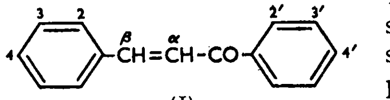
196. *Chalcones and Related Compounds. Part I. Preparation of Nitro-, Amino-, and Halogeno-chalcones.*

By W. Davey and J. R. Gwilt.

Preparation of mononitrochalcones by an improved method is described and the mononitration of chalcone has been investigated. Amino- and halogeno-chalcones have been prepared by various methods and the most satisfactory preparative conditions established.

Chalcone (I) (ω-benzylideneacetophenone) and substituted chalcones have been prepared and certain reactions of this typical αβ-unsaturated ketone system studied. The results will be described in this and in subsequent publications. Preliminary studies were devoted to the establishment of the optimum preparative conditions for substituted chalcones and, whilst condensation of the appropriate benzaldehyde and acetophenone in aqueous ethanol by means of sodium hydroxide [1] represents the most satisfactory approach, dismutation of uncondensed aldehyde occurs under strongly alkaline conditions, particularly with the nitrobenzaldehydes.[2] Since magnesium hydroxide suspensions [3] or aqueous sodium carbonate failed to effect condensation, dismutation has been minimised by the use of benzylidene diacetates, prepared by the addition of acetic anhydride to the benzaldehyde in presence of phosphoric acid,[4] and good yields of chalcones, free from gums, have been obtained. At least 1·5 equivalents of sodium hydroxide, relative to diacetate, were necessary for high yields, and in the preparation of cinnamylideneacetophenone at least 3 equivalents of alkali, relative to cinnamylidene diacetate, were necessary. The results obtained are given in Table 1. 2-Nitrochalcone was less pure than the other nitrochalcones, but the very ready dismutation of *o*-nitrobenzaldehyde made use of the diacetate essential.

Nitration of chalcone with nitric acid in acetic anhydride at low temperatures on a somewhat larger scale than that used by previous workers [5] yielded a mixture of 2- and 4-nitrochalcone, together with some oil. Solubility studies showed that ether or benzene was a suitable solvent to separate these isomers and a mixed melting point curve for mixtures of the two isomers was prepared. Attempts to identify 2-nitrochalcone by indigo formation [3,6] were not successful.



(I)

The direct condensation [1] of aminobenzaldehydes with acetophenones, or of benzaldehydes with aminoacetophenones, gives impure products.[7] Protection of the aldehyde group by diacetate formation in the alkaline condensation gave gums from which low

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[1] *Org. Synth.*, Coll. Vol. I, 2nd Edn., p. 78.

[2] Davey and Gwilt, *J.*, 1950, 204.

[3] *Idem, J. Soc. Chem. Ind.*, 1950, **69**, 330.

[4] *Idem, J.*, 1955, 1385.

[5] Goldschmidt, *Ber.*, 1895, **28**, 986; Tanasescu and Georgescu, *J. prakt. Chem.*, 1934, **139**, 189; Le Fèvre, Markham, and Pearson, *J.*, 1933, 344.

[6] Shriner and Kurosawa, *J. Amer. Chem. Soc.*, 1930, **52**, 2538; Janovsky, *Ber.*, 1891, **24**, 971; Best and Nicholson, *Ind. Eng. Chem. Anal.*, 1935, **7**, 190.

[7] Giua and Bagiella, *Gazzetta*, 1921, **51**, II, 116; Scholtz and Huber, *Ber.*, 1904, **37**, 392.

yields (23—44%) of aminochalcones were extracted by hot mineral acid. By the use of acetylation to protect the amino-group, alkaline condensation has been achieved in satisfactory yields (68—84%). Ease of hydrolysis of acetamido-groups in the resulting chalcones varied markedly with their position.

Aminochalcones were also prepared by reduction of the nitrochalcones and a comparative study of reduction methods was made for 3-nitrochalcone; yields were <40% (iron–acetic acid), 46% (neutral iron,[8] increased to 51% by preforming ferrous chloride), 51% (ferrous hydroxide[9]), 44% (sodium hydrogen sulphide[10]), and 76% (stannous chloride–hydrochloric acid.[11]). The stannous chloride–hydrochloric acid reduction was also the most satisfactory route for the other nitrochalcones, 52—79% yields being obtained, depending on the position of the nitro-group. Aminochalcones were obtained from the stannichlorides by treatment with excess of ammonia solution, followed by extraction with benzene[12] or preferably acetone.[13] Overall yields of aminochalcones from the nitrobenzaldehyde or nitroacetophenone are shown in Table 2, stannous chloride–hydrochloric acid–acetic acid reduction being the most satisfactory procedure.

