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]

LINCOLN, NEBRASKA

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

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

BY NORMAN H. CROMWELL AND GERALD D. MERCER[1]

RECEIVED MARCH 16, 1957

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

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

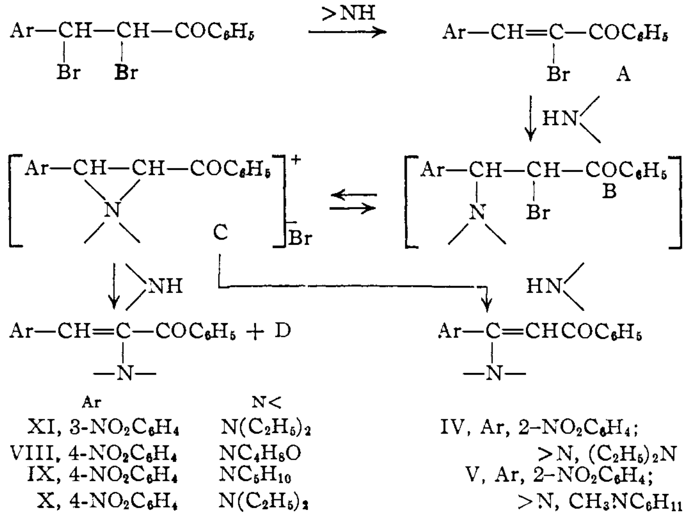
(2) See N. H. Cromwell, *Chem. Revs.*, **38**, 83 (1946), and ref. cited therein.

(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).



Ar	N<
XI, 3-$NO_2C_6H_4$	$N(C_2H_5)_2$
VIII, 4-$NO_2C_6H_4$	NC_4H_8O
IX, 4-$NO_2C_6H_4$	NC_5H_{10}
X, 4-$NO_2C_6H_4$	$N(C_2H_5)_2$

IV, Ar, 2-$NO_2C_6H_4$; >N, $(C_2H_5)_2N$

V, Ar, 2-$NO_2C_6H_4$; >N, $CH_3NC_6H_{11}$

manner to produce the corresponding α,β-di-(N-piperidino) ketone VII and the α-(N-piperidino)-α,β-unsaturated ketone IX.

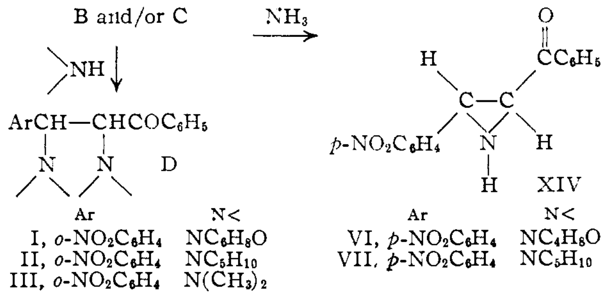
With anhydrous ammonia, 2,3-dibromo-3-(*p*-nitrophenyl)-propiophenone produced *trans*-2-(*p*-nitrophenyl)-3-benzoylethylenimine (XIV), previously prepared by Wieland[7] but assigned a piperizine structure without further investigation. A molecular weight determination and the measurement of absorption spectra (infrared and ultraviolet) clearly established the structure of this ethylenimine ketone.

Discussion of Reactions.—It has been shown[2] that α-bromochalcone or 2,3-dibromo-3-phenylpropiophenone reacts with secondary amines to produce either mixtures of α-amino-α,β-unsaturated ketones and α,β-diaminoketones (*i.e.*, morpholine and piperidine) or only the α-amino-α,β-unsaturated ketone (*i.e.*, diethylamine). An endocyclic α,β-unsaturated ketone, 8-bromoperinaphthenone-7, was found to react with secondary amines (*i.e.*, morpholine and piperidine) to produce either α-amino- or β-amino-α,β-unsaturated ketones, depending upon the conditions employed.[8] Recently it has been reported that 3-bromo-1,-1-dimethyl-2-keto-1,2-dihydronaphthalene reacts with morpholine to give a β-amino-α,β-unsaturated ketone.[9]

It seems probable that the first step in the reaction of amines with each of the 2,3-dibromo-3-arylpropiophenones (*o*-nitro, *m*-nitro and *p*-nitro) involves the loss of hydrogen bromide to produce the corresponding α-bromonitrochalcone (A). The second step in the presence of excess reagent is the addition of the amine to produce the reactive 2-bromo-3-amino-3-nitrophenylpropiophenones (B). With primary amines[5,10] or ammonia the last step in the sequence of reactions in all three series involves a ring closure to produce the ethylenimine ketone. Both the *m*-nitrophenyl and *p*-nitrophenyl series of bromo ketones react with diethylamine, morpholine and piperidine in the normal[2] manner to produce the expected results, *via* the intermediate quaternary ethylenimmonium ion, since α-amino-α,β-unsaturated ketones are included in the products.

