to continue for a number of hours. The catalyst was filtered, washed with alcohol, and the solution concentrated to the beginning of crystallization. In general the resultant solutions were concentrated to dryness and the solid products recrystallized from dilute alcohol.

Use of low catalyst ratio. 1-o-Bromobenzoyl-2-isopropylhydrazine (XVIII). A solution of 4.2 g. (0.0164 mole) of 1-*o*-bromobenzoyl-2-isopropylidenehydrazine was hydrogenated in the presence of 0.1 g. 5% platinum on carbon. Uptake of hydrogen was completed in 6–7 hr. The slow uptake of the final 10–20% of hydrogen was enough to indicate that with this decreased catalyst ratio the possibility of overhydrogenation would be negligible.

The reaction mixture was filtered and worked up as described in the previous example.

The *p*-bromo derivative XIX was also prepared in the same manner. In one experiment using a 10% catalyst ratio we did get XIX in 62% yield but we were never able to duplicate the results. With a 7% catalyst ratio we obtained a mixture of products. The poor solubility of 1-*p*-iodobenzoyl-2-isopropylidenehydrazine made reduction with a low catalyst ratio not feasible.

Use of excess hydrogen chloride. 1-p-Bromobenzoyl-2-isopropylhydrazine (XIX). A mixture of 2.55 g. (0.01 mole) 1-*p*-bromobenzoyl-2-isopropylidenehydrazine, 55 cc. of absolute alcohol containing 0.03 mole dry hydrogen chloride and 0.1 g. (4% ratio) of 5% platinum on carbon was hydrogenated under 2 atm. pressure. After reduction was complete the suspension was treated with water to dissolve the hydrochloride salt. The mixture was then filtered from the catalyst and the solvent evaporated to dryness. The residue was treated with hot water and filtered from any insoluble material. It was then neutralized with aqueous ammonia or sodium bicarbonate, cooled, filtered, and washed with cold water. There was no difference in melting point between the product before and after recrystallization.

When a 5% catalyst ratio was used, 4.7% ionic bromine was found by analysis. When a 6% ratio was employed it was noted that more over-hydrogenation was occurring. The crude product isolated from this experiment melted at 136–140° and was raised to 141–142° after recrystallization. The yield of unrecrystallized product was much lower than usual. See footnote (a) Table II.

1-p-Iodobenzoyl-2-isopropylhydrazine (XX). A suspension of 1.51 g. (0.005 mole) of 1-*p*-iodobenzoyl-2-isopropylidenehydrazine in 100 cc. 95% ethanol containing (0.15 mole) acetic acid and 0.075 g. 5% platinum on carbon was hydrogenated under 2 atm. pressure. When uptake was complete the material appeared to be in solution. The solution was filtered from the catalyst and concentrated to dryness. The residue was treated with 100 cc. of water and 2–3 cc. of concd. hydrochloric acid, stirred for a few minutes, and filtered. The filtrate was neutralized with sodium bicarbonate, cooled, and filtered. After washing with water and drying the product melted at 162–164°.

Acknowledgment. The authors wish to thank Mr. E. F. Shelberg and Mr. Orville Kolsto for the microanalyses, and Mr. W. Washburn for infrared examination of the compounds in Table I.

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Preparation of *N*-(Aryl)amino Acids from Nitroaryl Compounds and Alcohols

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Received April 20, 1960

The redoxidative condensation of primary and secondary alcohols with aromatic nitro compounds by means of sodium alkoxides is described. The reaction offers a synthesis of *N*-(aryl)amino acids.

Suter and Dains[1] in 1928 reported that reduction of *m*- and *p*-halonitrobenzenes with alcohol-alkoxide mixtures gave substituted azoxybenzenes, but that *N*-(*o*-haloaryl)amino acids were formed as the primary products from the *o*-halonitrobenzenes; the reaction was also accompanied by the formation of the substituted anilines:

(1)

Suter and Dains[1] stated that only primary alcohols of the type RCH_2CH_2OH yielded amino acids, *i.e.*, isobutyl and cinnamyl alcohols failed to undergo this condensation.

In our hands, the synthesis of *N*-(aryl)amino acids by this method gave yields of only 10–32%, whereas 40–60% were reported. The condensation was therefore reinvestigated, and the effect of the structure of the alcohol and of the nitro compound on the course of the reaction was determined.