TABLE 1. *Alkaline condensation of diacetates with acetophenone.*

Diacetate	Ratio NaOH/diacetate (equivs./mole)	Yield (%)	Diacetate	Ratio NaOH/diacetate (equivs./mole)	Yield (%)
Benzylidene ...	2·6	92	*o*-Nitrobenzylidene	0·6	0
	6·5	88		2·8	78
Cinnamylidene	2·3	0	*m*-Nitrobenzylidene	1·1	10
	3·0	58		1·8	92
			p-Nitrobenzylidene	0·6	53
				2·7	100

TABLE 2. *Yields (%) of aminochalcones by various routes.*

Amino-chalcone	By reduction of nitro-chalcone	By alkaline condensation NH$_2$-group protected	NH$_2$-group not protected	Amino-chalcone	By reduction of nitro-chalcone	By alkaline condensation NH$_2$-group protected	NH$_2$-group not protected
2-	41	—	16	2′-	45	—	10
3-	73	76	33	3′-	75	63	50
4-	79	23	11	4′-	54	(84) *	(31) *

* Calc. on *p*-aminoacetophenone, prepared from acetanilide by a method similar to that of Kaslow, Genzer, and Goodspeed (*Proc. Indiana Acad. Sci.*, 1950, **59**, 139; *Chem. Abs.*, 1951, **45**, 8534).

TABLE 3. *Yields (%) of halogenochalcones from amines by diazotisation in hydrochloric or phosphoric acid.*

Aminochalcone	Halogenochalcone	HCl	H$_3$PO$_4$	Aminochalcone	Halogenochalcone	HCl	H$_3$PO$_4$
3-Amino-	3-Chloro-	—	46	3′-Amino-	3′-Chloro-	18	52
4-Amino-	4-Chloro-	33	—	,,	3′-Bromo-	6-	36
,,	4-Bromo-	—	57	4′-Amino-	4′-Chloro-	29	57
,,	4-Iodo-	47	—	,,	4′-Bromo-	51	54

Dankova *et al.*[14] reported m. p. 96—97° for 2-aminochalcone and m. p. 119—120° for its hydrochloride, but the present authors have found m. p. 115° for the free amine while attempts to prepare a hydrochloride yielded resins (m. p. >300°). In some instances, reduction of 3-nitrochalcone by iron and acetic acid gave a product, m. p. 147°, which appeared to be a labile form of 3-aminochalcone, m. p. 159°; two hydrochlorides, m. p. 186° and 198°, were obtained, each of which yielded the stable aminochalcone (m. p. 159°)

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[8] West, *J.*, 1925, 494.

[9] *Org. Synth.*, Coll. Vol. III, p. 56.

[10] Haworth and Lapworth, *J.*, 1922, 76.

[11] Dilthey and Berres, *J. prakt. Chem.*, 1925, **111**, 340.

[12] Pfeiffer, *Annalen*, 1925, **441**, 228.

[13] Rupe and Porai-Koschitz, *Z. Farbst. Ind.*, 1906, **5**, 317.

[14] Dankova, Bokova, Preobrazhenskii, Petreshenko, Il'shtein, and Shvetsov, *Zhur. obshchei Khim.*, 1951, **21**, 787.

TABLE 4. *Overall yields (%) of halogenochalcones (based on original nitrobenzaldehyde or nitroacetophenone) by various routes.*

Chalcone	*via* Amine and diazotisation: Aminochalcone not isolated	*via* Amine and diazotisation: Aminochalcone pre-isolated	Halogeno-benzaldehyde or -acetophenone and alkaline condensation
3-Chloro-	48	35	71
3-Bromo-	27	—	62
4-Chloro-	—	26	49
4-Bromo-	—	45	53
4-Iodo-	—	37	52
3′-Chloro-	48	39	89
3′-Bromo-	30	27	61
4′-Chloro-	—	31	71
4′-Bromo-	35	38	49

TABLE 5. *Effect of the nature and position of certain substituents on the melting points of corresponding chalcones.*

(Italic figures denote new compounds).

