Reaction of Certain Electrophiles with Some Imines Derived from Cyclohexanone and Isobutyraldehyde[1]

JOHN P. CHUPP AND ERIKA R. WEISS

Monsanto Company, Agricultural Division, Research Department, St. Louis, Missouri 63166

Received October 23, 1967

Acid chlorides and alkyl and aryl isocyanates and isothiocyanates were allowed to react with imines derived from cyclohexanone and isobutyraldehyde. A variety of N-(1-alkenyl)amides (**2**, **8**), N-(1-alkenyl)ureas and thioureas (**3**, **5**, **12**), 2-enaminocarbamides (**4**, **6**), and triazinones (**11**) were formed and isolated as reaction products, depending upon the nature of the imine, type of electrophile, and reaction conditions. The results are compared with the reported work on the reaction of these reagents with N,N-disubstituted enamines from the same carbonyl compounds. The products can be rationalized as arising from three possible modes of attack by the electrophile on the imine: (1) nitrogen attack, with α-hydrogen elimination; (2) α-carbon attack, and (3) C=N attack followed by ring formation.

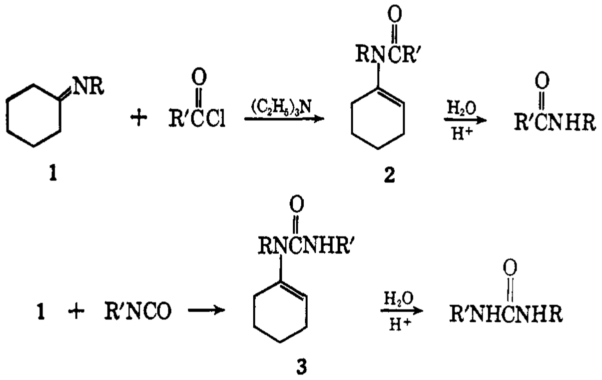
The imines of cyclohexanone and isobutyraldehyde are for the most part easily prepared[2] and, unlike many aliphatic imines, not subject to rapid polymerization and condensation reactions. We wished therefore to compare the behavior of the imines of these two carbonyl compounds toward certain electrophiles with those reported for the corresponding enamines. In the latter instance, it was shown that final substitution products with various acid chlorides,[3] isocyanates,[4] and the like involved electrophilic substitution on the olefinic carbon α to the carbon bearing the enamino nitrogen.

It would be anticipated that the imines could react by at least three possible modes. Imines, having a reactive carbon bearing a labile hydrogen (enolizable imines), such as those derived from cyclohexanone and isobutyraldehyde, could be expected to form products arising from acid chloride or isocyanate attack at the α position in exact analogy to results reported for the enamines. Alternatively, these electrophilic reagents could irreversibly react at the imino nitrogen and through loss of α hydrogen give stable enamides or enureas. Finally, the imines could react at the C=N bond to form cyclic products in analogy to reaction of isocyanates with aromatic Schiff bases or methylene imines.[4b,5]

The literature contains some work relative to reaction of these electrophiles with imines containing enolizable hydrogen. Thus, N-alkyl-N-alkenylamides are formed by the action of certain acid halides on aldimines.[6] On the other hand, it is reported that ketimines (from cyclohexanone) give carbon acylated products.[7] Studies on the effect of isothiocyanates and isocyanates on acetophenone anil indicate that only α-carbon attack occurs. Anils of benzoylthioacetanilide and benzoylmalonanilides, respectively, were isolated.[8]

It was found that when N-alkyl-N-cyclohexylidenamines were allowed to react with various acid chlorides or isocyanates, neutral N-acylated enamides (**2**) and enureas (**3**) could be isolated in fair yields (Scheme I).

SCHEME I



(See Table I for compilation and structure of compounds.) Anils of cyclohexanone showed no evidence of giving enureas with isocyanates but, rather, α-carbon attack occurred with formation of the 3′,4′-dichloro-2-(*p*-chloroanilino)-1-cyclohexene-1-carboxanilide (**4**). Structures were confirmed by elemental and spectral analysis with further confirmation by hydrolysis to known amides or ureas.[9]

Reaction of **1** with isothiocyanates was more complicated. Alkyl isothiocyanates gave cyclohexenylthioureas which on attempted distillation reverted to **1** and isothiocyanate. Certain arylisothiocyanates initially form **5**, but on heating rearrange to the vinylogous thiourea **6**, perhaps as a result of reversible thermal dis-

---

[1] Presented before the Division of Organic Chemistry at the First Midwest Regional Meeting, American Chemical Society, Kansas City, Mo., Nov 5, 1965, Abstract No. 440.

[2] (a) W. F. Bruce and R. N. Blomberg, U. S. Patents 2,700,681 and 2,700,682 (1955); (b) H. Weingarten, J. P. Chupp, and W. A. White, *J. Org. Chem.*, **32**, 3246 (1967); (c) K. L. Campbell, A. G. Sommers, and B. K. Campbell, *J. Amer. Chem. Soc.*, **66**, 82 (1944).