The products derived from a representative redoxidative condensation of *o*-chloronitrobenzene and 1-propanol included *N*-(*o*-chlorophenyl)alanine (31.9%), *o*-chloroaniline (51.3%), and 2,2′-dichloroazobenzene (16.7%). In several experiments the aromatic amine and the amino acid were formed in approximately equimolar amounts. The isolation of azo rather than azoxybenzenes among the products of the reaction is at variance with previous results,[1] however. The identification of 2,2′-dichloroazobenzene (m.p. 134–136°)[2,3] and 2,2′,5,5′-tetrachloroazobenzene (m.p. 182.5–184°)[4] was based on the correspondence of the melting points with literature values. The reported melting points of the related azoxy com-

(1) C. M. Suter and F. B. Dains, *J. Am. Chem. Soc.*, **50**, 2733 (1928).

(2) K. Brand, *J. prakt. Chem.*, [2], **67**, 148 (1902).

(3) D. Vorländer and F. Meyer, *Ann.*, **320**, 129 (1902).

pounds are considerably lower, *i.e.*, 56°[2] and 145–147°,[4,5] respectively (Table I).

TABLE I

PREPARATION OF *N*-(*o*-CHLOROPHENYL)ALANINE FROM *o*-CHLORONITROBENZENE AND 1-PROPANOL[a]

Ar-NO_2, Mole	*n*-C_3H_7OH, Moles	Sodium, Mole	Temp.	Amino Acid,[b] % Yield
0.1	0.07	0.3	25–27	20.5
0.2	2.6	0.4	35	30.5
0.2	1.06	0.4	55–65	24.3
0.2	2.6	0.4	54–57	20.5
0.2	2.1	0.3	60–65	25.8
0.2	2.1	0.3	65–66	—[c]
0.2	2.1	0.1	76	—[d]
0.2	2.4	0.3	76–77	31.9[e]

[a] Benzene (300–450 ml.) was utilized in all experiments. [b] *N*-(*o*-Chlorophenyl)alanine. [c] Propionaldehyde, 0.2 mole, was added simultaneously with the nitro compound. Tar formation predominated. [d] Sodium propionate, 0.2 mole, was added simultaneously with the nitro compound. Tars resulted. [e] *o*-Chloroaniline, b.p. 72–75°/5 mm. (51.3%) and 2,2′-dichloroazobenzene, m.p. 134–136° (16.7%) were also obtained. Ref. 2,3 report m.p. 136–137°.

Variation of the temperature within the range 25–80° had little influence on the yields of the *N*-(aryl)amino acids. The use of benzene (25–2500 ml.), which Suter and Dains[1] employed to accelerate the reduction of the nitroaromatic by the alkoxide,[5] and to decrease the ionizing effect of the excess alcohol, was also without apparent influence on the reaction. Some benzene was valuable, however, to insure homogeneity of the reaction mixture. Simultaneous addition of propionaldehyde along with the nitro compound to 1-propanol–sodium *n*-propoxide mixtures increased the high boiling residues, rather than the amino acid conversion.

The poor yields of amino acid obtained with 1-propanol in this condensation prompted a study of the reaction of secondary alcohols with nitroaromatics. Providing that the secondary alcohol has the requisite structure, *i.e.*, at least one methylene group adjacent to the carbinol function, the redoxidative condensation with nitroaromatics should be possible. In addition, the postulated aliphatic dehydrogenation product, a ketone, should be less readily self-condensed, and therefore, more available for reaction with the aromatic species.

3-Pentanol was chosen for this study since the expected amino acid would be the same as that derived from 1-propanol. Further, the symmetry of the alcohol might give rise to increased conversions (Table II).

In this connection, Dunbar and Arnold[7] have shown that dehydrogenation of secondary alcohols over copper chromite gives higher conversions to ketones than do normal primary alcohols to aldehydes. These investigators also found that 3-pentanol, representing a balanced structure with respect to the alkyl groups, gave the highest conversion to ketone on dehydrogenation.