The presence of an electron-attracting nitro group on the 3-aryl group in the 2,3-dibromo-3-(nitrophenyl)-propiophenones would be expected to activate the hydrogen atom in the 3-position and thus facilitate the loss of hydrogen bromide from the intermediate 2-bromo-3-amino-3-(nitrophenyl)-propiophenones (B) to produce β-aminonitrochalcones. However, since only the 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone behaved in this manner, it seems possible that a steric effect as well as the electrical effect of the *o*-nitro group is involved in determining the course of these reactions to produce the β-amino α,β-unsaturated ketones (IV) and (V). It is possible (but not certain) that the intermediate formation of the usual ethylenimmonium bromides[2] is not involved in the loss of hydrogen bromide from the intermediate 3-diethylamino- and 3-(N-methylcyclohexylamino)-2-bromo-3-(*o*-nitrophenyl)-propiophenones.

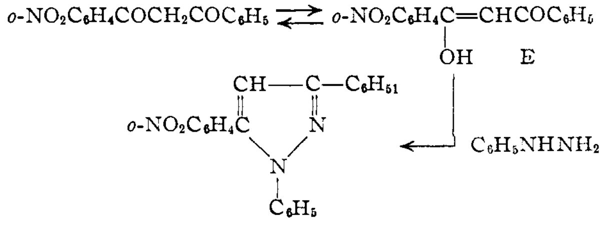
Steric controls[11] which are expected to operate in the formation of the 3-amino-2-bromo-3-arylpropiophenones suggest that the main products to be expected from the reactions involving ammonia are the *trans*-2-aryl-3-benzoylethylenimines (*i.e.*, XIV).



Ar	N<
I, *o*-$NO_2C_6H_4$	NC_4H_8O
II, *o*-$NO_2C_6H_4$	NC_5H_{10}
III, *o*-$NO_2C_6H_4$	$N(CH_3)_2$

Ar	N<
VI, *p*-$NO_2C_6H_4$	NC_4H_8O
VII, *p*-$NO_2C_6H_4$	NC_5H_{10}

It was of interest to find that *o*-nitrodibenzoylmethane reacted with phenylhydrazine to produce the known 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole. This result implies that *o*-nitrodibenzoylmethane reacts as the enol E.



Bodforss[12] came to a similar conclusion with regard to the reaction of *m*-nitrodibenzoylmethane and phenylhydrazine. Although the course of the reaction suggested by Bodforss has been disputed by Barnes and Dodson,[13] we are inclined to

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(7) H. Wieland, *Ber.*, **37**, 1150 (1904).

(8) N. H. Cromwell, D. B. Capps and S. E. Palmer, THIS JOURNAL, **73**, 1226 (1951).

(9) N. H. Cromwell and R. D. Campbell, *J. Org. Chem.*, **22**, 520 (1957).

(10) N. H. Cromwell, THIS JOURNAL, **69**, 258 (1947).

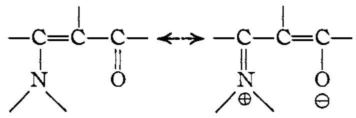
(11) N. H. Cromwell, W. Franklin and R. P. Cahoy, *ibid.*, **79**, 922 (1957).

(12) S. Bodforss, *Ber.*, **49**, 2795 (1916).

(13) R. Barnes and L. Dodson, THIS JOURNAL, **65**, 1585 (1943).