[3] (a) A. Stork and H. K. Landesmann, *ibid.*, **78**, 5128 (1956); (b) S. Hunig, *Chem. Ber.*, **90**, 2833 (1957), and succeeding papers.

[4] (a) S. Hunig, *Angew. Chem.*, **71**, 312 (1959); (b) D. Clemens and W. Emmons, *J. Org. Chem.*, **26**, 767 (1961); (c) G. Berchtold, *ibid.*, **26**, 3043 (1961); (d) M. Perelman and S. A. Mizak, *J. Amer. Chem. Soc.*, **84**, 4988 (1962).

[5] (a) R. Huisgen, K. Herbig, and M. Morikgwa, *Chem. Ber.*, **100**, 1107 (1967); (b) H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press Inc.. New York, N. Y., Chapters 4 and 5.

[6] H. Breederveld, *Rec. Trav. Chim.*, **79**, 401 (1960).

[7] R. W. Layer, *Chem. Rev.*, **63**, 489 (1963); see also V. E. Harvey, El Cerrito, and S. A. Ballard, U. S. Patent 2,418,173 (1947), and British Patent 638,091 (1950) [*Chem. Abstr.*, **41**, 4510 (1947); **44**, 9476 (1950)]. However, at least some N acylation apparently occurs because N-cyclohexylhexanamide was obtained after hydrolysis of the reaction mixture from N-cyclohexylidenecyclohexylamine and caproyl chloride. The intermediate acyl enamide was not fully characterized. A. A. Brizzolara, Jr., "An Investigation of Some Reactions of Enamines," Columbia University, Ph.D. Thesis, 1960.

[8] J. Moszew, A. Inasinski, K. Kubiczek, and J. Zawrzykraj, *Rocz. Chem.*, **34**, 1169 (1960); *Chem. Abstr.*, **55**, 1533*a* (1961).

[9] Thus, the possibility that the isocyanate–imine adducts are 4-amino-2-azetidinones[4d] rather than enureas (**3**, **12**) is ruled out by consideration of the ir 6.0 μ (C=O), nmr δ 5.8 (C=C**H**), and facile hydrolysis to 3-alkylureas. The β-lactams display ir 5.7 μ (C=O), nmr, δ 4.4–5.3 (Cβ–**H**), and hydrolyze to carboxamides similar to **10**. Spectral evidence, especially ir 6.0 μ (C=N, C=O), and nmr, δ 7.5–7.8 (C**H**=N), also serve to differentiate iminoanilide (**9**) from the alternate β-lactam structure.