TABLE II

PREPARATION OF *N*-(*o*-CHLOROPHENYL)ALANINE FROM *o*-CHLORONITROBENZENE[a] AND 3-PENTANOL

3-Pentanol, Mole	C_6H_6, Ml.	Sodium, Mole	Temp.	Amino Acid, % Yield
0.78	300	0.12	51–55	37.6
0.74	300	0.25	54–58	42.7
0.74	300	0.39	53–55	49.4
0.74	300	0.25	70–74	50.3
0.69	250	0.25	40–42	41.2[b]
0.22	300	0.22	60–64	36.2
0.46	300	0.20	51–54	38.2
0.46	2500	0.25	40–49	37.1
0.46	150	0.25	80–83	34.7
0.74	75	0.25	87–88	40.3
0.55	25	0.20	87–88	48.7
3.34	250	2.0	65–72	43.8[c]
0.46	200	0.2	50–55	60.3[d]

[a] The amount of *o*-$ClC_6H_4NO_2$ used was 0.1 mole except where noted. [b] Reverse addition of sodium 3-pentoxide solution to *o*-$ClC_6H_4NO_2$. [c] *o*-$ClC_6H_4NO_2$ (1.0 mole) was used. A 42.8% yield of *o*-chloroaniline was also obtained. [d] 3-Pentanone, 0.1 mole, added simultaneously with the *o*-$ClC_6H_4NO_2$.

In agreement with these considerations, the redoxidative condensation of 3-pentanol–sodium 3-pentoxide mixtures with *o*-chloronitrobenzene gave 34–50% yields of the *N*(*o*-chlorophenyl)-alanine. The addition of 3-pentanone to these reactions resulted in a further increase in the amino acid yield (60%). Reverse addition of the alcohol–sodium alkoxide mixture to the nitro compound did not improve the yield of the amino acids. Aluminum isopropoxide and tripotassium phosphate were ineffective condensing agents.

The exact stoichiometry of the reaction was difficult to determine. It was found that alcohol: nitroaromatic mole ratios of 2–10:1 gave qualitatively similar results. The optimum mole ratio of sodium:alcohol was 1:2.5.

The course of the redoxidative condensation of unsymmetrical alcohols, $RCH_2CHOHCH_3$, with nitroaromatics paralleled the course of the base-catalyzed aldol condensation of unsymmetrical ketones with a second carbonyl compound. In the redoxidative condensation, 2-butanol was attacked on the α-methyl group and not at the α-methylene group. Thus, 2,5-dichloronitrobenzene and 2-butanol gave *N*-(2,5-dichlorophenyl)glycine (28%); *N*-(*o*-chlorophenyl)glycine (36–38%) was formed from *o*-chloronitrobenzene and 2-butanol. The same products are formed from these nitro compounds and 2-propanol in 20–38% yields. From a study of the aldol condensation, Gettler

(4) T. De Crauw, *Rec. trav. chim.*, **50**, 753 (1931).
(5) P. Gagnon, K. Keirstead, and B. Newbold, *Can. J. Chem.*, **35**, 1304, 1423 (1957).
(6) J. W. Brühl, *Ber.*, **37**, 2066 (1904).
(7) R. Dunbar and M. Arnold, *J. Org. Chem.*, **10**, 501 (1945).

TABLE III

PREPARATION OF *N*-ARYLGLYCINES

$ArNO_2$, Mole		ROH R	ROH Moles	Na, Mole	C_6H_6, Ml.	Temp.	$ArNHCH_2COOH$, % Yield
2,5-Cl_2	0.1	2-C_3H_7	1.0	0.37	150	30–32	9.1
2,5-Cl_2	0.1	2-C_3H_7	1.0	0.37	400	35–37	21.8
2,5-Cl_2	0.1	2-C_3H_7	1.0	0.43	425	36–38	20.4
2,5-Cl_2	0.2	2-C_4H_9	1.6	0.43	400	30–36	28.6[a]
o-Cl	0.1	2-C_4H_9	0.5	0.20	300	50–51	38.3[b]
o-Cl	0.1	2-C_4H_9	0.5	0.25	200	56–61	36.6[c]
o-Cl	0.2	[d]	0.5	0.5	450	53–56	55.9

[a] 2,5-Dichloroaniline, b.p. 90–94° (5 mm.); m.p. 47–48.5° (46%), and 2,5-dichloroacetanilide, m.p. 131.5–133° (17%), were also obtained. *Anal.* Calcd. for $C_8H_7Cl_2NO$: C, 47.10; H, 3.43; N, 6.88. Found: C, 47.44; H, 3.95; N, 6.94. C. Graebe and S. Gourevitz, *Ber.*, **33**, 2025 (1900) report melting point for $C_8H_7Cl_2NO$ as 132°. [b] 2-Butanone added simultaneously with the nitro compound. [c] *o*-Chloroacetanilide, m.p. 87–88°, isolated in 6% yield. K. Orton and G. Owen, *J. Chem. Soc.*, **125**, 767 (1924) report 86.8°. [d] 2,4-Pentanediol was used in this experiment.

and Hammett[8] have established that under certain conditions the attack of benzaldehyde on 2-butanone in a basic medium is also at the α-methyl group (Table III).