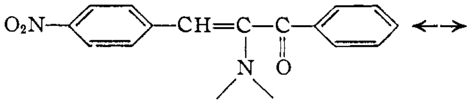
believe that Bodforss' description of these reactions is correct. The fact that 2,3-dibromo-3-phenyl-*m*'-nitropropiophenone reacts with a mixture of potassium hydroxide and phenylhydrazine to produce the same pyrazole[13] as does *m*-nitrodibenzoylmethane[12] cannot be taken as conclusive evidence for the structure of the pyrazole. The dibromide may have undergone an initial reaction with potassium hydroxide to produce *m*-nitrodibenzoylmethane. We believe that Bodforss' assignment of the 1,3-diphenyl-5-(*m*-nitrophenyl)-pyrazole structure to this derivative is correct.

Discussion of Absorption Spectra.—2-Nitrochalcone[5,6] has been shown to have only one maximum in the ultraviolet at 262 mμ, which is to be associated with the vinyl–benzoyl chromophore. The β-amino-2-nitrochalcones (IV) and (V) both showed benzoyl absorption in the range of 243–247 mμ and a new intense maximum at 340 mμ. Both of these β-amino-α,β-unsaturated ketones have carbonyl stretching frequencies near 1635 cm.$^{-1}$ in the infrared. As has been suggested previously,[14,15] such results indicate that the resonance implied by (F) ⟷ (G) makes an important contribution to both the ground and excited states of β-amino-α,β-unsaturated ketones.

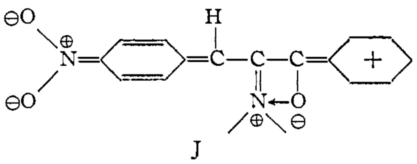


F G

The α-amino-α,β-unsaturated ketones (VIII) and (IX) also showed vinyl–benzoyl absorption at 255 mμ and moderately strong bands near the visible-ultraviolet boundary of the spectrum, 390–425 mμ. These longer wave length bands may be ascribed[14] to chromophores involving the whole molecule, and resonance implied by H ⟷ J is suggested as making a considerable contribution to the excited state.



H



J

It is important to observe that the presence of the nitro group in the *p*-position, which would be expected to support a negative charge through interaction with the benzene ring, greatly enhances light absorption in this part of the spectrum. Although α-diethylamino-3-nitrochalcone (XI) also has an ultraviolet absorption band at 400 mμ, the intensity is much lower than for the α-amino-4-nitrochalcones. Resonance interaction of the *m*-nitro group with the benzene ring is, of course, not expected. Ketone XI also shows a moderately strong nitrocinnamoyl band at 313 mμ. The infrared carbonyl stretching frequencies of all of these α-aminochalcones were between 1677 and 1682 cm.$^{-1}$. This shift to higher frequencies with respect to the carbonyl values for nitrochalcones (1671 cm.$^{-1}$ or less)[5,6] indicates that the resonance H ⟷ J makes little or no contribution to the ground state and that instead the inductive and coulombic field effects[16] of the α-amino groups increase the double bond character of the carbonyl group in the α-aminochalcones.[15] This shift in carbonyl frequency also may be associated with a steric inhibition of conjugation between the benzoyl and vinyl groups caused by the presence of the α-amino group.[5]

3-(*p*-Nitrophenyl)-propiophenone shows benzoyl absorption in the ultraviolet at 246 mμ and a slightly less intense band at 274 mμ, possibly to be associated with the nitrophenyl grouping. The ethylenimine derivative XIV showed similar absorption characteristics with an increase in wave length and intensity for the benzoyl and nitrophenyl bands. The infrared carbonyl stretching frequency of the ethylenimine ketone XIV was found at 1680 cm.$^{-1}$ as compared with a value of 1686 cm.$^{-1}$ for 3-(*p*-nitrophenyl)-propiophenone. These ultraviolet and infrared studies imply that hyperconjugation of the three-ring with the carbonyl and *p*-nitrophenyl groups makes a small contribution to both the ground and excited states of XIV, and that it has a *trans* configuration.[5]

The infrared spectrum for the copper chelate XV of *o*-nitrodibenzoylmethane showed the characteristics to be expected of such materials.[17]