Subst. position	Substituent					Subst. position	Substituent				
	Cl	Br	I	NO_2	NH_2		Cl	Br	I	NO_2	NH_2
2	52°	*72°*	*80°*	124°	*115°*	2′	94°	Oil	*113°*	124°	147°
3	75	84	*90*	148	159	3′	*93*	*94*[b]	*85*	129	*124*
4	114	123	*137*	164	151	4′	100	104	*115*	146	108

with aqueous ammonia. Mannich and Dannehl [15] have described a labile form of 2-aminochalcone, but in the present work only the stable form was obtained. Two forms of 3-acetamidochalcone, m. p. 104° [13] and m. p. 119°,[16] have been reported; in the present work the form of lower m. p. was obtained from the alkaline condensation of *m*-acetamidobenzaldehyde and acetophenone.

Decomposition of chalcone diazonium salts gave somewhat low yields of halogenochalcones (Table 3) and the most satisfactory route to these compounds was *via* the appropriate halogeno-benzaldehyde or -acetophenone, followed by the usual alkaline condensation (Table 4). Table 5 details the melting points now obtained for all the *ar*-monohalogenochalcones, together with those for the nitro- and amino-compounds, and suggests some semblance of order in these melting points.

EXPERIMENTAL

m-*Aminobenzaldehyde*.—(*a*) *m*-Nitrobenzaldehyde (10 g.) was reduced by stannous chloride–hydrochloric acid,[17] and the precipitated stannichloride treated with excess of ammonia (*d* 0·88). The residue was washed with 10% aqueous ammonia until chloride-free and extracted with ether. Removal of the ether yielded 6·1 g. (76%) of *m*-aminobenzaldehyde, m. p. indeterminate. Borsche and Sell [18] claim a crystalline form, m. p. 28—30°; other workers have obtained only the amorphous polymer.

(*b*) A freshly prepared mixture of sodium sulphide solution (50 g. in 50 ml. of water) and hydrochloric acid (25 ml.; *d* 1·18) was added to a solution of *m*-nitrobenzaldehyde (20 g.) in 95% (v/v) alcohol (140 ml.). Next morning, the bulk of the alcohol was distilled off and excess of water added. The gummy product was purified by dissolution in hydrochloric acid and reprecipitation with ammonia to yield 5·6 g. (35%) of *m*-aminobenzaldehyde.

(*c*) *m*-Nitrobenzaldehyde (13 g.) was dissolved in acetic acid (*d* 1·05; 50 ml.), water (360 ml.) and degreased activated iron powder (20 g.) were added, and the mixture was heated on the water-bath for 8 hr. The amine was isolated and purified in the usual way (4·7 g., 45%).

(*d*) Calcium chloride (10 g. of dihydrate in 15 ml. of water) and zinc dust (150 g.) were

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[15] Mannich and Dannehl, *Ber.*, 1938, **71**, *B*, 1899.
[16] Kaufmann and Burckhardt, *ibid.*, 1913, **46**, 3812.
[17] *Org. Synth.*, Coll. Vol. II, p. 130.
[18] Borsche and Sell, *Ber.*, 1950, **83**, 78.

added to a solution of *m*-nitrobenzaldehyde (15 g.) in 78% (v/v) alcohol (500 ml.), and the mixture refluxed for 1·5 hr. The solution was filtered, the bulk of the alcohol distilled off, and the amine precipitated with water, to yield 5·1 g. (43%) of *m*-aminobenzaldehyde as a gum-free yellow powder, melting over the range 83—155°.

The aldehyde (5 g.) was dissolved in acetic anhydride (25 ml.) and stirred with phosphoric acid (2 ml.; *d* 1·75) at 60° for 1 hr., then kept overnight at room temperature, and diluted with water to yield 5·0 g. (76%) of *m*-acetamidobenzaldehyde, m. p. 82° (Friedländer and Fritsch [19] give m. p. 84°).

o-Acetamidoacetophenone (5·3 g., 81%) was obtained by heating the amine (5 g.) for 0·5 hr. with acetic anhydride (15 ml.) and had m. p. 76°. Gevekoht [20] gave m. p. 76—77°.

m-*Aminoacetophenone*.—(*a*) Reduction of *m*-nitroacetophenone (10 g.) in 25%(w/v) acetic acid (400 ml.) with electrolytic iron powder (20 g.; 80—150 mesh) for 8 hr. on the water-bath, followed by addition of excess of alkali and steam-distillation, yielded 5·5 g. (68%) of *m*-aminoacetophenone, m. p. 97°. Elson *et al.*[21] gave m. p. 98—99° (see also Morgan *et al.*[22] and Phillips [23]).