The nature of the alkyl substituent on the α-methylene carbon of the alcohol had the expected effect—the yield of the desired amino acid decreased with increased size of the substituent. 2-Octanol and 2,5-dichloronitrobenzene gave a meager yield (18%) of 2-(2,5-dichloroanilino)-heptanoic acid. *n*-Dodecanol was completely unreactive. Unsuccessful redoxidative condensations were also attempted with *tert*-butyl alcohol and cyclopentanol. This redox reaction, however, was applicable to glycols. The yield of *N*-(*o*-chlorophenyl)glycine from 2,4-pentanediol and *o*-chloronitrobenzene was somewhat higher (56 *vs.* 35–45%) than from the reactions with 2-propanol or 2-butanol.

Special efforts were made to isolate scission fragments from the alcohol. Hydrocarbons derived from the aliphatic alcohols[9] were not isolated. Formaldehyde or acetaldehyde probably condensed too rapidly under the strongly basic conditions to permit isolation. 1-Phenylethanol underwent extensive oxidation; benzoic acid and acetophenone were the major products. 2-Phenylethanol yielded traces of phenylacetic acid; no amino acid was formed. A complex acidic fraction was obtained from 1,5-diphenyl-3-pentanol which could not be resolved. Infrared analysis of the residues from these reactions frequently indicated the presence of *N*-acylaromatic amines. Subsequently, *o*-chloroacetanilide and 2,5-dichloroacetanilide were isolated and identified from 2-butanol reactions. The formation of the *N*-acylamines partially accounts for the scission fragments from the reactant alcohols.

Suter and Dains[1] associated the electronegativity of the *ortho*-substituent of the nitroaromatic compound with the ability to undergo the condensation reaction. Our evidence indicated that an electronegative *ortho*-substituent is not a necessary criterion. Thus, nitrobenzene reacted with 3-pentanol to yield *N*-phenylalanine (40%), and 1-nitronaphthalene gave *N*-(1-naphthyl)alanine (50%) on reaction with 1-propanol. However, a successful condensation was limited by the presence of an oxidizable group on the aromatic ring. Infrared analyses of the acidic fractions indicated the presence of amino acids from the reactions of *o*-nitrotoluene and *o*-nitroanisole; isolation of analytical samples was not possible, however. Furthermore, 2,4-dinitrochlorobenzene and 1,4-dichloro-2,6-dinitrobenzene gave excessive tar formation under redoxidative condensation conditions (Table IV).

In one experiment with nitrobenzene and 3-pentanol, a trace of an acid melting at 137.5–139° was obtained. The structural assignment for this product as 2-(anilino)butyric acid is based on elemental analysis and correspondence with literature data.[10] (See Table V.) In an effort to arrive at a mechanistic interpretation of this complex reaction, compounds derived from the various reduction stages of nitrobenzene in alkaline solution were treated with 3-pentanol–sodium 3-pentoxide mixtures. The addition of mixtures of 3-pentanone and β-phenylhydroxylamine, azobenzene, azoxybenzene, or hydrazobenzene (1:1 mole ratio) to the basic solution did not yield amino acid. Earlier investigators[1] have shown that sodium butoxide did not reduce 4,4′-dichloroazoxybenzene under redoxidative conditions.

o-Chloronitrosobenzene and *p*-nitrosodimethylaniline did not yield amino acids when treated with 1-propanol–sodium *n*-propoxide mixtures. Dains and Kenyon[11] have reported the reduction of nitrosobenzene with sodium in 1-propanol gave azoxybenzene, together with smaller amounts of aniline and tars.

(8) J. D. Gettler and L. P. Hammett, *J. Am. Chem. Soc.*, **65**, 1824 (1943).

