Anal. Calcd. for $C_{28}H_{37}NO_6$: C, 71.90; H, 7.98. Found: C, 72.47; H, 8.54.

Saponification of this oil gave optically inactive **2-hydroxy-3-benzyloxypropanilide**, m.p. 77–78.5°.

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.82; H, 6.32; N, 5.16. Found: C, 70.73; H, 6.42; N, 5.22.

Methyl Cyclopropyl Ketone.—After 17 months at −20° and 1 month at 25° the odor of isocyanide was still quite strong and a work up of the product failed to detect any product other than traces of the isocyanide polymer.

EVANSTON, ILLINOIS RECEIVED JANUARY 14, 1950

[A CONTRIBUTION FROM THE WEIZMANN INSTITUTE OF SCIENCE]

The Action of *t*-Butyl Hypochlorite on Organic Compounds. II. Aromatic Aldehydes[1]

BY DAVID GINSBURG

The action of *t*-butyl hypochlorite on a number of aromatic aldehydes has been investigated. In methoxy-, dimethylamino- and hydroxyaldehydes, nuclear chlorination takes place, whereas in other aldehydes, the hydrogen of the aldehyde group is substituted by chlorine and the corresponding acid chloride is formed.

In continuation of previous experiments, the reaction of aromatic aldehydes with *t*-butyl hypochlorite was studied. The only reference in the published literature to such a reaction was a note by Clark[2] who reported—without experimental details—that benzaldehyde is converted to benzoyl chloride.[2a] Indeed, in some cases, *t*-butyl hypochlorite has been known to effect substitution of hydrogen by chlorine.[3]

Table I summarizes the results obtained. In most cases, the products could be identified by their physical constants. Where this was impossible, an exact proof was provided; the pertinent results are recorded in the Experimental Section.

It can be seen from the table that, on the whole, the hydroxyl, methoxyl and dimethylamino groups activate the nucleus (nuclear chlorination) whereas hydrogen, chlorine or the methyl group activate the aldehyde group (formation of the acid chloride). When the *methoxyl* group is present, the chlorine enters para to it. If the para position is occupied, ortho chlorination occurs.[4]

The *hydroxyl* group is usually ortho directing but in the case of salicylaldehyde, the chlorine atom enters para to the hydroxyl group and not in the other ortho position. In vanillin, it can be seen that the directive influence of the hydroxyl group outweighs that of the methoxyl group since 5-chlorovanillin is obtained. Veratraldehyde conforms to the behavior of the monomethoxy aldehydes, yielding 6-chloroveratraldehyde.

The *dimethylamino* group in *p*-dimethylaminobenzaldehyde (occupied *p*-position!) directs the chlorine atom into the *ortho*-position.

m- and *p*-nitrobenzaldehydes were not attacked by *t*-butyl hypochlorite. Also the carboxyl group exerts a deactivating influence. Thus, benzoic, *p*-toluic and *p*-nitrobenzoic acids were recovered unchanged from the mixture with *t*-butyl hypochlorite.

The *solvent* influences the course of the reaction. In a non-polar solvent such as carbon tetrachloride, also the aldehydes containing a methoxyl group yield the acid chlorides.

Clark's observation that benzaldehyde yields benzoyl chloride upon chlorination with *t*-butyl hypochlorite was duplicated but only under the condition that the *t*-butanol formed in the reaction was removed *in vacuo* (at low temperature); otherwise benzoic acid becomes the main reaction product. This is also the case for anisaldehyde. The formation of benzoic (and anisic) acid is not due to hydrolysis at elevated temperature, as it occurs not only in 90% acetic acid, but also in carefully dried carbon tetrachloride. The following formulas account for these observations:

$$\text{(a)}\quad RCHO + t\text{-BuOCl} \longrightarrow RCOCl + t\text{-BuOH}$$

$$\text{(b)}\quad RCOCl + t\text{-BuOH} \longrightarrow RCOOH + t\text{-BuCl}$$

The chlorination reaction (a) is practically instantaneous. If aniline is added to the reaction mixture soon after the chlorinating agent, a nearly quantitative yield of benzanilide or *p*-anisanilide is obtained. Equally, if, after the addition of the chlorinating agent the *t*-butanol formed is removed *in vacuo*, a high yield of the acid chloride is obtained. If, however, the reaction mixture is heated for some time, the final product is the aromatic acid and, during the heating, *t*-butyl chloride distils off continually.