TABLE I

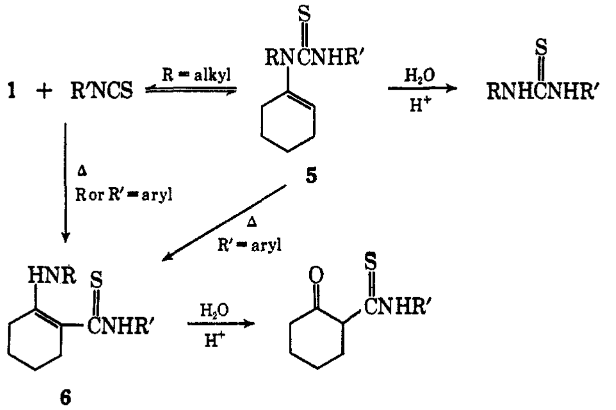
REACTION OF ELECTROPHILES WITH IMINES FROM CYCLOHEXANONE AND ISOBUTYRALDEHYDE

Compd	R	R′	X	Yield, %	Mp or bp (mm), °C	Calcd, %						Found, %						Pertinent nmr (CCl_4), δ
						C	H	Cl	N	S	Mol wt	C	H	Cl	N	S	Mol wt	
2a	CH_3	$2,4\text{-}Cl_2C_6H_3OCH_2$	O	61	107–108	57.33	5.45	22.57	4.46			57.21	5.55	22.64	4.39			5.7 (m, $=CH$) 3.0 (s, NCH_3)
2b	$(CH_3)_2CH$	$ClCH_2$	O	32	50–51			16.44	6.49					16.54	6.34			5.7 (m, $=CH$)
3a	CH_3	CH_3	O	95	65 120–130 (1)	64.25	9.59		16.65		168	64.14	9.53		16.56		160	5.6 (m, $=CH$, NH) 2.6 (d, $NHCH_3$) 2.9 (s, NCH_3)
3b	CH_3	$3,4\text{-}Cl_2C_6H_3$	O	74	Oil	56.19	5.39		9.36			55.57	5.41		9.36			5.9 (m, $=CH$) 2.9 (s, NCH_3)
3c	CH_3	$2\text{-}(NO_2)C_6H_4$	O	90	120.5–122	61.07	6.22		15.26			60.87	6.24		15.61			5.9 (m, $=CH$) 3.0 (s, NCH_3)
4				70	147–150	57.66	4.33	26.88	7.08			58.01	4.18	26.85	7.05			11.8 (m, $4\text{-}ClC_6H_4NH$)
5a	CH_3	C_2H_5	S	86	43–44				14.13	16.17					14.15	15.86		6.0 (m, NH) 5.7 (m, $=CH$) 3.3 (s, NCH_3)
5b	CH_3	$3,4\text{-}Cl_2C_6H_3$	S	85	107–108	55.33	5.12	22.49	8.89	10.17	315	53.30	5.06	22.50	8.87	10.04	297	5.9 (m, $=CH$) 3.4 (s, NCH_3)
5c	$n\text{-}C_4H_9$	$3,4\text{-}Cl_2C_6H_3$	S	92	95–96	57.13	6.20		7.84	8.97	357	56.50	6.12		7.89	9.16	363	5.8 (m, $=CH$)
6a	CH_3	$3,4\text{-}Cl_2C_6H_3$	S	57	160–161	53.33	5.12	22.49	8.89	10.17	315	53.37	5.13	22.47	8.83	10.14	323	12.8 (m, CH_3NH) 2.9 (d, NCH_3)
6b	$n\text{-}C_4H_9$	$3,4\text{-}Cl_2C_6H_3$	S		140–141	57.13	6.20		7.80	8.97		57.32	6.21		7.80	8.97		12.9 (m, C_4H_9NH)
6c	$4(CH_3)C_6H_4$	$3,4\text{-}Cl_2C_6H_3$	S	67	153–154	61.38	5.15	18.12	7.16	8.19		61.42	5.21	17.98	6.99	8.15		13.6 (m, p-tolyl-NH)
8				48	50–51.5	59.54	7.99	17.58	6.94			59.41	7.88	17.73	7.03			[a]
9a	$(CH_3)_2C{=}CH$	$3,4\text{-}Cl_2C_6H_3$	O	91	90–95	57.52	5.79	22.64	8.94			57.53	5.80	22.64	8.94			[a]
9b	$(CH_3)_3C$	$3,4\text{-}Cl_2C_6H_3$	O	78	62–64	57.15	6.39	22.49	8.89			57.22	6.46	22.53	8.90			11.1 (s, NH) 7.6 (s, $CH{=}N$) 1.28 [s, $C(CH_3)_2$]
11a	CH_3	$4\text{-}ClC_6H_4$	O	80	Oil	63.04	8.09		12.97		324	62.68	8.05		12.81		321	[a]
11b	C_2H_5	$3,4\text{-}Cl_2C_6H_3$	O	93	110–113	59.1	7.52	18.4	10.9		386	58.90	7.37	18.53	10.6		393	[a]
12a	CH_3	$4\text{-}ClC_6H_4$	O	96	78–82	60.37	6.33	14.85	11.74		239	60.56	6.14	14.58	11.57		240	5.8 (m, $=CH$) 2.9 (s, NCH_3) 1.7, 1.8 [$=C(CH_3)_2$]
12b	$(CH_3)_2CH$	$3,4\text{-}Cl_2C_6H_3$	O		80–81	55.82	6.02	23.54	9.30		301	55.91	5.63	23.55	9.15		305	5.8 (m, $=CH$) 1.7, 1.9 [$=C(CH_3)_2$] 1.1 [d, $CH(CH_3)_2$]
12c	$(CH_3)_2CH$	$3,4\text{-}Cl_2C_6H_3$	S	80	115			22.35	8.83		317			22.21	8.56		333	5.9 (m, $=CH$) 1.7, 1.9 [$=C(CH_3)_2$]

[a] See Experimental Section.

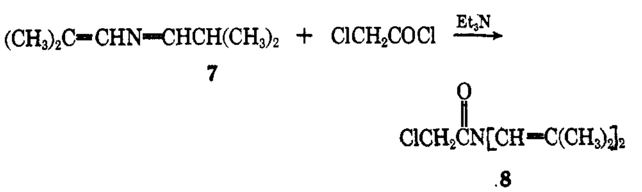
sociation to starting isothiocyanate and imine, followed by irreversible formation of 6 (Scheme II).[10]

SCHEME II



In contrast to 1, anils of cyclohexanone with isothiocyanates gave only 2-anilino-1-cyclohexenthiocarboxamides (6). The anils thus behave similarly to those described in ref 8.

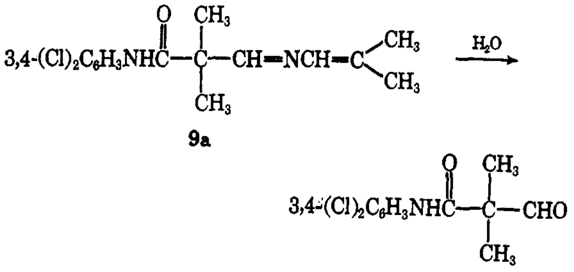
The structure of the imine from isobutyraldehyde largely determined the mode of attack of the various electrophiles. 7 is both an imine and enamine and its reaction with chloroacetyl chloride gave 8. This reaction represents an extension of Brederveld's method[6]



$$\underset{7}{(CH_3)_2C{=}CHN{=}CHCH(CH_3)_2} + ClCH_2COCl \xrightarrow{Et_3N} \underset{8}{ClCH_2\overset{O}{\overset{\|}{C}}N[CH{=}C(CH_3)_2]_2}$$

for the preparation of N,N-dialkenylamides. Reaction of isocyanate with 7 does not give dialkenylurea, but rather reaction occurs at the α carbon to produce 9a.