(9) H. D. Zook, J. March, and D. F. Smith, *J. Am. Chem. Soc.*, **81**, 1617 (1959).

(10) W. v. Miller, J. Plöchl, and L. Sender, *Ber.*, **25**, 2035 (1892); O. Nastvogel, *Ber.*, **22**, 1795 (1898); **23**, 2010 (1890).

(11) F. B. Dains and W. D. Kenyon, *J. Am. Chem. Soc.*, **53**, 2357 (1931).

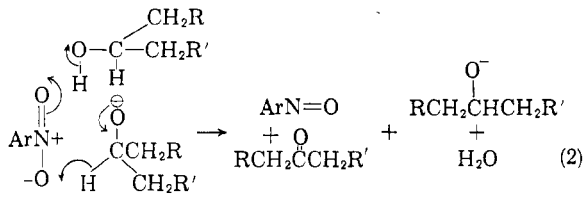
TABLE IV

MISCELLANEOUS PREPARATIONS OF *N*-(ARYL)AMINO ACIDS

$ArNO_2$, Mole		ROH R	ROH Moles	Na, Mole	C_6H_6, Ml.	Temp.	*N*-(Aryl)amino Acid	Yield, %
o-CH_3O	0.1	3-C_5H_{11}	0.83	0.39	300	50–52	[a]	
o-CH_3	0.5	3-C_5H_{11}	1.65	1.0	150	77–80	[a]	
2,5-Cl_2	0.1	*n*-C_3H_7	1.07	0.3	300	39–45	*N*-(2,5-Dichlorophenyl)alanine	50.0[b]
2,5-Cl_2	0.1	3-C_5H_{11}	0.8	0.37	300	50–52	*N*-(2,5-Dichlorophenyl)alanine	52.9
H	0.1	3-C_5H_{11}	0.46	0.25	200	43–55	2-(Anilino)butyric acid	trace
H	0.5[c]	3-C_5H_{11}	1.65	1.0	125	74–77	*N*-Phenylalanine	40.4
2,5-Cl_2	0.1	2-C_8H_{17}	0.56	0.38	300	53–55	2-(2,5-Dichloroanilino)-heptanoic acid	20.5
2,5-Cl_2	0.1	2-C_8H_{17}	0.56	0.38	300	53–55	2-(2,5-Dichloroanilino)-heptanoic acid	18.7
$C_{10}H_7$[d]	0.1	*n*-C_3H_7	1.08	0.2	300	80	*N*-(1-Naphthyl)alanine	50.3

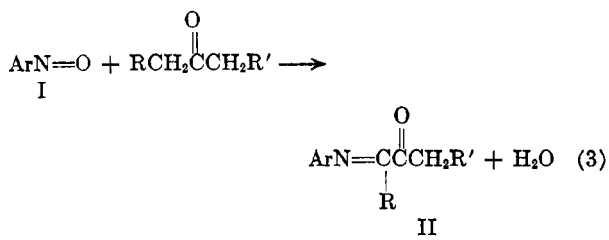
[a] Complex acidic fractions resulted. Amino acid evident from infrared analysis; not isolated. [b] 2,2′,5,5′-Tetrachloroazobenzene, m.p. 182.5–184°, was isolated in trace amounts. De Crauw[4] reports the m.p. as 189°. [c] 3-Pentanone, 0.5 m., was added with the nitro compound. [d] 1-Nitronaphthalene; all other runs were substituted benzenes.

The following mechanism is suggested for this redoxidative condensation. It is based on the assumption that the initial step is an alkoxide-catalyzed reduction of the nitro group to nitroso group, with oxidation of alcohol to carbonyl compound.



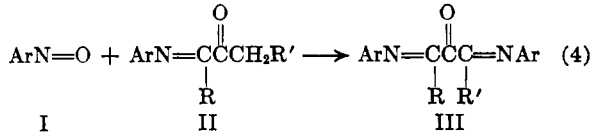
(2)

Nitroso compound (I) can condense with carbonyl compound giving the monoanil of an α-diketone (II). Solvent cage entrapment of these primary reaction products might "aid" this step.



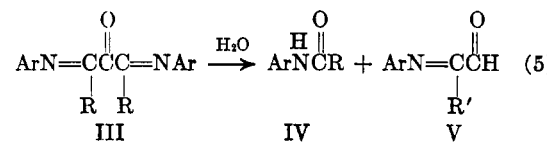
(3)

Condensation with a second molecule of nitroso compound may occur at the other methylene group *alpha* to the carbonyl function.

