Kodak Co. White Label product which had been recrystallized several times from absolute alcohol and dried in a vacuum desiccator over potassium hydroxide and phosphorus pentoxide. The material melted at 145.2–146.7° in a sealed tube. Taylor and Grant[8] reported a melting point of 143.4°. The pyridinium chloride was stored as a standard solution in acetonitrile. Titration of aliquots with either standard base or silver nitrate showed no change in acid or chloride concentration over a period of many weeks. Pyridinium perchlorate prepared from aqueous perchloric acid and pyridine melted at 298.6–299.6°.[9] The neutral equivalent of this material was 179.2. The calculated value is 179.6°. N-Methylpyridinium chloride was prepared by passing methyl chloride into pyridine at a temperature of 55–60°. The hygroscopic salt after recrystallization from acetonitrile and drying in a vacuum desiccator over phosphorus pentoxide melted at 139.7–140.8°. A Volhard titration showed the presence of 27.3% chlorine. The calculated value is 27.4%. The salt was stored in acetonitrile solution. Tetraethylammonium chloride was prepared from the bromide and decomposed without melting.[10] A Volhard determination showed the presence of 21.2% halogen (calculated 21.4%). Tetraethylammonium perchlorate was prepared from silver perchlorate and tetraethylammonium bromide.[11] After several recrystallizations from 95% ethanol, the product gave no precipitate with either hydrochloric acid or acidified silver nitrate. The material, after drying at 57° (1 mm.), decomposed in the range 310–330° without melting. (Healey and Martell reported a melting point with decomposition of 345°.) A Dumas nitrogen analysis showed the presence of 6.45% nitrogen (calculated 6.11%).

Kinetic Procedures.—The reaction was studied by following the rate of disappearance of the absorption band of acetyl cyanide which falls near 304 mμ in acetonitrile solution. The ultraviolet measurements were made with a Beckman quartz spectrophotometer model DU, in which the 10-cm. cell compartment had been replaced with a water-tight compartment provided with quartz windows and two outlets for circulating water from a thermostat.[12] Long-necked 1-cm. Beckman silica cells sealed with ground-glass stoppers were used for reaction vessels. Distilled water was circulated in a closed system from a copper coil placed in a thermostat to the compartment by means of an Eastern centrifugal pump, model B1. The speed of the pump was regulated with a Variac. Because of small particles and bubbles in the water, more reproducible optical density values could be obtained by turning off the circulating pump during the short time the reading was being taken. It was established that the temperature of the water in the compartment did not vary by more than ±0.03° under these conditions. The thermostat was set at 25.0° with a Precision thermometer which had been checked against three different Anschütz thermometers. Time was measured with a Presion timer.

In preparing solutions all liquids were transferred by pipet in an attempt to minimize the amount of water in the system. In a typical run the appropriate amount of pyridine was weighed into a volumetric flask. Standard pyridinium chloride and standard neutral salt solution were pipetted in, the flask was three-quarters filled with acetonitrile and weighed. Approximately the desired amount of hydrogen cyanide was added from the ice-jacketed buret (which was protected from atmospheric moisture with a calcium chloride tube and a ground-glass joint at the tip which fitted the volumetric flask). The flask was again weighed and filled to the mark with solvent. This solution was diluted by pipetting aliquots into two other volumetric flasks which were filled nearly to volume and thermostated. The contents of one was used for the solvent cell, and to the other was added the acetyl cyanide by pipet. The solutions were immediately transferred into the Beckman cells and measurements were begun.

Acknowledgment.—We gratefully acknowledge the support of this research by the B. F. Goodrich Co.

(8) M. D. Taylor and L. P. Grant, *J. Chem. Ed.*, **32**, 93 (1955).

(9) F. Arndt and P. Nachtung, *Ber.*, **59B**, 448 (1926).

(10) W. E. Thompson and C. A. Krause, THIS JOURNAL, **69**, 1016 (1947).

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(12) We wish to thank Mr. Gideon Fraenkel who designed this water-tight cell compartment.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, ST. LOUIS RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

Preparation of 2-Substituted Acetamides

BY A. J. SPEZIALE AND P. C. HAMM

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A variety of 2-substituted acetamides were prepared for the most part from the parent 2-chloroacetamides by displacement reactions.

It has been shown that a wide variety of N-substituted and N,N-disubstituted 2-chloroacetamides possess outstanding activity as pre-emergence, grass-specific herbicides[1] and that the related chloropropionamides and butyramides are almost completely devoid of this type of action.[2] It was of interest, therefore, to determine the variations in activity by replacing the α-chlorine and hydrogen atoms in the 2-chloroacetamides by other functional groups. This paper deals with the synthesis of compounds of this type. Among the groups introduced are other halogen atoms, hydroxy, alkoxy, amino, phthalimido, nitrile, thiocyanate, alkylthio, thiosulfate and isothiouronium.