Experimental[5]

General Chlorination Procedure.—The aldehyde (0.04 mole) is dissolved or suspended (in cases of low solubility) in the solvent (10 ml.) used for the reaction (see table) and *t*-butyl hypochlorite (5 ml.) added with stirring. Usually there is an induction period (30–120 seconds) before a strong exothermic reaction sets in. The reaction mixture is concentrated and the product is isolated by either crystallization or distillation. The products are purified so easily, that in all probability no isomers are formed in addition to those indicated in the table.

Example: Chlorination of Benzaldehyde in Carbon Tetrachloride.—The general procedure was followed: benzaldehyde (4.3 g.) was treated with *t*-butyl hypochlorite (4.4 g.). Immediately after all the hypochlorite had been added, excess aniline was added to the reaction mixture. A nearly quantitative yield of benzanilide (7.5 g.), m. p. 161°, was obtained. The m. p. was not depressed on admixture with an authentic sample. When the *t*-butanol was removed *in*

---

(1) Paper I in this series, Ritter and Ginsburg, THIS JOURNAL, **72**, 2381 (1950).

(2) Clark, *Chem. News*, **143**, 265 (1931).

(2a) It has been brought to our attention by one of the Referees that there are three dissertations in the M.I.T. library on this subject: Bixley, M.S. Thesis, M.I.T. (1927); Clark, Ph.D. Thesis, M.I.T. (1930); Sumner, Ph.D. Thesis, M.I.T. (1934).

(3) For references, *cf.* Ref. 1.

(4) Differences in the directing influence of methoxyl and hydroxyl groups have been observed in other instances, *e.g.*, in bromination (*cf.*, E. Bergmann, *J. Chem. Soc.*, 1284 (1948)) and in the Friedel–Crafts reaction (*cf.* Ch. Weizmann, Haskelberg and Berlin, *ibid.*, 398 (1939)).

(5) All melting and boiling points are uncorrected.

TABLE I

REACTION OF AROMATIC ALDEHYDES WITH *t*-BUTYL HYPOCHLORITE

A = 90% AcOH; B = *t*-BuOH; C = CCl_4; D = mixed m. p. with authentic sample not depressed; E = see Experimental Section

(a) RC_6H_4CHO derivatives R =	Solvent	Product	Proof of Structure	Yield, %
H	A	C_6H_5COOH	D	95
H	C	C_6H_5COCl or C_6H_5COOH	E	96
o-Cl	A	*o*-ClC_6H_4COOH	D	90
o-Cl	B	*o*-ClC_6H_4COOH	D	92
o-Cl	C	*o*-ClC_6H_4COOH	D	94
m-Cl	A	*m*-ClC_6H_4COOH	D	87
p-CH_3	A	*p*-$CH_3C_6H_4COOH$	D	83
o-OH	A	5-Cl-2-HOC_6H_3CHO	E	79
o-CH_3O	A	5-Cl-2-$CH_3OC_6H_3CHO$	M.p. 81°; m.p. semicarbazone 239°[a]	84
o-CH_3O	C	2-$CH_3OC_6H_4COOH$	D	93
m-OH	A	2-Cl-3-HOC_6H_3CHO	M.p. 139°; m.p. semicarbazone 239°[b]	73
m-CH_3O	A	6-Cl-3-$CH_3OC_6H_3CHO$	M.p. 62–63°; m.p. semicarbazone 242°[c]	68
p-OH	A	3-Cl-4-HOC_6H_3CHO	M.p. 132–133°; m.p. semicarbazone 210°[d]	82
p-CH_3O	A	3-Cl-4-$CH_3OC_6H_3CHO$	M.p. 62°; m.p. oxime 115°[e]	77
p-CH_3O	C	*p*-$CH_3OC_6H_4COCl$ or *p*-$CH_3OC_6H_4COOH$	E	94
p-AcO	A	*p*-$AcOC_6H_4COOH$	M.p. 199–200°	86
p-AcO	C	*p*-$AcOC_6H_4COOH$	M.p. 199–200°	91
m-NO_2	A, B, C	No reaction		..
p-NO_2	A, B, C	No reaction		..
p-$(CH_3)_2N$	B	3-Cl-4-$(CH_3)_2NC_6H_3CHO$	E	65
(b) Other aldehydes				
Vanillin	A	5-Cl-vanillin	M.p. 164–166°; m.p. semicarbazone 204°[f]	81
Vanillin	B	5-Cl-vanillin	M.p. 164–166°; m.p. semicarbazone 204°[f]	84
Vanillin	C	5-Cl-vanillin	M.p. 164–166°; m.p. semicarbazone 204°[f]	82
Veratraldehyde	A	6-Cl-veratraldehyde	M.p. 140°[g]	84
Veratraldehyde	B	6-Cl-veratraldehyde	M.p. 140°[g]	77
Veratraldehyde	C	Veratric acid	M.p. 180°	85
1-Naphthaldehyde	A	5-Cl-1-Naphthaldehyde	E	69
2-HO-1-Naphthaldehyde	A	3(?)-Cl-2-HO-1-Naphthaldehyde	E	73