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

Experimental

2,3-Di-*sec*-amino-3-(*o*-nitrophenyl)-propiophenones.—The 2,3-di-N-morpholino- (I), the 2,3-di-N-piperidino- (II) and the 2,3-bis-dimethylamino-3-(*o*-nitrophenyl)-propiophenone (III) were prepared by stirring a suspension of 10 g. (0.0242 mole) of 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone[4] in 50 ml. of abs. ethanol with 0.097 mole of the corresponding amine for 15 minutes with ice-bath cooling. These reaction mixtures were allowed to stand in the refrigerator for 24 hr. The yellow-orange colored solids were removed by filtration and the filtrates concentrated to yield several more crops. These crude materials were combined in each run, washed with water and recrystallized from benzene–alcohol mixtures using charcoal to decolorize the solutions; see Table I for yields, anal. and m.p. Attempts to isolate α-amino or β-amino α,β-unsaturated ketones from these three reaction mixtures were unsuccessful. These products, I, II and III, also were obtained in slightly lower yields from α-bromo-2-nitrochalcone.[5]

Several attempts to prepare 2-bromo-3-morpholino-3-(*o*-nitrophenyl)-propiophenone by mixing α-bromo-2-nitrochalcone with one molar equiv. of morpholine in dry ether produced only small amounts of the diamino ketone I. Treatment of 2-nitrochalcone with N-bromomorpholine using Southwick's[18] procedure failed to give the α-halo-β-amino ketone in this case, and only small amounts of I could be isolated.

β-Diethylamino-(IV) and β-(N-Methylcyclohexylamino)-2-nitrochalcone (V).—The dibromoketone (0.05 mole) was

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[14] N. H. Cromwell and W. R. Watson, *J. Org. Chem.*, **14**, 411 (1949).

[15] N. H. Cromwell, *et al.*, THIS JOURNAL, **71**, 3337 (1949).

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

[17] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 126.

[18] P. L. Southwick and W. L. Walsh, THIS JOURNAL, **77**, 405 (1955).

TABLE I

PHYSICAL AND ANALYTICAL DATA

Amino ketones	No.	Yield, %	M.p., °C.	Formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
3-(*o*-Nitrophenyl)-propiophenone										
2,3-Di-(N-morpholino)-	I	78	182–183	$C_{23}H_{27}N_3O_5$	64.92	6.40	9.88	65.27	6.51	10.19
2,3-Di-(N-piperidino)-	II	77	159–160	$C_{25}H_{31}N_3O_5$	71.23	7.41	9.97	71.31	7.40	9.89
2,3-Bis-(dimethylamino)-	III	75	144–145	$C_{19}H_{23}N_3O_3$	66.84	6.79	12.31	66.69	6.56	12.59
2-Nitrochalcone										
β-Diethylamino-	IV	76	112–113	$C_{19}H_{20}N_2O_3$	70.35	6.22	8.64	70.59	6.30	8.56
β-(N-Methylcyclohexylamino)-	V	63	145–146	$C_{22}H_{24}N_2O_3$	72.50	6.64	7.69	72.86	6.92	7.55
3-(*p*-Nitrophenyl)-propiophenone										
2,3-Di-(N-morpholino)-	VI	43	183	$C_{23}H_{27}N_3O_5$	64.92	6.40	9.88	65.31	6.23	9.76
2,3-Di-(N-piperidino)-	VII	26	165–166	$C_{25}H_{31}N_3O_3$	71.23	7.41	9.97	71.39	7.37	9.95
4-Nitrochalcone										
α-(N-Morpholino)-	VIII	30	159–160	$C_{19}H_{18}N_2O_4$	67.44	5.36	8.28	67.63	5.49	8.64
α-(N-Piperidino)-	IX	52	106–107	$C_{21}H_{21}N_2O_3$	71.41	5.99	8.33	71.62	6.29	8.51
α-Diethylamino-	X	99	102–103	$C_{19}H_{20}N_2O_3$	70.35	6.22	8.64	20.37	6.20	8.49
3-Nitrochalcone										
α-Diethylamino-	XI	90	92–93	$C_{19}H_{20}N_2O_3$	70.35	6.22	8.64	70.62	6.26	8.54