Since the N-substituted 2-chloroacetamides were available from previous work,[3] methods of synthesis for many of the 2-substituted acetamides were designed to use these available compounds. Several different N-substituents which had previously been shown to be highly active as 2-chloroacetamides were chosen to determine the scope of phytotoxicity.

The herbicidal activity of these compounds and the correlation of their activities with those of the 2-chloroacetamides is reported elsewhere.[2]

The 2-haloacetamides which were prepared during the course of this investigation and not reported previously are listed in Table I. Other 2-substituted acetamides which were synthesized, for the most part, from the parent 2-chloro- or 2-iodoacetamides are given in Table II. The preparation

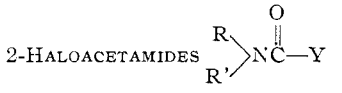
(1) P. C. Hamm and A. J. Speziale, *J. Agri. Food Chem.*, **4**, 518 (1956).

(2) P. C. Hamm and A. J. Speziale, *ibid.*, **4**, in press (1956).

(3) A. J. Speziale and P. C. Hamm, THIS JOURNAL, **78**, 2556 (1956).

TABLE I

2-HALOACETAMIDES



No.	Y	R	R'	Yield, %	M.p., °C.	B.p., °C.	Mm.	$n^{25}D$	Formula	Halogen, % Calcd.	Halogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
II	FCH_2[a]	Allyl	Allyl	73	.....	99	1.0	....	$C_8H_{12}FNO$	...	...	8.90	9.00
III	$BrCH_2$	Allyl	Allyl	85	.....	99	1.2	1.5131	$C_8H_{12}BrNO$	36.64	36.73	..	..
IV	ICH_2	H	Cyclohexyl	82	123–124	..	..	....	$C_8H_{14}INO$	...	...	5.24	5.13
V	ICH_2	H	Furfuryl	90	94–95	..	..	....	$C_7H_8INO_2$	47.78	47.73	..	..
VI	ICH_2[b]	Pentamethylene		89	.....	..	..	1.5765	$C_7H_{12}INO$	...	...	5.54	5.66
VII	ICH_2	H	*p*-Methoxyphenyl	96	147–148	..	..	....	$C_9H_{10}INO_2$	...	...	4.81	4.78
VIII	Cl_2CH	Allyl	Allyl	93	.....	93	1.2	1.5021	$C_8H_{11}Cl_2NO$	34.08	34.32	6.73	6.54
IX	Cl_3C	H	Propyl	89	43–44	92	1.7	....	$C_5H_8Cl_3NO$	52.02	51.70	..	..
X	Cl_3C	Propyl	Propyl	81	.....	95	1.0	1.4850	$C_8H_{14}Cl_3NO$	43.16	43.48	..	..
XI	Cl_3C	Allyl	Allyl	75	.....	83	1.0	1.5082	$C_8H_{10}Cl_3NO$	43.88	44.12	..	..
XII	Cl_3C	H	Dodecyl	95	48–49	..	..	....	$C_{14}H_{26}Cl_3NO$	32.16	31.77	..	..

[a] Fluoroacetyl chloride prepared according to W. E. Truce, THIS JOURNAL, **70**, 2828 (1948). [b] Product could not be distilled under reduced pressure.

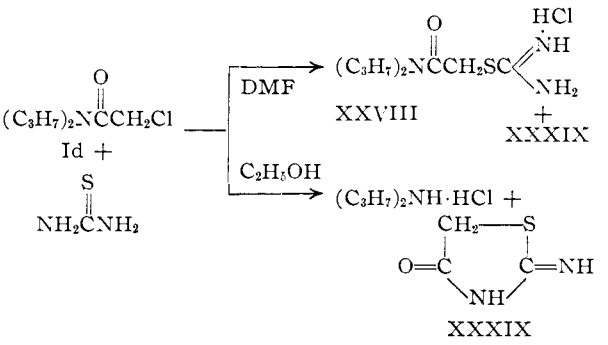
of a representative member of each type of compound is given.

In the preparation of 2-amino-N-substituted-acetamides (XXXII), following the procedures of Haworth *et al.*,[4] and Sheehan,[5] the melting points and physical characteristics of the amine hydrochlorides XXXIa,c did not agree with those reported.[4] The intermediate N-(substituted)-phthalimides XXX were synthesized from potassium phthalimide and the appropriate 2-chloroacetamide in dimethylformamide. With the availability of the N-substituted-2-chloroacetamides,[3] this method appeared more feasible than that which employed phthaloyl glycine[4,5] in the preparation of compounds of type XXX. Treatment of XXX with hydrazine hydrate and hydrochloric acid[5] gave the 2-aminoacetamide hydrochlorides (XXXI) which were converted to the free bases by the use of Amberlite IRA 400 (OH) ion-exchange resin.