[a] Buu-Hoï reports m.p. 81°; semicarbazone m.p. 238–240° (*Compt. rend.*, **221**, 202 (1945)). [b] Hodgson and Beard report m.p. 139.5°; semicarbazone m.p. 236–237° (*J. Chem. Soc.*, 149 (1926). [c] Hodgson and Beard report m.p. 62°; semicarbazone m.p. 236° (*idem.*). [d] Biltz reports m.p. 139°; semicarbazone m.p. 210° (*Ber.*, **37** 4032 (1904)). This reaction took place explosively on one occasion, again pointing to the need for caution when employing *t*-butyl hypochlorite; *cf.* Teeter, *et al.*, *Ind. Eng. Chem.*, 41, 851 (1949). [e] Pfeiffer and Segall report m.p. 62.5–63° (*Ann.*, **460**, 133 (1928)); Gatterman reports oxime m.p. 115° (*ibid.*, **357**, 349 (1907)). [f] Hann and Spencer report m.p. 165°, semicarbazone m.p. 198–199° (THIS JOURNAL, **49**, 535 (1927). *Cf.* Raiford and Lichty, *ibid.*, **52**, 4576 (1930)). [g] Raiford and Perry report m.p. 140–141° (*J. Org. Chem.*, **7**, 354 (1942)).

vacuo, on completion of the reaction, an 80–90% yield of benzoyl chloride was obtained, b. p. 195–198°. If, however, the reaction mixture was refluxed for 2 hours after the chlorinating agent had been added, only benzoic acid was isolated.

5-Chloro-2-hydroxybenzaldehyde.—This compound was obtained by chlorination of salicylaldehyde; its m. p. was 100° (Durrows[6] reports 100°). Methylation with dimethyl sulfate in sodium hydroxide solution yielded an aldehyde, the semicarbazone of which showed no m. p. depression when mixed with the semicarbazone of 5-chloro-2-methoxybenzaldehyde obtained by chlorination of 2-methoxybenzaldehyde (see table).

5-Chloro-1-naphthaldehyde.—The aldehyde could not be induced to crystallize, but yielded a crystalline semicarbazone, m. p. 239°. Permanganate oxidation of the oily aldehyde yielded 5-chloro-1-naphthoic acid, m. p. 245°.[7,8]

3(?)-Chloro-2-hydroxy-1-naphthaldehyde.—The compound obtained melted at 81° and its semicarbazone at 228°. The only monochlorinated derivative of 2-hydroxy-1-naphthaldehyde described in the literature is the 4-chloro compound which melts at 118–119°.[9] The aldehyde of m. p. 81° was oxidized with chromic acid in acetic acid. Exhaustive extraction of the oxidation mixture with ether permitted isolation of a small quantity of phthalic acid (50 mg. of the anhydride, m. p. 130–131°, from 1 g. of material). The remaining aqueous liquid contained most of the chlorine of the starting material in form of chloride ion. It is therefore concluded that the chlorine atom must be in the same ring as the other substituents.