TABLE II

SUMMARY OF ULTRAVIOLET AND INFRARED SPECTRA

Compound	Ultraviolet max.[a] No.	λ, mμ	ε × 10^{-3}	Infrared bands[b] Band	Wave no.	Rel. % abs.
2-Nitrochalcone	IV	247	16.4	C=O	1635	83
β-Diethylamino-		340	23.6	C=C	1618	57
				Ar	1600	50
β-(N-Methylcyclo-hexylamino)-	V	243	16.4	C=O	1636	88
		340	24.3	C=C	1620	69
				Ar	1600	60
4-Nitrochalcone		316	28.8[c]	C=O	1650	23[d]
(*trans*)				C=C	1605	25
				Ar	1593	27
α-[N-Morpholino]-	VIII	255	19.5	C=O	1682	15
		390	12.5	ArC=C	1593	26
α-[N-Piperidino]-	IX	255	19.5	C=O	1677	40
		413	13.8	ArC=C	1587	68
α-Diethylamino-	X	258	19.5	C=O	1677	35
		425	15.7	ArC=C	1597	37
3-Nitrochalcone	XI	256	22.3	C=O	1677	31
α-Diethylamino-		313	17.2	ArC=C	1595	45
		400	2.5			
2-(*p*-Nitrophenyl)-3-Benzoylethylen-imine (*trans*)	XIV	255	20.5	N—H	3300	9[e]
		279	19.4	C=O	1680	26
				Ar	1612	21
3-(*p*-Nitrophenyl)-propiophenone		246	12.3	C=O	1686	75
		274	10.7	Ar	1597	36
Bis-[1-(*o*-nitrophenyl)-3-phenyl-1,3-propanedione]copper	XV			Ar	1600	45[d]
				C=O	1560	60
				C=C	1530	65

[a] The ultraviolet spectra were determined with a Cary model 11 spectrophotometer in the range of 220–450 mμ in 95% ethanol using 10^{-4} molar solutions. [b] The infrared spectra were determined over the range of 4000–600 cm.$^{-1}$ at 25° using 0.10-mm. matched cells with a Perkin–Elmer model 21 instrument and 12–20 mg./ml. CCl_4 solutions, unless otherwise indicated. [c] See W. Black and R. Lutz, THIS JOURNAL, **77**, 5134 (1955). [d] Determined as a Nujol mull. [e] Determined with a satd. soln. in CCl_4.

suspended in 100-ml. amounts of abs. ethanol and treated with 0.21 mole of diethylamine and 0.15 mole of N-methylcyclohexylamine, respectively. These reaction mixtures were allowed to stand in the dark at room temperature for two days. The solvent was removed under reduced pressure and the oil–solid residues mixed with 400 ml. of ether. The ether solutions were filtered to remove the by-product amine hydrobromides, washed with water and dried over anhyd. magnesium sulfate. Concentration of these ether solutions by evaporation followed by the addition of petroleum ether, b.p. 30–60°, caused the crystallization of the crude products which were recrystallized from 95% ethanol; see Table I for m.p.'s, yields and analyses. These yellow colored products were obtained in slightly lower yields using α-bromo-2-nitrochalcone in place of the dibromoketone.

2,3-Di-*sec*-amino-3-(*p*-nitrophenyl)-propiophenones.—The 2,3-di-N-morpholino- (VI) and the 2,3-di-N-piperidino-3-(*p*-nitrophenyl)-propiophenone (VII) were prepared by stirring at room temperature for 3 hr., suspensions of 12.39 g. (0.030 mole) of 2,3-dibromo-3-(*p*-nitrophenyl)-propiophenone in 250 ml. of abs. ethanol with 0.120 mole of the corresponding amine. The working up of these reaction mixtures in the usual manner produced both the diamino ketones VI and VII and the corresponding α-amino-α,β-unsaturated ketones, **α-morpholino-*p*-nitrochalcone (VIII) and α-piperidino-*p*-nitrochalcone (IX)**; these products were recrystallized from 95% ethanol, see Table I for yields, m.p.'s and analytical data.

α-Diethylamino-4-nitrochalcone (X) and α-Diethylamino-3-nitrochalcone (XI).—These orange-red products were obtained by mixing 2,3-dibromo-3-(*p*-nitrophenyl)-propiophenone and the *m*-nitrophenyl analog with three molar equivalents of diethylamine in abs. ethanol at ice-bath temperature. The reaction mixtures were allowed to stand for two days at room temperature and the products isolated in the usual manner and recrystallized from 95% ethanol; see Table I for data.