(*b*) Reduction of *m*-nitroacetophenone (10 g.) with ferrous sulphate (150 g. of heptahydrate in 250 ml. of water) and ammonia (55 ml.; *d* 0·88) under reflux for 1 hr., followed by steam-distillation, yielded 5·7 g. (71%), m. p. and mixed m. p. 97°.

(*c*) Reduction of *m*-nitroacetophenone (10 g.) by Morgan and Moss's method [22] yielded 6·7 g. (82%), m. p. and mixed m. p. 97°.

The amine (4·6 g.), refluxed with acetic acid (10 ml.) and acetic anhydride (20 ml.) for 0·5 hr., yielded *m*-acetoamidoacetophenone (5·4 g., 92%), m. p. 127°. Rupe *et al.*[24] gave m. p. 128—129°.

p-*Acetamidoacetophenone*.—(*a*) Acetanilide (10 g.) and zinc chloride (25 g.) were refluxed in acetic anhydride (100 ml.) for 1·5 hr., then poured into water. The resulting black oil was extracted repeatedly with boiling water and alcohol, to yield *p*-acetamidoacetophenone (4·0 g., 30%), m. p. 169° (Raiford *et al.*[25] gave m. p. 169°; cf. Klingel [26] and Kunckell [27]).

(*b*) Acetanilide (25 g.) in carbon disulphide (250 ml.) was refluxed with acetyl chloride (50 ml.) and aluminium chloride (100 g.) for 8 hr. The carbon disulphide was decanted off and the residue treated with water, to yield the ketone (25 g., 76%), m. p. and mixed m. p. 169°.

p-*Aminoacetophenone*.—The preceding acetyl derivative (10 g.) was refluxed for 1 hr. with N-sodium hydroxide (100 ml.), neutralised, and left overnight to yield *p*-aminoacetophenone (3·5 g., 69%), m. p. 106° (Drewsen [28] gave m. p. 106°; cf. Kaslow *et al.*[29]).

Preparation of Chalcone.—To benzylidene diacetate (10 g.) and acetophenone (7 g.) in 95% alcohol (100 ml.) 10% (w/v) sodium hydroxide solution (50 ml.) was added with stirring and, after 30 min., diluted with water (800 ml.). The precipitated chalcone (9·2 g., 92%) had m. p. and mixed m. p. 56° *Org. Synth.*[1] gives m. p. 55—57°).

Increase of alkali concentration to 50% gave a reduced yield (8·8 g., 88%; m. p. 55°).

The standard method [1] using benzaldehyde gave a yield of 92% (m. p. 55°).

Preparation of Nitrochalcones.—(a) *From nitrobenzaldehydes*. By the standard method,[1] from nitrobenzaldehyde (10 g.) and acetophenone (9 g.) with the other materials *pro rata*.

(b) *From nitrobenzylidene diacetates*. The diacetate (10 g.) was suspended in a solution of acetophenone (5 g.) in 95% alcohol (60 ml.), and 20% (w/v) sodium hydroxide solution (20 ml.) was added slowly. The mixture was stirred for 15 min., diluted with about 2 vols. of water, acidified with hydrochloric acid, and filtered. 2- and 3-Nitrochalcone were recrystallised from aqueous acetic acid, other nitrochalcones from alcohol or aqueous alcohol.

Yields and m. p.s are given in Table 6.

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[19] Friedländer and Fritsch, *Monatsh.*, 1903, **24**, 1.
[20] Gevekoht, *Ber.*, 1882, **15**, 2083.
[21] Elson, Gibson, and Johnston, *J.*, 1930, 1128.
[22] Morgan and Moss, *J. Soc. Chem. Ind.*, 1923, **42**, 461T.
[23] Phillips, *Manuf. Chem.*, 1952, **23**, 476.
[24] Rupe, Braun, and Zembruski, *Ber.*, 1901, **34**, 3522.
[25] Raiford and Davis, *J. Amer. Chem. Soc.*, 1928, **50**, 158.
[26] Klingel, *Ber.*, 1884, **17**, 1613.
[27] Kunckell, *Ber.*, 1900, **33**, 2641.
[28] Drewsen, *Annalen*, 1882, **212**, 150.
[29] Kaslow, Genzer, and Goodspeed, *Proc. Indiana Acad. Sci.*, 1950, **59**, 139; *Chem. Abs.*, 1951, **45**, 8534.