To illustrate further the sequences of reactions for XXXIa,c, N,N-diallyl-1,3-dioxo-2-isoindolineacetamide (XXXb) was prepared in 92% yield. The amine hydrochloride XXXIb was obtained as an oil which on treatment with alkali gave the free base XXXIIb which formed a picrate. 2-Amino-N,N-diallylacetamide (XXXIIb) was further charbacterized by chloroacetylation to N-(diallylcaramoylmethyl)-2-chloroacetamide (XXXIII) which, on reaction with potassium phthalimide in dimethylformamide, gave N-(diallylcarbamoylmethyl)-1,3-dioxo-2-isoindolineacetamide (XXXIV).

In the reaction of 2-chloro-N,N-dipropylacetamide (Id) with thiourea, it was found that the use of dimethylformamide (DMF) or alcohol as solvents gave strikingly different results. When equivalent amounts of Id and thiourea were refluxed in 95% ethanol, only dipropylamine hydrochloride and XXXIX were obtained in 74 and 86% yields, respectively. However, in dimethylformamide at 30°, a 21% yield of pseudothiohydantoin (XXXIX) and 75% yield of the desired isothiouronium salt XXVIII were isolated.

Since the isothiouronium salt XXVIII was recovered unchanged when a sample was refluxed in ethanol, it is probably not an intermediate to XXXIX. While ethyl chloroacetate,[6a] chloroacetamide,[6b] chloroacetic acid[6c] and dichloroacetic acid[6d] react with thiourea to give XXXIX, this appears to be the first reported instance in which this reaction occurs with N-substituted-2-chloroacetamides Id.



In the preparation[3] of 4-(chloroacetyl)-morpholine (Ic) from chloroacetyl chloride and morpholine at −10 to −20°, there was isolated 4,4-bis-(4-morpholinocarbonylmethyl)-morpholinium chloride (XLIc) in 5% yield from crude Ic by filtration prior to distillation. The morpholinium chloride XLIc was synthesized according to scheme (Ic—XLIc) and shown to be identical with the material isolated from crude Ic. It is postulated that XLIc was also formed in this manner during the preparation and isolation of Ic.

The isolation of XLIIe from the distillation residue in the preparation of XXXVe from Ie and XLe is further evidence that the series of reactions (I—XLII) occur in the preparation of I and XX-XV. In this instance, however, the quaternary halide XLIe was not isolated but rather eliminated ethyl chloride during the distillation of XXXVe to give the tertiary amine XLII.

The 2-haloacetamides showed, in general, the expected reactivity toward nucleophilic reagents in the replacement of the halogen atom. These reactions, performed with a variety of such reagents, should provide a simple synthetic method for

(4) R. D. Haworth, D. H. Peacock, W. R. Smith and R. MacGillivray, *J. Chem. Soc.*, 2972 (1952).

(5) J. C. Sheehan and V. S. Frank, THIS JOURNAL, **71**, 1856 (1949); J. C. Sheehan and W. L. Richardson, *ibid.*, **76**, 6329 (1954).

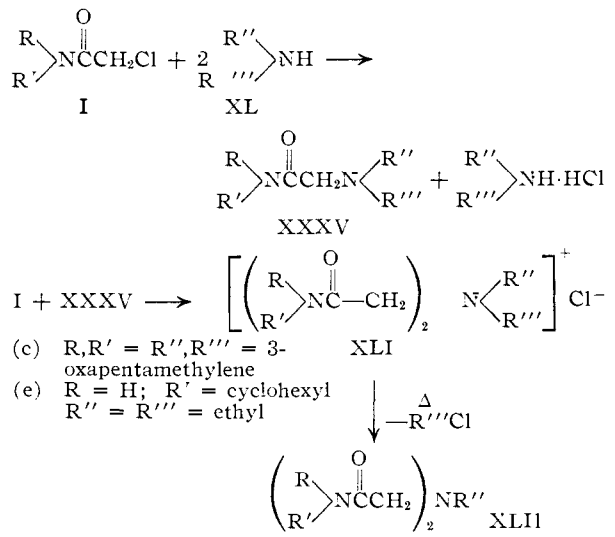
(6) (a) C. F. H. Allen and J. A. VanAllan, *Org. Syntheses*, **27**, 71 (1947); (b) E. Mulder, *Ber.*, **8**, 264 (1875); (c) R. Andreasch, *Monatsh.*, **8**, 424 (1887); (d) A. E. Dixon, *J. Chem. Soc.*, **63**, 815 (1893).