$3,4\text{-}(Cl)_2C_6H_3NCO + 7 \longrightarrow$

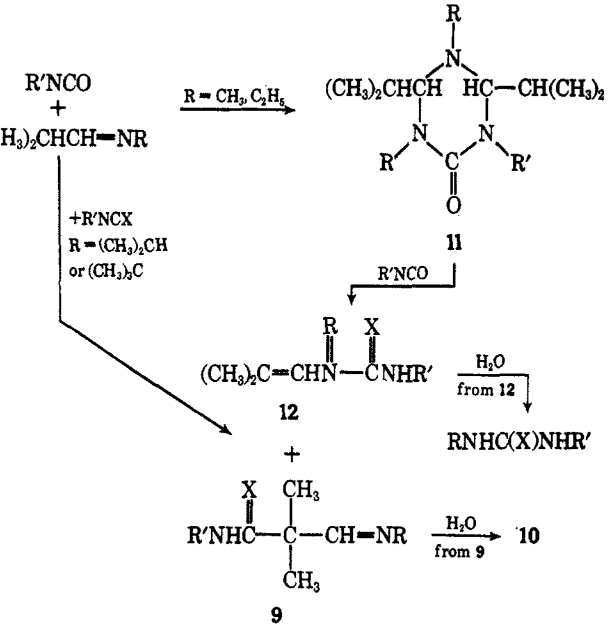


$$\underset{9a}{3,4\text{-}(Cl)_2C_6H_3NH\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-CH{=}NCH{=}C(CH_3)_2} \xrightarrow{H_2O} \underset{10}{3,4\text{-}(Cl)_2C_6H_3NH\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-CHO}$$

The amidic proton is seemingly hydrogen bonded with the imino nitrogen as evidenced by the unusually low absorption of this proton in the nmr, δ 10.3–10.6 (see NH, 9a, 9b).

N-Isobutylidene-N-methylamine reacts with isocyanates at room temperature to form triazinones (11), in analogous fashion to that found for certain imines possessing no α hydrogen.[4a,5] However, further reaction of 11 with isocyanate gives alkenylureas (12), possibly through electrophilic attack of isocyanate on the basic ring nitrogen, followed by ring opening *via* α-hydrogen elimination. N-Ethyl-N-isobutylidenamine behaves similarly, although anilide (9) is found to some extent [determined by nmr measurement of the ratio $(CH_3)_2C{=}C$ (from 12) to $-C(CH_3)_2-$ (from 9)]. N-Isopropylisobutylidenamine with greater bulk than the N-methyl or -ethyl homologs gives, with isocyanates on heating, a mixture of alkenylurea (12) and anilide (9) in a ratio of approximately 3:2. No apparent triazinone formation was observed. Curiously, 3,4-dichlorophenyl isothiocyanate on heating with N-isopropylisobutylidenamine gave only 12 and no 9. Finally, N-*t*-butylisobutylidenamine gave only 9 with isocyanate (Scheme III).

SCHEME III



Experimental Section

All melting points were taken on a Fisher-Johns block. All microanalytical work was performed by the Galbraith Laboratories, Knoxville, Tenn. Ir spectra were determined on a Beckman IR-Va and nmr spectra on a Varian Model A-60 spectrometer with chemical shifts reported in parts per million from tetramethylsilane as an internal standard.

Imines Derived from Cyclohexanone and Isobutyraldehyde.—The preparation of these materials have been previously described.[2a,b,11]

Materials 2a,b.—The preparation of these materials from the respective N-alkylcyclohexylidenamine[3a] and acid chloride can be illustrated by the preparation of 2a.

N-(1-Cyclohexen-1-yl)-2-(2,4-dichlorophenoxy)-N-methylacetamide (2a).—2,4-Dichlorophenoxyacetyl chloride (35.0 g, 0.146 mol) was placed in 200 ml of benzene, cooled to 0–5°, and N-methylcyclohexylidenamine (16.7 g, 0.15 mol) contained in 100 ml of benzene was added dropwise, with cooling. After addition the mixture was stirred for 15 min; then triethylamine (15 g, 0.15 mol) was added dropwise at 0–5°. After addition, the reaction mixture was refluxed for 1 hr. The reaction mixture was filtered, the salt cake was washed with benzene, and the combined filtrate and washings were washed twice with *ca.* 200 ml of water. After drying over anhydrous magnesium sulfate and subsequent removal of solvent under vacuum, the residue was recrystallized twice (charcoal) from hexane.