TABLE 6. *Yields of nitrochalcones.*

Posn. of NO_2	Yield (%) from :			Published results (refs. in parentheses)	
	aldehyde	diacetate	M. p.	Yield (%)	M. p.
2-	(48)	78	128—130°	46 (*a*)	119—120° to 126° (14, *b*—*d*)
3-	96	92	148	—	120°, 145—146° (*c*, *d*)
4-	94	100	164	79 (*a*)	150°, 163·5°, 164° (*d*, *e*)
2′-	87	91	124	—	124° to 129° (*d*, *f*, *g*)
3′-	97	99	129	—	110°, 125—127°, 131° (*d*, *e*, *g*, *h*)
4′-	92	95	146	—	146·5—147° to 150° (*d*, *g*, *i*)

(*a*) Dippy and Lewis, *Rec. Trav. chim.*, 1937, **56**, 1000. (*b*) Tanasescu and Baciu, *Bull. Soc. chim. France*, 1937, **4**, 1742. (*c*) Sorge, *Ber.*, 1902, **35**, 1067. (*d*) Weygand and Schacher, *Ber.*, 1935, **68**, 2498. (*e*) Le Fèvre *et al.*, see ref. 5. (*f*) Engler and Dorant, *Ber.*, 1895, **28**, 2500. (*g*) Dilthey, Neuhaus, and Schommer, *J. prakt. Chem.*, 1929, **123**, 235. (*h*) Barnes and Dodson, *J. Amer. Chem. Soc.*, 1943, **65**, 1585. (*i*) Weygand, *Annalen*, 1927, **459**, 115.

Cinnamylidene Diacetate.—Cinnamaldehyde (11 g.) was added during 5 min. to a stirred mixture of acetic anhydride (80 ml.) and phosphoric acid (2 ml.; *d* 1·75). The whole was poured into water. The diacetate, which solidified, was filtered off (yield, 19·0 g., 97%) and had m. p. 86° (Späth [30] gave m. p. 86°). A slight yellow colour was removed by washing the product with a little ice-cold alcohol (no change in m. p.).

Cinnamylideneacetophenone.—(*a*) From cinnamylidene diacetate, by the same method as for nitrochalcones, cinnamylideneacetophenone was obtained in 58% yield, with m. p. 97°, rising to 102° on one recrystallisation from aqueous ethanol. Stobbe and Rucker [31] give m. p. 102—103°.

(*b*) From cinnamaldehyde by the same method, the acetophenone was obtained in 84% yield, with m. p. 93°, rising to 102° on one recrystallisation.

Nitration of Chalcone.—To chalcone (50 g.), in acetic anhydride (500 ml.) containing phosphoric acid (5 ml.; *d* 1·75) at $-5°$, nitric acid (35 ml.; *d* 1·52) was added at such a rate that the temperature did not exceed $-5°$. Stirring was continued for 30 min. at $-5°$ and the mixture poured into ice-water (5 l.). The precipitated oil ($\sim$56 g.) was washed with a little cold ethanol, leaving 47 g. of material, m. p. 124°. Fractionation from ethanol yielded only 2- (m. p. and mixed m. p. 128°) and 4-nitrochalcone [m. p. 160°; m. p. (from benzene) and mixed m. p. 164°]. From the mixed m. p. curve the relative proportions of the 2- and 4-nitrochalcone were approximately 60 : 40. Hence overall yields were: 2-nitrochalcone 46%, 4-nitrochalcone 31%, unidentified material 23%.

2- and 4-Nitrochalcone form a eutectic mixture approximately in the ratio 70 : 30, with m. p. 112°.

Solubilities of 2- and 4-nitrochalcones were determined by evaporating known amounts of saturated solutions, with the following results (g./100 ml.): in C_6H_6 at 20°, 2- 3·7, 4- 0·7; in C_6H_6 at 40°, 2- 5·1, 4- 1·8; in ether at 20°, 2- 1·0, 4- 0·13.

Aminochalcones by Direct Condensation.—Generally, the methods used for the preparation of nitrochalcones (see above) proved successful except that the crude products contained much gum. This was extracted with hot 2N-hydrochloric acid, and the aminochalcones were reprecipitated by addition of 2N-sodium hydroxide to the cold solution and recrystallised from alcohol (charcoal) (see Table 2).

