*p*-nitrophenyl)-propiophenone was dissolved in 100 ml. of glacial acid and warmed to 50°. To this solution was added 16 g. of bromine in 50 ml. of glacial acetic acid. The temperature of the reaction mixture was maintained at 50° for 1 hr., cooled and poured into 500 ml. of cold water. The oily solid residue was crystallized from ethanol; wt. 32.23 g. (96% yield), m.p. 100–101°.

Anal. Calcd. for $C_{15}H_{12}NO_3Br$: C, 53.91; H, 3.62; Br, 23.92. Found: C, 54.08; H, 3.62; Br, 24.32.

2-Phenyl-1,2,3,4-tetrahydroquinoline Hydrochloride (XIII).—A 3.0-g. sample of 3-(*o*-nitrophenyl)-propiophenone was dissolved in 50 ml. of ethyl acetate and shaken with 45 lb./in.^{2} of hydrogen in the presence of 0.5 g. of W-2 Raney nickel catalyst for 3 hr. at room temperature. The oily product isolated from the reaction mixture was converted to its hydrochloride salt upon passing dry hydrogen chloride gas into a dry ether solution of it; wt. 1.15 g. (40% yield), m.p. 220–225°, recrystallized from abs. ethanol.

Anal. Calcd. for $C_{15}H_{16}NCl$: Cl, 14.67. Found: Cl, 14.43.

2-Phenylquinoline.—A 2.0-g. sample of 2-nitrochalcone was dissolved in 60 ml. of ethyl acetate, and hydrogenated in the presence of W-2 Raney nickel as outlined above to produce 1.3 g. (82% yield) of 2-phenylquinoline, m.p. 81–82°. This product was identical with samples prepared by (a) refluxing *o*-nitrochalcone for 16 hr. with 48% hydroiodic acid (31% yield) or (b) by refluxing 3-(*o*-nitrophenyl)-propiophenone with the same reagent for 20 hr. (30% yield).[10]

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[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Amino Derivatives of Nitrochalcones. I. Synthesis, Structure Studies and Absorption Spectra

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2,3-Dibromo-3-(*o*-nitrophenyl)-propiophenone and the corresponding α-bromo-2-nitrochalcone react with morpholine, piperidine or dimethylamine to produce the expected 2,3-diamino-3-(*o*-nitrophenyl)-propiophenones, while secondary amines with greater steric requirements, such as diethylamine and N-methylcyclohexylamine, react to produce β-amino-2-nitrochalcones. The corresponding bromine derivatives of 3-nitro and 4-nitrochalcone react with both classes of secondary amines in the normal manner to produce 2,3-diamino-3-nitrophenylpropiophenones and/or α-aminonitrochalcones. The structures of the amino chalcones were established by acid hydrolysis studies. A discussion of the ultraviolet and infrared absorption spectra of these and related compounds is given.

The reactions of secondary amines with α,β-dibromoketones and α-bromo-α,β-unsaturated ketones have been the subject of numerous investigations reported from this Laboratory[2] and from others.[3]

The reaction of 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone[4] with morpholine, piperidine and dimethylamine produced the corresponding α,β-diamino ketones I, II and III. Only one of the two possible racemates was isolated in each case in at least 75% yield, and it was not possible to isolate either α-amino- or β-amino-α,β-unsaturated ketones from the highly colored reaction mixtures. These same products I, II and III also were obtained in slightly lower yields from α-bromo-2-nitrochalcone.[5]

When 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone was allowed to react with secondary amines having higher steric requirements, yellow colored products were produced which analysis, absorption spectra studies and acid hydrolysis showed were β-amino-*o*-nitrochalcones. Thus β-diethylamino- (IV) and β-(N-methylcyclohexylamino)-2-nitrochalcone (V) were produced in good yields using the corresponding amines. These same products were obtained in nearly the same yields from α-bromo-2-nitrochalcone.

The unsaturated amino ketones IV and V were difficult to hydrolyze, but long heating with dilute sulfuric acid produced the known *o*-nitrodibenzoylmethane which readily gave a copper chelate. This 1,3-diketone reacted with phenylhydrazine to give the known 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole.[5,6]

In contrast with the *o*-nitro compound, both 2,3-dibromo-3-(*m*-nitrophenyl)-propiophenone and 2,3-dibromo-3-(*p*-nitrophenyl)-propiophenone reacted with diethylamine to produce the corresponding α-diethylamino-3-nitrochalcone (XI) and α-diethylamino-4-nitrochalcone (X), respectively. The structures of these products X and XI were established by analysis, absorption spectra studies and their acid hydrolysis to the corresponding 1,2-diketones. Compound X was hydrolyzed to *p*-nitrobenzylphenyl diketone (XII) which produced 2-(*p*-nitrobenzyl)-3-phenylquinoxaline (XIII) on heating with *o*-phenylenediamine. The α-amino-α,β-unsaturated ketone XI produced the corresponding 1,2-diketone which was converted to the known 2-(*m*-nitrobenzyl)-3-phenylquinoxaline on warming with *o*-phenylenediamine.

2,3-Dibromo-3-(*p*-nitrophenyl)-propiophenone reacted with morpholine to give a mixture of 2,3-di-(N-morpholino)-3-(*p*-nitrophenyl)-propiophenone (VI) and α-(N-morpholino)-4-nitrochalcone (VIII), which were separated readily by fractional recrystallization. Piperidine behaved in a similar

(1) Standard Oil Co. (of Indiana) Fellow, 1955–1956.

(2) See N. H. Cromwell, *Chem. Revs.*, **38**, 83 (1946), and ref. cited therein.

(3) (a) R. Lutz, *et al.*, *J. Org. Chem.*, **14**, 982 (1949); (b) **16**, 1442 (1951).

(4) R. Sorge, *Ber.*, **35**, 1065 (1902); W. Dilthey, L. Neuhaus and W. Schommer, *J. prakt. Chem.*, **123**, 235 (1930); I. Tanasescu and A. Georgescu, *ibid.*, **139**, 189 (1934).

(5) N. H. Cromwell and G. D. Mercer, THIS JOURNAL, **79**, 3815 (1957).

(6) N. H. Cromwell and R. A. Setterquist, *ibid.*, **76**, 5752 (1954).