Table II

2-Substituted Acetamides $RR'NC(=O)CH_2Y$

No.	Y	R	R′	Yield, %	M.p., °C.	B.p., °C.	B.p., Mm.	$n^{25}D$	Formula	Nitrogen, % Calcd.	Nitrogen, % Found	Halogen, % Calcd.	Halogen, % Found
XIII	OH	Allyl	Allyl	76	......	88	1.1	1.4850	$C_8H_{13}NO_2$	...	...[a]	...	...
XIV	OC_2H_5	Allyl	Allyl	82	....	75	0.6	1.4660	$C_{10}H_{17}NO_2$	7.65	7.48[b]	...	...
XV	CN[c]	Pentamethylene		52.5	88–89	...	...	....	$C_8H_{12}N_2O$	...	...	...	...
XVI	CN	H	2-Chloroallyl	29	44–45	170	0.4	....	$C_6H_7ClN_2O$	17.66	17.43	22.35	22.47
XVII	SCN	H	Furfuryl	73	72.5–73.5	...	...	....	$C_8H_8N_2O_2S$	14.28	14.17	...	...
XVIII	SCN	Allyl	Allyl	71	......	146	0.7	1.5241	$C_9H_{12}N_2OS$	14.27	14.41	...	...
XIX	SC_2H_5	H	Tetrahydrofurfuryl	68	......	163–165	3.2	1.5112	$C_9H_{17}NOS$	...	...[d]	...	...
XX	SC_4H_9	H	3-Methoxypropyl	89	......	132	0.5	1.4855	$C_{10}H_{21}NO_2S$	6.39	6.25	...	...
XXI	$SO_2C_4H_9$	H	3-Methoxypropyl	60	......	202	1.0	....	$C_{10}H_{21}NO_4S$	5.57	5.88[e]	...	...
XXII	$SCH_2CH_2NH_2$	Allyl	Allyl	100[f]	......	...	...	1.5292	$C_{10}H_{18}N_2OS$	...	...[g]	...	...
XXIII	$S(CH_2)_2NHCOCH_2Cl$	Allyl	Allyl	97[f]	......	...	...	1.5398	$C_{12}H_{19}ClN_2O_2S$	...	...	12.19	12.14
XXIV	$SO_2(CH_2)_2NHCOCH_2Cl$	Allyl	Allyl	49[f]	......	...	...	....	$C_{12}H_{19}ClN_2O_4S$	...	...	10.98	10.88
XXV	$SCH_2CH(NH_2)CO_2H$[h]	Allyl	Allyl	72[f]	......	...	...	....	$C_{11}H_{18}N_2O_3S$	...	...	...	...
XXVI	SSO_3Na	Allyl	Allyl	81	......	...	...	....	$C_8H_{12}NNaO_4S_2\cdot H_2O$	4.80	4.82[i]	...	...
XXVII	SSO_3Na	3-Oxapentamethylene		88	......	...	...	....	$C_6H_{10}NNaO_5S_2H_2O$	4.99	5.16	...	...
XXVIII	$SC(=NH)NH_2\cdot HCl$	Propyl	Propyl	75	138	...	...	....	$C_9H_{19}N_3OS\cdot HCl$	16.55	16.23	13.97	13.92
XXIX	$SC(=NH)NH_2\cdot HCl$	Pentamethylene		59	164–166	...	...	....	$C_8H_{15}N_3OS\cdot HCl$	17.67	17.30	14.91	14.86
XXXa	Phthalimido	Ethyl	Ethyl	90	154.2–155.2[j]	...	...	....	$C_{14}H_{16}N_2O_3$	10.76	10.62	...	...
XXXb	Phthalimido	Allyl	Allyl	92	102–103	...	...	....	$C_{16}H_{16}N_2O_4$	9.85	9.89	...	...
XXXc	Phthalimido	3-Oxapentamethylene		88	200–201[k]	...	...	....	$C_{14}H_{14}N_2O_4$	10.22	10.16	...	...
XXXIa	$NH_2\cdot HCl$	Ethyl	Ethyl	83	116–117[m]	...	...	....	$C_6H_{14}N_2O\cdot HCl$	16.71	16.54[m]	21.27	21.43
XXXIb	$NH_2\cdot HCl$	Allyl	Allyl	..[l]	......	...	...	....	$C_8H_{14}N_2O\cdot HCl$	...	...	...	...
XXXIc	$NH_2\cdot HCl$	3-Oxapentamethylene		62	240–243[n]	...	...	....	$C_6H_{12}N_2O_2\cdot HCl$	15.51	15.36[n]	19.63	19.54
XXXIIa	NH_2[o]	Ethyl	Ethyl	79	......	66	0.5	1.4622	$C_6H_{14}N_2O$	...	...	...	...
XXXIIb	NH_2[p]	Allyl	Allyl	76	......	115–120	1.0	1.4930	$C_8H_{14}N_2O$	...	...	...	...
XXXIIc	NH_2[q]	3-Oxapentamethylene		..	......	...	...	....	$C_6H_{12}N_2O_2$	...	...	...	...
XXXVe	$N(C_2H_5)_2$[r]	H	Cyclohexyl	78	......	114–117	1.0–1.2	1.4749	$C_{12}H_{24}N_2O$	13.19	12.65	...	...
XXXVI	$^+N(C_2H_5)_2CH_3I^-$	H	Cyclohexyl	100[s]	74–76	...	...	....	$C_{13}H_{27}IN_2O$	...	...	35.82	35.25
XXXVII	$^+N(C_2H_5)_3I^-$	H	Furfuryl	89	144–145	...	...	....	$C_{13}H_{23}IN_2O_2$	...	...	34.66	34.40
XXXVIII	$^+N(C_4H_9)_3I^-$	H	*p*-Methoxy phenyl	87	100–101	...	...	....	$C_{21}H_{37}IN_2O_2$	...	...	26.64	26.40