Hydrolysis of β-Amino and α-Amino-α,β-unsaturated Ketones.—(a) **β-Diethylamino-2-nitrochalcone (IV)** (1.0 g.) was refluxed for 16 hr. in 20 ml. of 15% sulfuric acid. The acid solution was extracted with ether and made basic with sodium hydroxide to recover 0.49 g. of IV. Evaporation of the ether extract and recrystallization from 95% ethanol produced 0.090 g. (22% yield) of *o*-nitrodibenzoylmethane,[19] m.p. 115–116°. This product gave a deep-red color with alcoholic ferric chloride.

A 0.05-g. sample of *o*-nitrodibenzoylmethane was dissolved in 10 ml. of 50% acetone–water and treated with a saturated solution of cupric acetate in 50% acetone–water. **The bis-[1-(*o*-nitrophenyl)-3-phenyl-1,3-propanedione]-copper** was filtered from the solution and recrystallized from dioxane and benzene; m.p. 287–288°, wt. 0.045 g. (80% yield).

Anal. Calcd. for $C_{31}H_{21}N_2O_8Cu$: Cu, 10.58. Found: Cu, 10.69.

A 0.025-g. sample of *o*-nitrodibenzoylmethane was dissolved in 5 ml. of 1:1 alcohol–chloroform and one molar equivalent of phenylhydrazine and a drop of gl. acetic acid added. The mixture was warmed and allowed to stand at

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[19] S. Gabriel and W. Gerhard, *Ber.*, **54B**, 1613 (1921).

room temperature for a day. The yellow crystalline product was recrystallized from 95% ethanol, 0.02 g. (63% yield), m.p. 178–180°. This product was identical with an authentic sample of **1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole**.[6]

(b) **β-(N-Methylcyclohexylamino)-2-nitrochalcone** (V) was hydrolyzed in a similar manner, as in (a), to produce a 47% yield of *o*-nitrodibenzoylmethane. Almost half of the starting material was recovered after 12 hr. of reflux with 15% sulfuric acid.

(c) **α-Diethylamino-4-nitrochalcone** (X) (1.0 g.) was refluxed for 6 hr. with 20 ml. of 15% sulfuric acid and the reaction mixture cooled and extracted with ether. Evaporation of the ether extract produced an oily solid which was recrystallized from 95% ethanol after decolorizing with charcoal; m.p. 119–120°, wt. 0.70 **g.** (84.5% yield), *p-nitrobenzylphenyl diketone* (**XII**).

Anal. Calcd. for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12. Found: C, 67.09; H, 4.34.

A 0.027-g. (0.001 mole) sample of XII was heated for a few minutes with 0.108 g. (0.001 mole) of *o*-phenylendiamine in 5 ml. of abs. ethanol. Cooling the mixture produced **2-(*p*-nitrobenzyl)-3-phenylquinoxaline (XIII)**; recrystallized from 95% ethanol, m.p. 124–125°, wt. 0.292 g. (86% yield).

Anal. Calcd. for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 74.09; H, 4.29; N, 12.78.

(c) **α-Diethylamino-3-nitrochalcone (XI)** (1.0 g.) was refluxed with 20 ml. of 15% sulfuric acid for 3 hr., cooled and extracted with ether. Evaporation of the ether gave an oil which was dissolved in 5 ml. of abs. ethanol and warmed with 0.329 g. of *o*-phenylenediamine. Cooling produced **2-(*m*-nitrobenzyl)-3-phenylquinoxaline**,[12] recrystallized from 95% ethanol, m.p. 120–121.5°, wt. 0.83 g. (78% yield).

2-(*p*-Nitrophenyl)-3-benzoylethylenimine (**XIV**).—A 4.13-g. (0.010 mole) sample of 2,3-dibromo-3-(*p*-nitrophenyl)-propiophenone was suspended in 50 ml. of abs. ethanol and the mixture saturated with anhydrous ammonia and allowed to stand in the dark at room temperature for one week. The dibromide dissolved in about three days. The solvent was removed under reduced pressure and the residue mixed with water and extracted with ether. Evaporation of the ether and recrystallization of the oily residue from 95% ethanol produced 2.23 g. (78% yield) of XIV, m.p. 142–143°. This product appears to be identical with that reported by Wieland[7] as either the ethylenimine ketone or a dimer having a piperazine structure, which he preferred. A mol. wt. determination by the cryoscopic method showed the structure of this product actually to be XIV.