Although Borsche and Sell [18] claim to have obtained crystalline *m*-aminobenzaldehyde, it proved possible to prepare only the usual polymeric form, insoluble in alcohol. Accordingly for direct condensation the aldehyde (1·0 g.) was first dissolved in 5N-hydrochloric acid (10 ml.), and acetophenone (1·1 g.) in 95% alcohol (40 ml. v/v) was added. 10% (w/v) Sodium hydroxide solution (*ca.* 25 ml.) was added to basify the mixture which was then kept at 50° for 45 min. and left overnight at 20°. Filtration yielded 1·6 g. of gum. Extraction with hydrochloric acid followed by reprecipitation and recrystallisation from alcohol (charcoal) yielded 0·8 g. (44%) of 3-aminochalcone, m. p. and mixed m. p. 159°. Rupe and Porai-Koschitz [13] gave m. p. 159°.

The standard method [1] was also used for the preparation of aminochalcones from acetamidoacetophenones (see Table 2).

Hydrolysis of Acetamidochalcones.—(a) 3-*Aminochalcone.* The acetyl compound (5 g.) was

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[30] Späth, *Monatsh.*, 1915, **36**, 29.

[31] Stobbe and Rucker, *Ber.*, 1911, **44**, 869.

refluxed for 30 min. with a slight excess of 2N-sodium hydroxide, further quantities being added as required to maintain a slightly alkaline reaction. Cooling the mixture yielded 3·8 g. (90%) of 3-aminochalcone, m. p. (from alcohol) and mixed m. p. 159°.

(b) 4-*Aminochalcone*. Alkaline condensation of *p*-acetamidobenzylidene diacetate (5 g.) and acetophenone (2·5 g.) by the standard method [1] yielded a mixture of 4-aminochalcone and its acetyl derivative. The mixture was refluxed with 2N-sodium hydroxide as above, to yield 3·4 g. (68% referred to the diacetate) of 4-aminochalcone, m. p. 151° (from alcohol). Rupe and Porai-Koschitz [13] gave m. p. 151°.

(c) 4′-*Aminochalcone*. Procedure as for the 4-amino-compound gave an 84% yield (from *p*-acetamidoacetophenone), m. p. and mixed m. p. 106°. Scholtz and Huber,[7] and Dilthey *et al.*[32] gave m. p. 108°.

Reduction of Nitrochalcones.—The nitrochalcone (10 g.) was stirred with stannous chloride (40 g. of the dihydrate) and hydrochloric acid (100 ml.; *d* 1·18) and slowly warmed to 90°. The mixture was then generally homogeneous. The solution was left overnight at 0° and the stannichloride compound filtered off. It was mixed with excess of aqueous ammonia and the resultant paste drained at the pump and extracted with boiling acetone. The solvent was removed at room temperature and the residual chalcone recrystallised from alcohol (see Table 2).

2-*Aminochalcone*. 2-Nitrochalcone (5 g.) yielded 2-*aminochalcone* (2·3 g., 52%), m. p. 115° (Found: N, 6·2. $C_{15}H_{13}ON$ requires N, 6·3%). Dankova *et al.*[14] give m. p. 96—97° but their analytical figures do not confirm their having obtained this amine.

3-*Aminochalcone*. A form of m. p. 159° was obtained by reduction of 3-nitrochalcone as above. In some runs by the method of Marrian, Russell, and Todd [33] material (about 35%), m. p. 147° (from alcohol), was obtained. This had mixed m. p. 158° with authentic 3-aminochalcone of m. p. 159°, and mixed m. p. 120—125° with the original 3-nitrochalcone of m. p. 148°. This *form* was readily soluble in mineral acids (Found: C, 80·5; N, 6·3. $C_{15}H_{13}ON$ requires C, 80·7; N, 6·3%).

2N-Hydrochloric acid at 40° was saturated with 3-aminochalcone of m. p. 159°. When the filtrate was left at room temperature colourless plates of the *hydrochloride* were deposited, having m. p. 198° (from water) (Found: Cl^-, 13·9. $C_{15}H_{13}ON,HCl$ requires Cl, 13·7%). Addition of excess of ammonia yielded 3-aminochalcone, m. p. and mixed m. p. 159°. This (higher-melting) hydrochloride was also obtained on boiling the lower-melting amine with 2N-hydrochloric acid.