[a] *Anal.* Calcd.: C, 61.86; H, 8.43. Found: C, 61.81; H, 8.45. [b] *Anal.* Calcd.: C, 65.54; H, 9.35. Found: C, 64.94; H, 9.58. [c] Prepared by a different method m.p. 88–89°; J. W. Barrett, A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 1065 (1935). [d] *Anal.* Calcd.: S, 15.77. Found: S, 15.56. [e] *Anal.* Calcd.: S, 12.72. Found: S, 12.53. [f] Crude material could not be distilled or crystallized. [g] *Anal.* Calcd.: S, 14.99. Found: S, 15.11. [h] The *p*-toluenesulfonamide melted at 102–104°. *Anal.* Calcd. for $C_{18}H_{24}N_2O_5S_2$: N, 6.79; S, 15.54. Found: N, 6.81; S, 15.70. [i] *Anal.* Calcd.: S, 22.00. Found: S, 22.04. [j] Ref. 4, reported m.p. 151°. [k] Ref. 4, reported m.p. 200–201°. [l] Not isolated. [m] *Anal.* Calcd.: C, 43.24; H, 9.07. Found: C, 42.91; H, 9.03. Ref. 4 reported m.p. 101°, hygroscopic needles. [n] *Anal.* Calcd.: C, 39.89; H, 7.25. Found: C, 39.62; H, 7.26. Ref. 4 reported m.p. 106° hygroscopic needles. [o] *Picrate*, 88% yield on crude; m.p. 220° dec. *Anal.* Calcd. for $C_{12}H_{17}N_5O_8$: N, 19.49. Found: N, 19.19. Ref. 9 report the amine b.p. 85° (0.1 mm.) and the picrate m.p. 221° dec. [p] *Picrate*, m.p. 196–198° dec. *Anal.* Calcd. for $C_{14}H_{17}N_5O_8$: N, 18.27. Found: N, 18.06. [q] Only crude material isolated, *picrate*, m.p. 221° dec. *Anal.* Calcd. for $C_{12}H_{15}N_5O_9$: C, 38.61; H, 4.05; N, 18.76. Found: C, 38.86; H, 4.36; N, 18.50. [r] *Oxalate*, m.p. 135.8–136.8°. Calcd. for $C_{12}H_{24}N_2O\cdot C_2H_2O_4$: N, 9.29. Found: N 9.25. [s] Crude yield.



the preparation of diverse 2-substituted acetamides.

Experimental[7]

2-Haloacetamides.—These compounds are listed in Table I. The 2-iodoacetamides were prepared from the 2-chloroactamides[3] in the usual manner with potassium iodide in acetone. The other haloacetamides were synthesized from the appropriate amine and acyl chloride as described previously.[3]

N,N-Diallylglycolic Amide (XIII).—A mixture of 15.2 g. (0.2 mole) of glycolic acid and 45 g. (0.47 mole) of diallyl amine was heated at reflux (111–150°) for 34 hr. during which time amine–water azeotrope was distilled slowly at 86–93°. Excess amine was then distilled under reduced pressure, and the liquid residue was dissolved in ether, dried and distilled. The infrared spectrum showed characteristic absorption in hydroxyl and amide regions.

Attempts to prepare XIII from N,N-diallyl-2-chloroacetamide by replacement of the chlorine atom in alkaline media failed. With an equivalent of 5% sodium hydroxide solution at room temperature, a mixture of products (infrared) in low yield resulted. When an excess of 10% sodium carbonate solution was used at 62–63° for 37 hr., the replacement reaction took place, but only to about 85% completion (infrared and analysis of product).

N,N-Diallyl-2-ethoxyacetamide (XIV).—To a sodium ethoxide solution prepared from 4.6 g. of sodium and 200 ml. of absolute ethanol, 34.7 g. of N,N-diallyl-2-chloroacetamide was added at 0–5° during 20 minutes. The mixture was stirred for 4 hr., allowed to warm to room temperature and sodium chloride removed by filtration. Excess alcohol was removed under reduced pressure, and the residue dissolved in ether. The ether solution was washed with dilute hydrochloric acid, sodium bicarbonate solution and water and dried over magnesium sulfate. Removal of the ether left a light yellow oil which distilled at 75° (0.6 mm.).

The alkylthioacetamides were prepared similarly and their sulfones by oxidation with 30% hydrogen peroxide in glacial acetic acid.