No other identifiable products could be isolated from this reaction mixture.

LINCOLN, NEBRASKA

[CONTRIBUTION FROM THE LABORATORY OF CHEMICAL PHARMACOLOGY, NATIONAL CANCER INSTITUTE[1]]

meso-Dihydroguaiaretic Acid and its Derivatives[2]

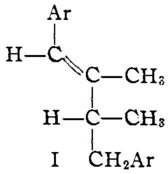
BY ANTHONY W. SCHRECKER

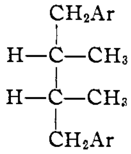
RECEIVED FEBRUARY 28, 1957

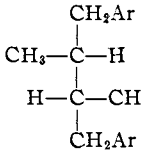
The contaminant of crude guaiaretic acid (I, R = H) has been identified as *meso*-dihydroguaiaretic acid (II, R = H). II (R = Me) and its DL-isomer have been synthesized by a stereospecific method. The infrared spectra of diastereoisomers in this series are discussed.

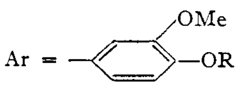
Guaiaretic acid (I, R = H), a key compound in the elucidation of the absolute configuration of lignans,[3] occurs in *Guaiacum officinale* L.[4] together with a number of related compounds.[5] Its isolation has, however, been complicated by the presence of a contaminant, which lowers the optical rotation of the crude product and from which it is not readily separated. Schroeter, who was the first to obtain pure I (R = H) (m.p. 99–100.5°, $[\alpha]_D$ −94° in ethanol),[6] informed Haworth[7] that his crude material was contaminated with an optically active (IIIa, R = H) and an inactive dihydro derivative of I (R = H), both of which occurred naturally in Guaiac resin; however, he never published these findings. He had previously prepared the dimethyl ethers of these dihydro compounds by reduction of I (R = Me) and assigned the *meso* configuration (II, R = Me) to the inactive ether, m.p. 100–101°, because of its mode of formation and because its diamino derivative could not be resolved.[6] Haworth,[7] however, prepared the same compound, m.p. 101–102°, by reduction of synthetic (DL)-I (R = Me) and named it "*dl*-dihydroguaiaretic acid dimethyl ether." He and Cartwright[8] later isolated I (R = Ac) and one of its dihydro derivatives from Guaiac resin after acetylation, but reported no optical rotations.[9]

Although it is generally assumed[4] that Schroeter's inactive dimethyl ether does possess the *meso* rather than the DL-configuration, confirmatory proof was desired. This was accomplished by a stereospecific synthesis of both II and IIIb (R = Me). In addition, the contaminant that lowers the rotation of crude I (R = H) was identified as its


I


II (*meso*)


IIIa, *active*
IIIb, DL



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[1] National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare.

[2] Presented in part at the XIVth International Congress of Pure and Applied Chemistry in Zurich, Switzerland, July 22, 1955; *cf.* Congress Handbook, p. 45.

[3] A. W. Schrecker and J. L. Hartwell, *J. Org. Chem.*, **21**, 381 (1956); THIS JOURNAL, **79**, 3827 (1957).

[4] For leading references, see (a) H. Erdtman in Paech and Tracey, "Modern Methods of Plant Analysis," Vol. III, Springer-Verlag, Berlin, 1955, p. 428; (b) W. M. Hearon and W. S. MacGregor, *Chem. Revs.*, **55**, 957 (1955).

[5] F. E. King and J. G. Wilson, Congress Handbook, XVIth International Congress of Pure and Applied Chemistry, Paris, 1957; *J. Chem. Soc.*, to be published.

[6] G. Schroeter, L. Lichtenstadt and D. Ireneu, *Ber.*, **51**, 1587 (1918).

[7] R. D. Haworth, C. R. Mavin and G. Sheldrick, *J. Chem. Soc.*, 1423 (1934).

[8] N. J. Cartwright and R. D. Haworth, *ibid.*, 948 (1947).

[9] Inactive dihydroguaiaretic acid dimethyl ether, m.p. 102–103°, was also obtained by methylation of nordihydroguaiaretic acid, isolated from *Larrea divaricata*: *cf.* C. W. Waller and O. Gisvold, *J. Am. Pharm. Assoc., Sci. Ed.*, **34**, 78 (1945).