2N-Hydrochloric acid was saturated with 3-aminochalcone of m. p. 147° at room temperature. On storage, an amorphous *hydrochloride* was deposited, of m. p. 186° (Found: Cl^-, 13·8%). A mixed m. p. with the higher-melting form was 198°. Shaking this salt with excess of ammonia yielded 3-aminochalcone, m. p. and mixed m. p. 159°. Adams, Cohen, and Rees [34] obtained a crude hydrochloride, m. p. 185—195° (decomp.), as the first product in the catalytic hydrogenation of 3-nitrochalcone.

3′-*Acetamidochalcone*.—*m*-Acetamidoacetophenone (5 g.) was dissolved in alcohol (20 ml.; 95% v/v) containing benzaldehyde (4 g.). 2N-Sodium hydroxide (5 ml.) was added and the mixture stirred at room temperature for 30 min., then just neutralised with 5N-hydrochloric acid, and most of the alcohol was distilled off, yielding 3′-*acetamidochalcone* (5·9 g., 92%), m. p. 138° (from alcohol) (Found: N, 5·4. $C_{17}H_{15}O_2N$ requires N, 5·3%). 3′-Aminochalcone, prepared by ferrous hydroxide reduction of 3′-nitrochalcone, was acetylated by boiling acetic anhydride: the m. p. and mixed m. p. with the above material were 138°.

3′-*Aminochalcone*.—3′-Acetamidochalcone (5 g.) was refluxed with a 2% aqueous suspension (50 ml.) of magnesium hydroxide for 1 hr., neutralised with 2N-sulphuric acid, and cooled, to yield 3′-*aminochalcone* (4·0 g., 98%), m. p. 124° (Found: N, 6·2. $C_{15}H_{13}ON$ requires N, 6·3%). This was also prepared by direct condensation of *m*-aminoacetophenone with benzaldehyde or benzylidene diacetate (yields 40% and 61% respectively), and by reduction of 3′-nitrochalcone with iron–acetic acid [32] (yield 26%), ferrous hydroxide [9] (yield 36%), or stannous chloride–hydrochloric acid as above (yield 78%). After recrystallisation all samples had m. p. and mixed m. p. 124°.

Halogenochalcones from Nitrochalcones.—(a) *Chlorochalcones*. Stannous chloride (80 g. of the dihydrate) in hydrochloric acid (100 ml.; *d* 1·16) was refluxed with the nitrochalcone

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[32] Dilthey, Neuhaus, Reis, and Schommer, *J. prakt. Chem.*, 1930, **124**, 81.

[33] Marrian, Russell, and Todd, *J.*, 1947, 1419.

[34] Adams, Cohen, and Rees, *J. Amer. Chem. Soc.*, 1927, **49**, 1097.

(10 g.) for 30 min., then left overnight at room temperature. Diazotisation at 0—5° with sodium nitrite (10 g. in 30 ml. of water) and treatment with cuprous chloride–hydrochloric acid gave little nitrogen, and a mixture of chlorochalcone and amine stannichloride (*ca.* 12 g.) was obtained from which chloro- and amino-chalcones were extracted by hot acetone.

TABLE 7. *Preparation of known halogenochalcones by alkaline condensation.*

Chalcone	Yield (%)	M. p.	Refs.	Chalcone	Yield (%)	M. p.	Refs.
2-Chloro-	83	52°	*a, b*	3-Bromo-	93	84°	*h*
3-Chloro-	94	75	*b, c*	4-Bromo-	99	123	*a*
4-Chloro-	89	114	*b, d, e,* 25	2′-Bromo-	62	Oil	*i*
4′-Chloro-	87	100	*e, f, g*	4′-Bromo-	94	104	*e—h, j*

(*a*) Weygand and Gunther, *Annalen*, 1927, **459**, 118; Pfeiffer and Kunze, *J. prakt. Chem.*, 1928, **119**, 119; Bickel, *J. Amer. Chem. Soc.*, 1946, **68**, 865. (*b*) Ref. *a* of Table 6. (*c*) Eaton, Black, and Fuson, *J. Amer. Chem. Soc.*, 1934, **56**, 687. (*d*) Von Walther and Raetze, *J. prakt. Chem.*, 1902, **65**, 280; Weitz and Scheffer, *Ber.*, 1921, **54**, 2339. (*e*) Dilthey, *J. prakt. Chem.*, 1921, **101**, 202; *f*, Allen and Frame, *Canad. J. Res.*, 1932, **6**, 605. (*g*) Brandstätter, *Monatsh.*, 1949, **80**, 1. (*h*) Stevens, *J.*, 1930, 2107. (*i*) Barnes and Payton, *J. Amer. Chem. Soc.*, 1936, **58**, 1300. (*j*) Kohler, Heritage, and Burnley, *Amer. Chem. J.*, 1910, **44**, 67.