1-(Cyanoacetyl)-piperidine (XV).—A mixture consisting of 32.3 g. of 1-(chloroacetyl)-piperidine, 15.6 g. of potassium cyanide and 100 ml. of ethanol was held at 75–80° for 2 hr. The potassium salts were removed by filtration and washed with ethanol. The combined filtrates were evaporated to dryness and the residue recrystallized from water.

Sodium 4-(Hydroxyacetyl)-morpholine Thiosulfate Monohydrate (XXVII).—This was prepared by a modification of the procedure for sodium glycolanilide thiosulfate.[8] A solution consisting of 16.4 g. of 4-(chloroacetyl)-morpholine, 24.8 g. of sodium thiosulfate pentahydrate and 200 ml. of 50% ethanol was heated under reflux for 4 hr., cooled and filtered to remove a small amount of suspended impurities. The solid residue, after concentration of the filtrate under reduced pressure, was extracted with five 100-ml. portions of boiling ethanol. Evaporation of the alcohol to dryness gave 23.3 g. (88%) of the Bunte salt as the monohydrate. A sample for analysis was recrystallized twice from ethanol containing a few ml. of water.

2-(Amidinothio)-N,N-dipropylacetamide Hydrochloride (XXVIII).—A solution of 11.2 g. of thiourea in 100 ml. of dimethylformamide was treated with 26.6 g. of 2-chloro-N,N-dipropylacetamide in 25 ml. of dimethylformamide at 30° with cooling. The mixture was stirred overnight during which solid material precipitated out. An aliquot of the reaction mixture was titrated with silver nitrate solution and the theoretical amount of chloride ion was shown to be present. The mixture was diluted with 200 ml. of dry acetone and the isothiouronium salt XXVIII was collected on a filter; yield 20 g. (53%); m.p. 136–138°. An additional 8.5 g. of material was obtained by dilution of the acetone filtrate with 500 ml. of ether; total yield 28.5 g. (75%). A portion of this material was recrystallized from dimethylformamide–acetone mixture.

On further dilution of acetone–ether mother liquor, a 21% yield of crude pseudothiohydantoin (XXXIX) was isolated. A purer product was obtained by filtering the alcohol insoluble portion; m.p. 200–205°.

Anal. Calcd. for $C_3H_4N_2OS$: N, 24.12; S, 27.60. Found: N, 23.98; S, 27.50.

In attempting to prepare the isothiouronium salt in 95% ethanol, only pseudothiohydantoin (XXXIX) and dipropylamine hydrochloride were isolated. A solution of 11.2 g. of thiourea in 50 ml. of 95% ethanol was heated to reflux and 26.6 g. of 2-chloro-N,N-dipropylacetamide in 10 ml. of alcohol was added in 5 minutes. Refluxing was continued for 1.5 hr. during which time crystals formed. After cooling to room temperature, there was collected 15.0 g. (86%) of XXXIX. The filtrate was concentrated to a small volume and diluted with 500 ml. of dry acetone. There was obtained in this manner 15.2 g. (74%) of pearly plates which were identified as dipropylamine hydrochloride; m.p. 268–272° dec.

Triethyl-(furfurylcarbamoylmethyl)-ammonium Iodide (XXXVII).—A solution of 5.3 g. of N-furfuryl-2-iodoacetamide in 50 ml. of dry benzene was treated with 3.0 g. of triethylamine in 30 ml. of dry benzene at 50–60°. After heating at 60–65° for about 4 hr., 10 ml. of benzene was removed by distillation to ensure dryness. The white crystalline iodide was collected on a filter and recrystallized from ethyl acetate–ethanol mixture.

XXXVIII was prepared similarly from the 2-iodoacetanilide and tributylamine, and XXXVI was prepared from XXXVe and methyl iodide in the usual manner.

4,4-Bis-(morpholinocarbonylmethyl)-morpholinium Chloride (XLIc).—In the preparation of 4-(chloroacetyl)-morpholine (Ic) a small amount of white solid (m.p. 204–205°) was isolated from the crude material prior to the final distillation.[3] This solid was shown to be the morpholinium chloride (XLIe) and a sample was synthesized as follows. To a solution of 16.3 g. (0.1 mole) of 4-(chloroacetyl)-morpholine in 50 ml. of 1,2-dichloroethane, there was added 17.5 g. (0.2 mole) of morpholine. After refluxing for 2 hr., the hydrochloride was recovered in quantitative yield. To the filtrate containing the intermediate 4-(morpholinoacetyl)-morpholine (XXXVc), 16.3 g. (0.1 mole) of 4-(chloroacetyl)-morpholine was added, and the resulting solution refluxed for 3 hr. The solvent was removed under reduced pressure and the residue treated with 100 ml. of acetone and filtered. There was obtained 3.8 g. of white crystalline material, m.p. 203–205°.