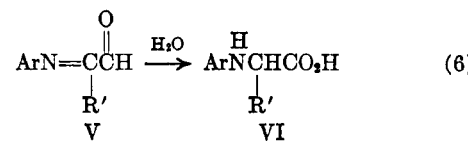


(4)

Hydrolysis[12] of this dianil of a vicinal tricarbonyl compound could result in cleavage of III. Visualized as a β-dicarbonyl compound "basic" cleavage (Equation 5), this would give one molecule of *N*-arylamide (IV), and V, the precursor of *N*-arylamino acids which might arise from primary alcohols, as shown by Equation 6.



(5)



(6)

The last equation represents an intramolecular Cannizzaro reaction. Considering Suter and Dain's work,[1] compound V corresponds to their suggested initial condensation product, and this concept is in accord with their postulate as to mechanism. Under the conditions of this reaction, the amide (IV) probably alcoholizes readily, giving free amine, $ArNH_2$. Azobenzene derivatives could form by the known arylnitroso-arylamine condensation.

Additional facts seem pertinent. Suter and Dains[1] did not report amide formation, but primary alcohols should give none. The secondary alcohols utilized in this investigation gave isolable amides in several instances, as related above.

Several preparations utilizing *N*-(*o*-chlorophenyl) alanine as an intermediate were attempted. The preparation of a meso-ionic compound (Sydnone)[13] failed. It was also impossible to rearrange *N*-nitroso-*N*-(*o*-chlorophenyl)-alanine according to the Fisher-Hepps procedure.[14] These results are attributed to steric hindrance about the *o*-chloro substituent.

(12) Reaction water or water added on work-up may effect this hydrolysis. The resultant cleavage might be initially an alcoholysis of III with subsequent saponification of esters, etc., on work-up.

(13) W. Baker and W. D. Ollis, *Quart. Rev.*, 11, 15 (1957).

(14) C. C. Tung, private communication.

TABLE V

ANALYTICAL DATA: *N*-(ARYL)AMINO ACIDS

Amino Acid	Empirical Formula	Mol. Wt.	M.P. Found	M.P. Lit.	Ref.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Neut. equiv.
N-Phenylalanine	$C_9H_{11}NO_2$	165	161–162[a]	163	10	65.50	64.92	6.67	6.80	8.48	8.25	166.2
N-(*o*-Chlorophenyl)alanine	$C_9H_{10}ClNO_2$	199.5	148–149[a]	150	1	—	—	—	—	—	—	—
N-(1-Naphthyl)alanine	$C_{13}H_{13}NO_2$	215	157–159	161	[b]	74.63	75.20	6.04	6.20	6.52	6.54	—
N-(2,5-Dichlorophenyl)-alanine	$C_9H_9Cl_2NO_2$	234	160–161.5[a]	163	1	—	—	—	—	—	—	—
N-(*o*-Chlorophenyl)glycine	$C_8H_8ClNO_2$	185.5	171–173	171	[c]	51.85	52.05	4.32	4.74	7.55	8.26	184 186
N-(2,5-Dichlorophenyl)-glycine	$C_8H_7Cl_2NO_2$	220	174–175.5	—	[d]	43.70	43.92	3.18	3.49	6.37	5.82	222
2-(Anilino)butyric acid	$C_{10}H_{13}NO_2$	179	137.5–139	139–41	10	67.10	66.45 67.19	7.27	7.13 7.33	7.83	8.48	174 176.5
2-(2,5-Dichloroanilino)-heptanoic acid	$C_{13}H_{17}Cl_2NO_2$	290	115–117	—	—	53.68	53.80	6.24	5.86	5.22	4.83	288

[a] Mixed melting point with an authentic sample was not depressed. [b] C. A. Bischoff and A. Hausdörfer, *Ber.*, **30**, 2309 (1897). [c] C. G. Schwalbe, W. Schultz, and H. Jochheim, *Ber.*, **41**, 3793 (1908). [d] Reported by H. E. Thompson, C. P. Swanson, and A. G. Norman, *Botan. Gaz.*, **107**, 4761 (1946), but no melting point was given.