TABLE 8. *New halogenochalcones and " mixed " chalcones.*

			Found (%)	Required (%)				Found (%)		Required (%)	
Chalcone	M. p.	Yield (%)	Hal	Hal	Chalcone	M. p.	Yield (%)	Hal	N	Hal	N
2′-Chloro-	94°	76	14·4	14·6	4′-Iodo-	115°	94	37·8	—	38·0	—
3′-Chloro-	93	96	14·3	14·6	4′-Bromo-2-chloro-	106	99	22·0 *	—	22·1	—
2-Bromo-	(72)	—	29·1	27·9	4 : 4′-Di-iodo-	216	91	54·7	—	55·2	—
3′-Bromo-	94	94	27·5	27·9	2-Chloro-3′-nitro-...	152	74	12·2	4·8	12·3	4·9
2-Iodo- ...	80	78	37·3	38·0	4′-Bromo-3-nitro-	172	93	24·0	4·1	24·1	4·2
3-Iodo- ...	90	92	37·9	38·0	4′-Chloro-3-nitro-...	145	90	12·3	4·7	12·3	4·9
4-Iodo- ...	137	92	37·9	38·0	4′-Chloro-4-nitro-...	164 †	92	12·3	4·8	12·3	4·9
2′-Iodo-...	113	53	38·4	38·0	4-Dimethylamino-						
3′-Iodo-...	85	89	37·7	38·0	3′-nitro-	170	89	—	9·3	—	9·5

* Total halogen, as Cl. † Mixed m. p. *ca.* 148° with 4-nitrochalcone (m. p. 164°).

(b) *Bromochalcones.* Reduction of nitrochalcones by stannous bromide–hydrobromic acid, diazotisation, and decomposition of the diazonium salt with cuprous bromide [17] gave the bromochalcones. The 3-, 3′-, and 4′-bromo-compound were thus obtained in 28, 31, and 38% yield respectively.

(c) *Iodochalcones.* Preliminary results were disappointing and direct condensation was therefore used.

Halogenochalcones from Aminochalcones.—(a) *Diazotisation in hydrochloric acid.* 3′-Aminochalcone (5 g.) in hydrochloric acid (50 ml.; *d* 1·16) was diazotised at 0—5° with sodium nitrite (2 g. in 10 ml. of water), and the solution decomposed by acid cuprous chloride.[17] Extraction of the resulting gum with hot ethanol (charcoal) gave 3′-chlorochalcone (1·0 g., 18%), m. p. and mixed m. p. 92°.

(b) *Diazotisation in phosphoric acid.* 3′-Aminochalcone (5 g.) in phosphoric acid (125 ml.; *d* 1·75) was diazotised by Hodgson and Walker's method,[35] with sodium nitrite (5 g.) in phosphoric acid (100 g.; *d* 1·75), and the diazonium compound decomposed by acid cuprous chloride as before, to yield a product from which 3′-chlorochalcone (3·0 g., 54%), m. p. and mixed m. p. 92°, was extracted. Further results of the use of this method are given in Table 3.

Halogenochalcones by Direct Condensation.—The general method [1] was modified to reduce contamination of the final chalcone. The appropriate aldehyde and acetophenone were dissolved in the minimum amount of ethanol at room temperature, sufficient 2N-sodium hydroxide added to render the stirred solution alkaline, and the whole stirred for 30 min. Neutralisation with 2N-hydrochloric acid was followed by dilution with water and storage overnight. The chalcone was filtered off and recrystallised to constant m. p. from ethanol or acetic acid. Yields were generally above 90% (see Tables 7 and 8).

THE POLYTECHNIC, REGENT STREET, LONDON, W.1.

[*Received, July 31st,* 1956.]

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[35] Hodgson and Walker, *J.*, 1933, 1620.