The acetone solution was treated with an additional 16.3 g. (0.1 mole) of 4-(chloroacetyl)-morpholine. After refluxing for 4 hr., the solvent was distilled and 200 ml. of benzene added. Removal of the benzene by distillation to ensure dryness left an oily residue which solidified immediately. An acetone suspension upon filtration gave 19.2 g. of product, m.p. 201–203°. An additional 5.3 g. was obtained from the mother liquors. The total yield was 28.3 g. (74%). A portion recrystallized from absolute methanol melted at 203–204°, and the melting point was not depressed on admixture with the material (m.p. 204–205°) obtained in the preparation of 4-(chloroacetyl)-morpholine.

Anal. Calcd. for $C_{16}H_{28}ClN_3O_5$: Cl, 9.36; N, 11.18. Found: Cl, 9.43; N, 11.18.

(7) Melting points are uncorrected. Analyses by Mr. A. Bybell and infrared spectra by Mr. O. Kinast.

(8) U. Weiss and S. Sokol, THIS JOURNAL, **72**, 1687 (1950).

N-Cyclohexyl-2-diethylaminoacetamide (XXXVe).—To 29.3 g. of diethylamine in 100 ml. of ethanol, 35.2 g. of 2-chloro-N-cyclohexylacetamide (Ie) was added during about 0.5 hr. at room temperature. The solution was held at 40–45° for 4 hr. and the solvent removed by distillation under reduced pressure. After addition of ether to the liquid residue, there was obtained 18 g. (82.5% of theory) of diethylamine hydrochloride by filtration. Evaporation of the ether gave crude XXXVe (85% yield) which was distilled.

The residue from the distillation of N-cyclohexyl-2-diethylaminoacetamide was heated with acetone and filtered. The white crystalline material, **2,2'-ethyliminobis-(N-cyclohexylacetamide) (XLIIe)** was dissolved in ethanol, filtered and precipitated on the addition of water; m.p. 156–157° (presoftening at 154°). The material was soluble in dilute acid but insoluble in dilute alkali and was chlorine free.

Anal. Calcd. for $C_{18}H_{33}N_3O_2$: C, 66.83; H, 10.28; N, 12.99; neut. equiv., 323.5. Found: C, 67.00; H, 10.33; N, 12.99; neut. equiv., 323.0.

N,N-Diallyl-1,3-dioxo-2-isoindolineacetamide (XXXb).—To 37.0 g. of potassium phthalimide in 250 ml. of dimethylformamide, there was added 34.7 g. of N,N-diallyl-2-chloroacetamide at 52–60° during 0.5 hr. The solution was held at 65–70° for 2 hr., cooled to room temperature and poured into 500 ml. of water. The phthalimido derivative was collected on a filter and washed with water, m.p. 100–101°. Recrystallization from aqueous ethanol raised the melting point to 102–103°. XXXa and XXXc were prepared similarly.

4-(Aminoacetyl)-morpholine Hydrochloride (XXXIc).—A solution of 36.6 g. of N-(morpholinocarbonylmethyl)-phthalimide in 500 ml. of absolute ethanol was treated with 10.0 g. of 85% hydrazine hydrate solution and heated at reflux for 2 hr. The solid residue, after removal of the solvent under reduced pressure, was heated at 50° for 10 minutes with 400 ml. of 2 *N* hydrochloric acid.[5] Phthalyl hydrazide (80%) was recovered by filtration at room temperature. The filtrate was concentrated to dryness at 20–25° (20 mm.) and the residue extracted with five 100-ml. portions of absolute ethanol. On cooling 15.0 g. (62% yield) of 4-(aminoacetyl)-morpholine hydrochloride was recovered as non-hygroscopic pearly plates. The melting point was not changed after several recrystallizations from absolute ethanol. XXXIa was prepared similarly and obtained as non-hygroscopic pearly plates.

N,N-Diallyl-2-aminoacetamide (XXXIIb).—N,N-Diallyl-2-aminoacetamide hydrochloride (XXXIb), prepared as described for the morpholine analog, was obtained as an oil which could not be induced to crystallize. It was dissolved in dilute alkali and the solution concentrated to a small volume at 20–25° (20 mm.). The residue was dissolved in ether–acetone mixture, filtered to remove sodium chloride, and after removal of the solvents, the free amine was distilled.

2-Amino-N,N-diethylacetamide (XXXIIa), the free amine, was prepared by passing 23.8 g. of 2-amino-N,N-diethylacetamide hydrochloride (XXXIa) in 150 ml. of water through Amberlite IRA (OH) resin in a 3 × 45 cm. column. The halogen free eluent was concentrated under reduced pressure and the residue distilled. There was obtained 14.7 g. (79% yield) of 2-amino-N,N-diethylacetamide.[9]

N-(Diallylcarbamoylmethyl)-1,3-dioxo-2-isoindolineacetamide (XXXIV).—N,N-Diallyl-2-aminoacetamide (7.4 g.) was chloroacetylated[3] to give 4.5 g. (41% yield) of **N-(diallylcarbamoylmethyl)-2-chloroacetamide (XXXIII)**, b.p. 177° (1.6 mm.). This material was converted to the phthalimido derivative XXXIV by heating at 80–90° for 1 hr. with 7 g. of potassium phthalimide in 100 ml. of dimethylformamide. The cooled mixture was poured into water and the solid collected on a filter and dried, yield 2.0 g. (30%). A sample recrystallized from aqueous ethanol melted at 136–137°.