1-(1-Cyclohexen-1-yl)-1,3-dimethylurea (3a).—N-Methylcyclohexylidenamine (15.7 g, 0.14 mol) was dissolved in 200 ml of toluene, and to this solution methyl isocyanate (8.4 g,

---

[10] Thermal dissociation has also been observed in certain enureas derived from 2-phenylpyrroline by S. J. Love and J. A. Moore, *J. Org. Chem.*, **33**, 2361 (1968).

[11] R. H. Hasek, E. U. Elam, and J. C. Martin, *ibid.*, **26**, 1822 (1961).

0.14 mol) was added at room temperature. The reaction was exothermic, with the temperature rising to 35°. After standing for 2 hr at ambient temperature, solvent was removed and the oily residue distilled at 120–130° (1 mm) to give 7 g of oil, which later solidified. This material was recrystallized from cold hexane. A second preparation afforded a 95% yield of oil, which solidified on seeding.

1-(Cyclohexen-1-yl)-3-(3,4-dichlorophenyl)-1-methylurea (3b).—N-Methylcyclohexylidenamine and 3,4-dichlorophenyl isocyanate (0.1 mol each) reacted exothermally in toluene at room temperature to give, upon removal of solvent, 22 g of light yellow oil which did not crystallize.

1-(1-Cyclohexen-1-yl)-3-(2-nitrophenyl-1)methylurea (3c).—In similar manner to the preparation of **3a** and **3b**, 2-nitrophenyl isocyanate with N-methylcyclohexylidenamine gave yellow crystals from ethanol.

Materials 5a–c.—The reactions of isothiocyanates with N-alkylcyclohexylidenamines, carried out in toluene or benzene at room temperature, were mildly exothermic. Several hours were usually required for complete disappearance of isothiocyanate as monitored by ir. Upon removal of solvent, the residue was purified by suitable recrystallization. However, care was taken with products arising from aryl isothiocyanates not to expose them to heat; recrystallization from cold (−10°) concentrated toluene or ether solution was found necessary to prevent rearrangement. The preparation of **5a** and **5b** are representative of the procedures used to make these materials.

1-(1-Cyclohexen-1-yl)-3-ethyl-1-methyl-2-thiourea (5a).—N-Methylcyclohexylidenamine (11.1 g, 0.1 mol) and ethyl isothiocyanate (8.7 g, 0.1 mol) reacted at room temperature to give, after removal of solvent, 17 g of an oil which later crystallized, mp 43–44°. On distillation of some of the oil, fractions were collected at 45–55° (10 mm) which was shown by ir to contain isothiocyanate and imine. Upon standing, **5a** was again formed from the distillate.

1-(1-Cyclohexen-1-yl)-3-(3,4-dichlorophenyl)-1-methyl-2-thiourea (5b).—N-Methylcyclohexylidenamine (10.3 g, 0.094 mol) was dissolved in 100 ml of toluene and at room temperature 3,4-dichlorophenyl isothiocyanate (19.1 g, 0.094 mol) was added dropwise. After standing several hours crystals formed, mp 107–108°. By partial evaporation of the toluene in the cold (−10°), 24.5 g of crystals, mp 107°, was obtained. **5b**, upon melting at 107°, resolidified and melted again at 135–140°.

Materials 6a,b.—These materials could be prepared directly from the appropriate aryl isothiocyanate and N-alkyl-N-cyclohexylidenamine by reacting equimolar amounts of these reagents in refluxing toluene or alcohol for several hours, followed by removal of solvent and recrystallization of the solid residue from hot alcohol. A small amount of 1-aryl-3-alkyl-2-thiourea derived from the respective aryl isothiocyanate was found as by-product. Alternatively, **5** (R′ = aryl) was dissolved in anhydrous ethanol, heated for several minutes at reflux, and **6** collected as crystals upon cooling.

3′,4′-Dichlorothio-2-*p*-toluidino-1-cyclohexene-1-carboxanilide (6c).—To 12 g of 3,4-dichlorophenyl isothiocyanate dissolved in tetrachloroethylene was added dropwise an equimolar amount of N-cyclohexylidene-*p*-toluidine. No appreciable exotherm was noticed, and, to cause the isothiocyanate to react, the material was heated to 70° for 3 hr. Crystals formed, and upon cooling 15.7 g of solid was isolated by filtration. Recrystallization from ethanol afforded product.

3′,4′-Dichloro-2-(*p*-chloroanilino)-1-cyclohexene-1-carboxanilide (4).—To 10.3 g of N-cyclohexylidene-*p*-chloroaniline contained in toluene was added an equimolar amount of 3,4-dichlorophenyl isocyanate dissolved in toluene. To cause disappearance of isocyanate (as monitored by ir), the material was refluxed for several hours, and after removal of toluene the solid remaining recrystallized from ethanol.

2-Chloro-N,N-bis(2-methylpropenyl)acetamide (8).—The procedure given above describing the preparation of **2a** was used. Upon distillation the product was collected at 97–108° (1 mm). The oil was recrystallized from hexane three times to give 47.5% yield of crystals: nmr (CCl_4), δ 1.57 (s, 6, $=CCH_3$), 1.74 (d, 6, *J* = 1 Hz, CCH_3), 3.95 (s, 2, $ClCH_2$), and 5.95 (m, 2, $=CH$).