Since both 3- and 4-chlorophthalic acids are more soluble in ether than phthalic acid, it should have been possible to isolate either of these compounds in the ether layer, had the chlorination occurred in the unsubstituted ring of the 2-hydroxy-1-naphthaldehyde.[10]

3-Chloro-4-dimethylaminobenzaldehyde.—Reaction of *t*-butyl hypochlorite with *p*-dimethylaminobenzaldehyde gave a nuclear-chlorinated derivative of m. p. 74°, which was characterized by a well-crystallized semicarbazone of m. p. 194–196°.

---

(6) Durrows, *J. Chem. Soc.*, **123**, 1426 (1923).

(7) Chlorination in the 5-position could be expected in view of the fact that bromination of 1-naphthaldehyde yields the 5-bromo-derivative (Ruggli and Preuss, *Helv. Chim. Acta*, **24**, 1345 (1941)). Equally, bromination of 1-naphthoic acid yields the 5-bromo derivative (Shoesmith and Rubli, *J. Chem. Soc.*, 3103 (1927)).

(8) The melting points of the known chloro-1-naphthoic acids are as follows: 2-Cl, 152–153°; 4-Cl, 210°; 5-Cl, 245°; 6-Cl, 216°; 7-Cl, 233.5–236.5°; 8-Cl, 171–171.5°.

(9) Burton, *J. Chem. Soc.*, 282 (1945).

(10) Blicke and Smith, THIS JOURNAL, **51**, 1869 (1929); "Beilstein," Vol. IX, pp. 792, 816.

Anal. Calcd. for $C_{10}H_{13}ON_4Cl$: Cl, 14.8. Found: Cl, 15.0.

Of the two possible isomers, 2-chloro-4-dimethylaminobenzaldehyde had been prepared before[11] by an unambiguous synthesis; m. p. 82°. The 3-chloro-compound was synthesized by the following method and was found identical (mixed m. p.'s of the aldehydes and the semicarbazones) with the above substance.

o-Chlorodimethylaniline was prepared by heating *o*-chloroaniline (13 g.), methyl alcohol (20 cc.) and concd. sulfuric acid (1 cc.) for 16 hours at 160–170° (sealed tube), addition of alkali, extraction with ether and fractional distillation, b. p. 205–206°; yield 5.5 g.[12] This quantity was kept at room temperature for 24 hours, mixed with phosphorus oxychloride (5.5 g.) and N-methylformanilide (4.8 g.). Ice-water and alkali was added, the product extracted with ether, and the aldehyde transferred into aqueous bisulfite solution. The latter was treated with sodium carbonate and the aldehyde extracted with ether and isolated in form of its semicarbazone, m. p. 195–196°. Regenerated from this derivative, it had m. p. 74°; yield 0.6 g.

---

[11] "Beilstein," Vol. XIV, p. 38.

[12] Heidlberg, *Ber.*, **20**, 149 (1887); Friedlaender, *Monatsh.*, **19**, 638 (1876).

REHOVOTH, ISRAEL RECEIVED MAY 26, 1950

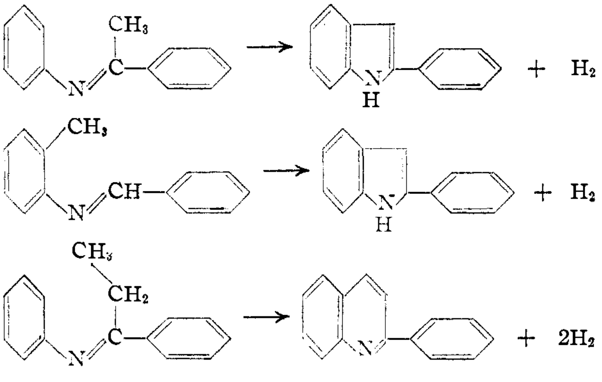
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POMONA COLLEGE]

Catalytic Synthesis of Heterocycles. V.[1] Dehydrocyclization of Anils to Nitrogen Heterocycles

BY CORWIN HANSCH, DONALD G. CROSBY, MICHAEL SADOSKI, ALBERT LEO AND DOUGLAS PERCIVAL

The vapor-phase catalytic dehydrocyclization of six aromatic anils to indoles and quinolines, using a chromium–copper catalyst at temperatures of 500–575°, has been carried out. Conversions of anil to heterocycle range from 5–30% per pass. A mechanism for the reaction is suggested. An improved method for the preparation of acetophenone anils is described.