Anal. Calcd. for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31. Found: C, 63.43; H, 5.80; N, 12.14.

(9) G. B. Marini-Bettolo and J. F. Cavalla, *Gazz. chim. ital.*, **84**, 896 (1954).

ST. LOUIS, MISSOURI

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF EMORY UNIVERSITY]

The Reaction of Enamines with Aromatic Diazonium Salts

BY JAMES W. CRARY,[1] OSBORNE R. QUAYLE[2] AND CHAS. T. LESTER

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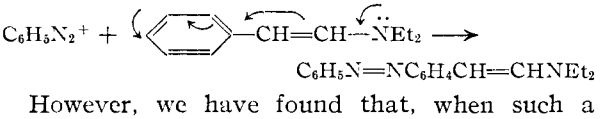
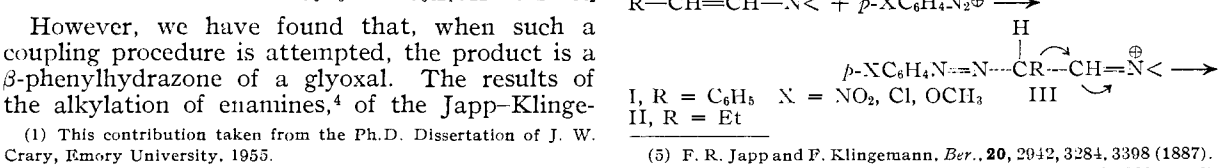
N,N-Diethylstyrylamine and 1-(1-butenyl)-piperidine have been treated with aromatic diazonium salts. Crystalline compounds, identified as the corresponding β-phenylhydrazones of phenylglyoxal and ethylglyoxal, were produced when *p*-nitro-, *p*-chloro- and *p*-methoxybenzenediazonium chloride salts were used. When the behavior of enamines possessing no β-hydrogen was investigated, *p*-substituted phenylhydrazones were the products identified: *viz.*, 1-(β-methylstyryl)-piperidine with 2,4-dinitrobenzenediazonium salt gave acetophenone 2,4-dinitrophenylhydrazone, and 1-(1-isobutenyl)-piperidine with *p*-nitrobenzenediazonium chloride gave acetone *p*-nitrophenylhydrazone. A mechanism for each of these reactions is proposed. The structures of the products were established by synthesis and by comparison of their infrared spectra to compounds of known structure.

N,N-Diethylstyrylamine is a vinylog[3] of N,N-diethylaniline. As such it might be expected to respond to electrophilic attack by a diazonium salt to form a *p*-substituted azo derivative



$$C_6H_5N_2^+ + \text{(C}_6\text{H}_5\text{)—CH=CH—NEt}_2 \longrightarrow C_6H_5N{=}NC_6H_4CH{=}CHNEt_2$$

However, we have found that, when such a coupling procedure is attempted, the product is a β-phenylhydrazone of a glyoxal. The results of the alkylation of enamines,[4] of the Japp–Klingemann reaction[5] between diazonium salts and β-ketoesters, and of the reaction between diazonium salts and unsaturated anilines and phenol ethers[6] all bear striking relationships to the reactions herein reported. The steps in the production of the β-phenylhydrazones may be rationalized as



$$R—CH{=}CH—\ddot{N}< + p\text{-}XC_6H_4N_2^{\oplus} \longrightarrow p\text{-}XC_6H_4N{=}N—\underset{\displaystyle H}{\underset{|}{C}}R—CH{=}\overset{\oplus}{N}< \longrightarrow$$

I, R = C_6H_5 X = NO_2, Cl, OCH_3 III

II, R = Et

(1) This contribution taken from the Ph.D. Dissertation of J. W. Crary, Emory University, 1955.

(2) Deceased, December 7, 1954.

(3) R. C. Fuson, *Chem. Revs.*, **16**, 1 (1935).

(4) G. Stork, R. Terrell and J. Szmuszkovicz, THIS JOURNAL, **76**, 2029 (1954).

(5) F. R. Japp and F. Klingemann, *Ber.*, **20**, 2942, 3284, 3398 (1887).

(6) (a) A. Quilico and N. Freri, *Gazz. chim. ital.*, **58**, 380 (1928); *C. A.*, **23**, 597 (1929); **59**, 600 (1929); **24**, 599 (1930); **60**, 606 (1930); *C. A.*, **25**, 932 (1931); (b) A. Quilico and E. Fleischner, *ibid.*, **59**, 39 (1929); **23**, 3675 (1929).