(7)

N-(*o*-Chlorophenyl)alanine and *N*-(2,5-dichlorophenyl)glycine were evaluated as biological toxicants. The glycine had markedly greater activity than the alanine as a contact herbicide, but both acids were inferior to 2,4-D. This is in accord with the findings of Takeda[15] who reported that the substitution of a nitrogen atom for the oxygen atom in the phenoxyacetic acids requires the presence of a *meta*-halogen atom, rather than *ortho*- or *para*-halogen atoms, for herbicidal activity.

EXPERIMENTAL

The synthesis of β-(*o*-chlorophenyl)hydroxylamine followed the directions in Organic Syntheses.[16] Dibenzalacetone was prepared by a known method.[17] 1,5-Diphenyl-3-pentanol was prepared by hydrogenation of dibenzalacetone over Raney nickel at 83–105° and 2400 p.s.i.g. hydrogen. The product distilling at 211–235° (5 mm.) was recrystallized from ethanol, m.p. 42–44°.[18] The conversion was 77.5%.

The following is a typical example of the redoxidative condensation. A 2-l. round-bottom flask fitted with a stirrer, water-cooled condenser and thermometer was charged with 360 ml. (293 g., 3.74 moles) of 3-pentanol. Sodium hydride (48 g., 2.0 moles as sodium) was added in small portions at 70–80°. After all the hydride had been added, 100 ml. of benzene was added and the mixture refluxed until formation of the alkoxide was complete. A solution of 157.5 g. (1.0 mole) of *o*-chloronitrobenzene in 150 ml. of benzene was added over 1.75 hr. at 65–72°. The mixture was refluxed for 2 hr. to complete the reaction.

Water was then added to the warm mixture; the organic and aqueous layers were separated. The benzene solution was washed with water until the aqueous washings were neutral. The combined aqueous solution was extracted with ether. The ether was combined with the benzene solution and dried over magnesium sulfate. The chilled aqueous solution was acidified to approximate *p*H 2. The precipitate was filtered, washed with water, and dried. The amino acid (87.2 g.) was recrystallized from benzene to give white crystals, m.p. 148.5–150°. The yield of *N*-(*o*-chlorophenyl)alanine was 43.8%.

The acidic fraction also yielded 3 g. of aliphatic acids which vapor phase chromatography showed to be a mixture of acetic and propionic acids.

The neutral fraction was distilled to remove ether and benzene. Steam distillation of the residue gave 54.5 g. (42.8%) of *o*-chloroaniline. The residual material, 39.1 g., could not be crystallized. It was separated into two fractions, 13.8 g. being soluble in hexane. This fraction had an infrared spectrum corresponding to an *N*-acylated *o*-chloro-

(15) A. Takeda, *Nogaku Kenkyu*, **41**, 82 (1953); *C.A.*, **49**, 11792 (1955); *J. Org. Chem.*, **22**, 1096 (1957).

(16) O. Kamm, *Org. Syntheses*, Coll. Vol. I, 445 (1941).

(17) C. R. Conard and M. A. Dolliner, *Org. Syntheses*, Coll. Vol. II, 167 (1948).

(18) L. Zechmeister and P. Rom, *Ann.*, **468**, 126 (1929).

aniline. It did not crystallize, however. The remainder of the residue was not investigated.

Caution should be exercised during the addition of the nitro compound to the alkoxide-alcohol solution. If the rate of addition is too rapid, a violent exothermic reaction often results. This is particularly the case at lower temperatures where an induction period has been observed before the reaction commenced. The temperature of the reaction is conveniently controlled by the rate of addition of the nitro compound.

When a carbonyl compound corresponding to the dehydrogenation product of the charged alcohol is employed in the reaction, it is added simultaneously with the nitro compound. This minimizes self-condensation products. The mole ratio of carbonyl compound to nitroaromatic was always 1:1. In those experiments where attempts were made to trap hydrocarbons from this reaction, two traps cooled in liquid nitrogen were placed at the head of the condenser. A T-tube was connected to the last trap, and a slow stream of nitrogen passed across the T to exclude moisture from the trap.

Frequently a deep purple coloration developed in the reaction mixture. This phenomenon was also observed by Gagnon and co-workers[6] during a study on the reduction of halonitroaromatics in alkaline solution. The color has been ascribed to impurities in the nitro compound, and in the case of *o*-chloronitrobenzene, has been shown to be due to the formation of a chlorotrihydroxydihydrophenazine.