[2-(3,4-Dichlorocarbaniloyl)-2-methylpropylidene]-(2-methylpropenyl)amine (9a).—3,4-Dichlorophenyl isocyanate (18.8 g, 0.1 mol) and 0.1 mol of N-isobutylidene-N-(2-methyl-1-propenyl)amine (**7**) were both dissolved in 100 ml of toluene; 0.25 ml of triethylamine was added. The mixture was refluxed for 8 hr, after which no isocyanate remained in the mixture. Upon removal of solvent, the residue recrystallized from hexane twice (charcoal), afforded white crystals: ir (CCl_4) 6.0 μ (C=O); nmr (CCl_4), δ 1.45 [s, 6, $C(CH_3)_2$], 1.83, 2.06 [2 s, 6, $=C(CH_3)_2$], 7.6 (s, 1, CH=N), and 10.3 [s (broad), 1, C(O)NH].

1-(*p*-Chlorophenyl)tetrahydro-4,6-diisopropyl-3,5-methyl-*s*-triazin-2(1H)-one (11a).—This material was prepared by reacting in benzene at room temperature a 2:1 mole ratio of N-isobutylidene-N-methylamine[12] with *p*-chlorophenyl isocyanate. Vacuum removal of solvent gave an oil: ir (CCl_4) 6.0 μ (C=O); nmr (CCl_4), δ 0.56–1.11 [4 d, 12, *J* = 7 Hz, $CH(CH_3)_2$], 2.32 (s, 3, C_2NCH_3), 2.90 (s, 3, $CNCH_3$ C=O), 3.70 (d, 1, *J* = 7 Hz, CHCHN), and 4.18 (d, 1, *J* = 7 Hz, CH–CHN).

1-(3,4-Dichlorophenyl)tetrahydro-4,6-diisopropyl-3,5-diethyl-*s* triazin-2(1H)one (11b).—This material was prepared by adding 0.2 mol of N-isobutylidene-N-ethylamine in ether to 0.1 mol of 3,4-dichlorophenyl isocyanate, dissolved in ether. After standing at room temperature several hours, the material was vacuum treated at room temperature to give 36.1 g of viscous oil which solidified on standing. Recrystallization was effected at room temperature from ether–pentane to give **11b**: ir (CCl_4) 6.0 μ (C=O); nmr (CCl_4), δ 3.7 (d, 1, *J* = 7 Hz, CHCHN), 4.3 (d, 1, *J* = 7 Hz, CH–CHN), 1.7–3.5 [m, 4, CH_3CH_2N and m, 2 $CH(CH_3)_2$], and 0.5–1.3 [d and t, 18, *J* = 7 Hz, $(CH_3)_2CH$ and CH_3CH_2].

3-(*p*-Chlorophenyl)-1-methyl-1-(2-methylpropenyl)urea (12a).—N-Isobutylidene-N-methylamine (10.3 g, 0.12 mol) was heated for *ca.* 1 hr in refluxing chlorobenzene with an equimolar amount of *p*-chlorophenyl isocyanate until no isocyanate remained in the mixture (as measured by ir). The material isolated after evaporation of solvent was an amber oil which was further purified by recrystallization from cold hexane to give pure **12a**: ir (CCl_4) 6.0 μ (C=O).

3-(3,4-Dichlorophenyl)-1-isopropyl-1-(2-methylpropenyl)urea (12b).—N-Isobutylidene-N-isopropylamine and 3,4-dichlorophenyl isocyanate (0.1 mol each) were mixed together and refluxed in 100 ml of tetrachloroethylene for 1 hr. After evaporation of the solvent, residual oil remaining was shown by nmr spectroscopy to have, in addition to spectral assignments for **12b** (see Table I), the following additional peaks for groups in compound [2-(carbaniloyl)-2-methylpropylidene]isopropylamine (**9**): nmr (CCl_4), δ 1.30 [d, 6, *J* = 7 Hz, $CH(CH_3)_2$] and 1.43 [s, 6, $C(CH_3)_2$]. The crude oil contained a ratio of **12b**:**9** as determined by nmr of *ca.* 3:2. Hydrolysis of a portion of the crude oil with hot 18% HCl gave a solid which upon recrystallization from methylcyclohexane gave **10** (identified by mixture melting point and ir). The solid remaining undissolved in hot methylcyclohexane was shown after recrystallization from aqueous ethanol to be 3-isopropyl-1-(3,4-dichlorophenyl)urea, mp 205°, as determined by mixture melting point and identical ir with those of an authentic sample. Elution of the bulk of the crude oil through a silicic acid column with carbon tetrachloride followed by recrystallization from cold hexane gave pure **12b**: ir (CCl_4) 6.0 μ (C=O).