Three equations illustrate the general reactions which are described in this paper



This first work has been limited to the investigation of anils between aromatic amines and aromatic carbonyl compounds. It is planned to attempt to extend this reaction to anils derived from mixed aliphatic–aromatic amines and carbonyl compounds.

Some work on the pyrolysis of anils has been reported. Pictet and Ankersmit[2] showed that by passing benzalaniline through a tube at 800° about 2% phenanthridine was formed. Benzal-α-naphthylamine was shown to give some naphthacridine by pyrolysis[3] while benzal *o*-toluidine was found to give 30% 2-phenylindole on passing through a hot tube.[4] It was hoped that a study of these reactions with modern dehydrogenation catalysts might increase the scope and usefulness of such reactions.

Experimental

All experiments were carried out in a Pyrex catalyst tube in a continuous flow system. The apparatus and procedure used have been previously described.[5] In each run, 10 ml. of fresh catalyst was used. It was readied for use by reduction *in situ* with a slow stream of hydrogen for 0.5 hour at 150–200° and then for 1 hour a few degrees above the temperature at which the run was to be made. Those anils which were not liquid at room temperature were introduced in the catalyst in the molten state, being held this way by surrounding the introduction tube with a steam jacket.

Catalyst Preparations (I).—This chromium on alumina catalyst has been previously reported.[6] (2) Activated charcoal[7] was extracted in a Soxhlet extractor with constant boiling hydrochloric acid for 24 hours. The charcoal was then dried, covered with 48% hydrofluoric acid in a platinum dish and evaporated to dryness. This hydrofluoric acid treatment was repeated three times in all. The catalyst support was then extracted thoroughly with boiling distilled water and dried. Charcoal treated in this way contained less than 0.2% ash, while the original material contained about 16% ash, 12% of which was silica. Sixty-nine grams of this charcoal was added to a boiling solution of 108.3 g. of $Cr(NO_3)_3 \cdot 9H_2O$ and 2.64 g. of $Cu(NO_3)_2.3H_2O$ in 150 ml. of distilled water. The mixture was boiled several minutes, then filtered, washed with distilled water and dried at 110°. (3) In 50 ml. of water, 31.4 g. of $Cr(NO_3)_3 \cdot 9H_2O$ was dissolved. With this solution 30 g. of acid treated charcoal was treated as above. (4) In 20 ml. of water were dissolved 18 g. of $Cr(NO_3)_3 \cdot 9H_2O$ and 1.75 g. of $Cu(NO_3)_2 \cdot 3H_2O$. This solution was heated to boiling and 23 g. of acid treated charcoal added with good mixing. This material was dried at 110° without filtering.

Preparation of Ketone Anils.—The general method of Reddelien[8] was modified for the preparation of these compounds. The appropriate ketone and amine were refluxed in an inert solvent with a small amount of the zinc salt of the amine. The water formed was removed by means of a water trap and when no more water formed the mixture was cooled and filtered.

2-Acetothienone Anil.—2-Acetothienone (63 g.), aniline (75 g.) and 2 g. of aniline–zinc chloride were refluxed for 40 hours in 200 ml. of toluene. Distillation gave 65% yield, b.p. 136–137° (11 mm.), m.p. 70°.

Anal. Calcd. for $C_{12}H_{11}NS$: C, 71.60; H, 5.51. Found: C, 71.74; H, 5.86.

Propiophenone o-Tolylimide.—Propiophenone (100 g.), *o*-toluidine (80 g.) and 2 g. of *o*-toluidine-zinc chloride were

---

[1] For the previous paper in this series see *Ind. Eng. Chem.*, **42**, 2114 (1950).

[2] Pictet and Ankersmit, *Ber.*, **22**, 3339 (1889); Pyle, *ibid.*, **60**, 287 (1927).

[3] Pictet and Ehrlich, *Ann.*, **266**, 155, 163 (1891).

[4] Pictet, *Ber.*, **19**, 1064 (1886).

[5] Hoog, Verheus and Zuiderweg, *Trans. Faraday Soc.*, **35**, 993 (1939).

[6] Hansch and Blondon, THIS JOURNAL, **70**, 1561 (1948).

[7] Type BP-6x8 obtained from the Pittsburgh Coke & Chemical Co.

[8] Reddelien, *Ber.*, **46**, 2715 (1913).