An authentic sample of *N*-(*o*-chlorophenyl)alanine was prepared by heating 89 g. (0.68 mole) of *o*-chloroaniline and 100 g. (0.55 mole) of ethyl α-bromopropionate in a round-bottom flask on a steam bath for 4 hr. The hot solution was washed with water to remove the amine hydrobromide. The organic material was returned to the flask and refluxed with a solution of 50 g. (0.89 mole) of potassium hydroxide in 250 ml. of water. The cooled solution was extracted with ether, and the aqueous layer acidified. *N*-(*o*-Chlorophenyl)alanine was recovered in the amount of 82.1 g. (75.0%), m.p. 148.5–149.5°. *N*-(2,5-Dichlorophenyl)alanine prepared from 2,5-dichloroaniline by this method melted at 161–162.5°.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Chemistry of Trinitromethane. I. Reactions with Unsaturated *N*-Methylolamides[1]

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Received May 23, 1960

Unsaturated *N*-methylolamides, such as *N*-methylolmethacrylamide and *N,N'*-bis(methylol)fumaramide undergo a Mannich type reaction with trinitromethane to give *N*-trinitroethylmethacrylamide (II) and *N,N'*-bis(trinitroethyl)-fumaramide (X) respectively. The reaction of *N*-methylolacrylamide and trinitromethane affords *N*-trinitroethylacrylamide (IV) and *N*-methylol-4,4,4-trinitrobutanamide (VIII). Nitration of compounds II and IV yield *N*-nitro-*N*-trinitroethyl-methacrylamide and *N*-nitro-*N*-trinitroethylacrylamide, respectively.

In 1953, we reported the preparation of unsaturated *N*-methylolamides.[2] The subject of this paper is their Mannich type reactions with trinitromethane (I).[3]

The synthesis of *N*-trinitroethylmethacrylamide (II) could not be accomplished by reacting methacrylamide with trinitroethanol or with a mixture of I and formaldehyde. Unstable oils were produced which were subsequently found to be reaction products of methacrylamide and I alone. However, treating *N*-methylolmethacrylamide (III) with I in aqueous medium gave compound II in an 80% crude yield.

The reaction of compounds III and I occurred over a wide *p*H range below 7. A *p*H range above 7 had to be avoided because it is well known that the trinitroethyl group is decomposed in basic medium to I and formaldehyde.[4] This also explains the failure to obtain II by reacting methacrylamide with I and formaldehyde, because the first step in this reaction, which is the formation of III, is base catalyzed[2] and the second step, the condensation of III with I can only proceed in acidic media.

The purification of II was difficult.The best results were obtained when small amounts of II (less than 2 g.) were treated at 2° with fuming nitric acid for 4 minutes and the mixture poured over crushed ice. Pure II decomposed on storage at 25° over a period of several months to a red semi-solid. Upon nitrating II with a mixture of anhydrous nitric acid and trifluoroacetic anhydride, *N*-nitro-*N*-trinitroethylmethacrylamide was obtained as a stable compound which did not discolor starch-iodide paper when heated for one hour at 65°; nor did it decompose upon storage for one year at 25°.[5]

The synthesis of *N*-trinitroethylacrylamide (IV) was difficult because of the ease of addition of I across the double bond present in acrylamide (V) or in *N*-methylolacrylamide (VI). Fusion of V with

(1) From the Ph.D. Thesis of Una E. Lynch, Purdue University, 1952.

(2) H. Feuer and U. E. Lynch, *J. Am. Chem. Soc.*, **75**, 5027 (1953).

(3) After this work was completed, two patents were issued which deal with the reaction of saturated amides with I and formaldehyde. R. Schenck and G. A. Wetterholm, Swed. Patent **148,217**, Dec. 28, 1954, and Nitroglycerin Aktiebolaget, Brit. Patent **813,477**, May 21, 1959.

(4) J. Reinhart, J. G. Meitner, and R. W. Van Dolah, *J. Am. Chem. Soc.* **77**, 496 (1953).

(5) C. R. Koller (Ph.D. thesis, Purdue University, 1950) has found that the stability of compounds containing a *N*-trinitroethyl group can be increased considerably by its conversion to a *N*-nitro-*N*-trinitroethyl group.