3-(3,4-Dichlorophenyl-1-isopropyl-1-(2-methylpropenyl)-2-thiourea (12c).—This material was obtained in analogous fashion to that for **12a**. There was no gross contamination of the crude as measured by nmr, and the crude oil solidified and was easily recrystallized from ethanol.

[2-(3,4-Dichlorocarbaniloyl)-2-methylpropylidene]-*t*-butylamine (9b).—3,4-Dichlorophenyl isocyanate (37.6 g, 0.2 mol), dissolved in *ca.* 50 ml of chlorobenzene was added to N-(2-methylpropylidene)-N-*t*-butylamine (25.4 g, 0.2 mol) contained in 100 ml of chlorobenzene. Reflux for *ca.* 30 min was necessary to cause complete reaction of the isocyanate. Upon removal of solvent, the residue (essentially all **9b** as indicated by nmr spectra) solidified and was recrystallized from cold pentane to give 48.9-g yield of white crystals **9b**: ir (CCl_4) 6.0 μ (C=O), CH=N).

Hydrolysis of Initial Reaction Products. Hydrolysis of 2-(2,4-Dichlorophenoxy)-N-(1-cyclohexen-1-yl)N-methylacetamide (2a).—**2a** (*ca.* 1.0 g) was placed in 5 ml of concentrated hydrochloric acid, heated momentarily. Solid began to dissolve, whereupon suddenly more solid precipitated. The mixture was diluted with once its volume of water and filtered and the solid washed with more water and dried, mp 112–114°. The material proved to be 2-(2,4-dichlorophenoxy)-N-methylacetamide as determined by ir and mixture melting point with an authentic sample.

---

[12] R. Tiollais, *Bull. Soc. Chim. Fr.*, 708 (1947).

Hydrolysis of 1-(1-Cyclohexen-1-yl)-3-(3,4-dichlorophenyl)-1-methylurea (3b).—**3b** (5 g) was placed in 20 ml of water and 20 ml of 10% hydrochloric acid added. The material was permitted to stand overnight with occasional stirring. The solid which formed was filtered off, washed with water, and recrystallized from benzene, mp 157–159°. The material proved to be 1-(3,4-dichlorophenyl)-3-methylurea as determined by ir and mixture melting point with an authentic sample.

Hydrolysis of 3′,4′-Dichloro-2-(*p*-chloroanilino)-1-cyclohexene-1-carboxanilide (4).—Approximately 2 g of **4** was heated on a steam bath with 20 ml of 18% hydrochloric acid for 2–3 hr, cooled, filtered, washed with water, and recrystallized from aqueous ethanol, followed by a second recrystallization from methylcyclohexane, mp 138–140°. The structure of 3′,4′-dichloro-2-oxocyclohexanecarboxanilide was assigned to this material from consideration of the following data: ir (CCl$_4$) 3.0 (NH), 5.9 (ketone C=O), and 6.0 μ (amide C=O).

Anal. Calcd for $C_{13}H_{13}Cl_2NO_2$: Cl, 24.8; N, 4.9. Found: Cl, 24.6; N, 4.9.

Hydrolysis of 1-(Cyclohexen-1-yl)-3-(3,4-dichlorophenyl)-1-methyl-2-thiourea (5b).—**5b** (*ca.* 2 g) was placed in 30 ml of 10% hydrochloric acid, and the mixture was allowed to stand overnight with occasional stirring. Upon filtering, the resulting solid was recrystallized from chloroform, mp 150–152°. The material proved to be 1-(3,4-dichlorophenyl)-3-methyl-2-thiourea as determined by ir and mixture melting point comparison with an authentic sample.

Hydrolysis of 3′,4′-Dichloro-2-(methylamino)thio-1-cyclohexene-1-carboxanilide (6a).—**6a** (*ca.* 1 g) was placed in 20 ml of 18% hydrochloric acid and heated gently on a steam bath for 10–15 min. The aqueous portion was decanted, and the residual tacky solid recrystallized from aqueous ethanol to give crystals, mp 112–114°. The structure of 3′,4′-dichloro-2-oxothiocyclohexanecarboxanilide was assigned this material from consideration of the following data: ir (CCl$_4$) 3.0 (NH), and 5.95 μ (C=O); nmr showed nine aliphatic hydrogens, one NH, and three aromatic hydrogens.

Anal. Calcd for $C_{13}H_{13}Cl_2NOS$: Cl, 23.60; N, 4.63; S, 10.6. Found: Cl, 23.97; N, 4.70; S, 10.6.

Hydrolysis of [2-(3,4-Dichlorocarbaniloyl)-2-methylpropylidene](2-methylpropenyl)amine (9a).—**9a** (*ca.* 5 g) was placed in 20 ml of 18% hydrochloric acid and heated on a steam bath for 15 min. The acid was decanted, and the residue heated further with water on the steam bath. The mixture was decanted again and the residual solid air dried, then recrystallized from methylcyclohexane, mp 102–104°. The structure of 3′,4′-dichloro-2,2-dimethylmalonaldehydanilide (**10**) was assigned to this material from consideration of the following data: ir (CCl$_4$) 3.0 (N-H), 5.85 (aldehyde C=O), and 5.96 μ (amide C=O); nmr spectra were consistent, showing six identical methyl protons, one aldehydic proton, one NH, and three aromatic protons.

Anal. Calcd for $C_{11}H_{11}Cl_2NO_2$: Cl, 27.4; N, 5.4. Found: Cl, 27.7; N, 5.5.

Hydrolysis of 2-(*p*-Chlorophenyl)-1-methyl-1-(2-methylpropenyl)urea (12a).—**12a** (*ca.* 1 g) was placed in 20 ml of 20% hydrochloric acid solution, and the mixture was refluxed for 15 min. The cooled solution was decanted and diluted with water. The resulting precipitate was separated and recrystallized from aqueous methanol to give 0.5 g of *p*-chlorophenyl-3-methylurea as identified by ir spectra and mixture melting point.

Registry No.—**2a,** 16241-20-6; **2b,** 16241-21-7; **3a,** 16240-17-8; **3b,** 16240-18-9; **3c,** 16240-19-0; **4,** 16286-17-2; **5a,** 16240-20-3; **5b,** 16240-21-4; **5c,** 16240-22-5; **6a,** 16240-23-6; **6b,** 16240-24-7; **6c,** 16240-25-8; **8,** 16240-26-9; **9a,** 16240-27-0; **9b,** 16240-28-1; **10,** 16240-29-2; **11a,** 16240-30-5; **11b,** 16240-31-6; **12a,** 2572-41-0; **12b,** 16240-33-8; **12c,** 16240-34-9; 3′,4′-dichloro-2-oxocyclohexanecarboxanilide, 16240-35-0; 3′,4′-dichloro-2-oxothiocyclohexanecarboxanilide, 16240-36-1; cyclohexanone, 108-94-1; isobutyraldehyde, 78-84-2.

The Reaction of 2-Phenyl-1-pyrroline with Phenyl Isocyanate

Steven J. Love[1] and James A. Moore

Department of Chemistry, University of Delaware, Newark, Delaware 19711

Received October 16, 1967

The reaction of phenyl isocyanate with 2-phenyl-1-pyrroline at 25° leads to 2-phenyl-1-phenylcarbamoyl-2-pyrroline (**2**). At higher temperatures the 3-substituted 2-pyrroline **4** is formed, and loss of isocyanate from **4** gives the 1-pyrroline-3-carboxanilide **5**. The 1-carbamoylpyrroline **2** undergoes rapid thermal elimination of phenyl isocyanate at 40°.

Although 2 + 2 cycloaddition reactions of isocyanates and olefins or of ketenes and azomethines are well-established preparative methods for azetidinones,[2] the cycloaddition of isocyanates and azomethines to form uretidinones have been reported on only a few occasions,[3,4] and the structural evidence for these products was extremely limited by contemporary standards. With a view to the possibility of obtaining a 1,6-diazabicyclo[3.2.0]heptane derivative by this cycloaddition process, we have studied the reaction of phenyl isocyanate with 2-phenyl-1-pyrroline (**1**). In previous work, a "well-defined" product was reported from the reaction of 2,5-dimethyl-1-pyrroline with phenyl isocyanate,[5] but the composition and structure of the compound were not specified.

The reaction of equimolar amounts of 2-phenyl-1-pyrroline and phenyl isocyanate at room temperature in hydrocarbon solution gave an unstable 1:1 product in 75% yield. The 1-phenylcarbamoyl-Δ^2-pyrroline structure **2** was indicated by the shift in the ultraviolet maximum from 243 mμ in **1** to 255 mμ **2**, a triplet nmr peak due to H-3 at δ 5.31, and acid hydrolysis to the ureido ketone **3**. Hydrolysis of **2** resulted in a significant amount of the original pyrroline as well.

At 110°, equimolar condensation led to a different 1:1 product and a compound containing one pyrroline and two isocyanate units, together with unreacted pyrroline and a trace of the hydrolysis product, **3**. The 1:1 and 1:2 products were obtained in a combined yield of about 40% (based on phenyl isocyanate), with the latter predominating in a ratio of about 3:1.

The minor (1:1) product was a base with ultraviolet absorption very similar to that of the pyrroline **1**; the pK_a' was 1.8 units lower than that of **2**. Schotten–Baumann benzoylation of the compound gave a product whose properties were consistent with the benzamido ketone **6**. These data suggest the Δ^1-pyrroline-3-carboxanilide structure **5** for the condensation product. Dickinson and Lang quite recently reported the

---

[1] National Science Foundation Predoctoral Fellow, 1965–1967.

[2] H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press Inc., New York, N. Y., 1967.

[3] A. Seiner and F. G. Shepheard, *J. Chem. Soc.*, 494 (1909).

[4] W. J. Hale and N. A. Lange, *J. Amer. Chem. Soc.*, **41**, 379 (1919).

[5] G. G. Evans, *ibid.*, **73**, 5230 (1951).