Reaction of Certain Isocyanates with Azomethines.
Evidence for a New Heterocyclic Adduct

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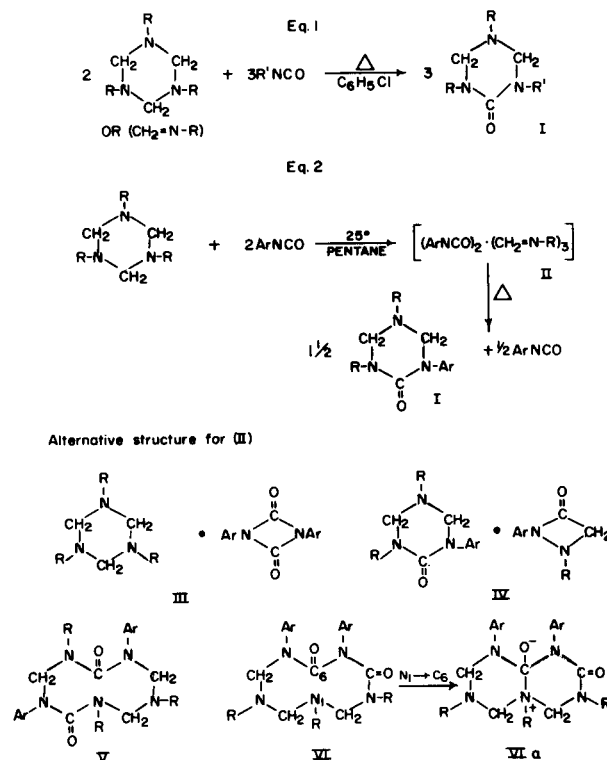
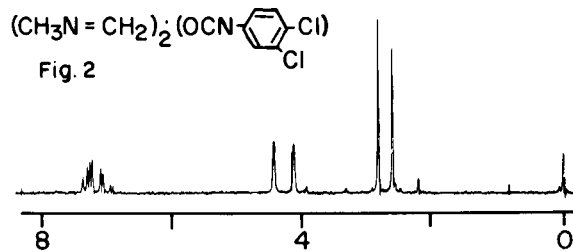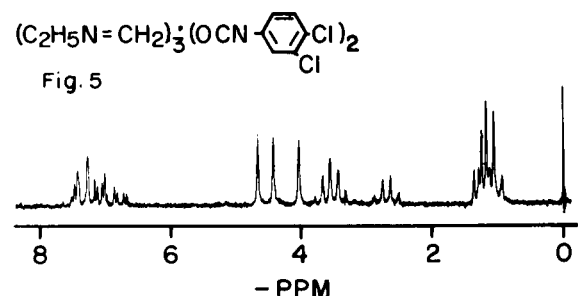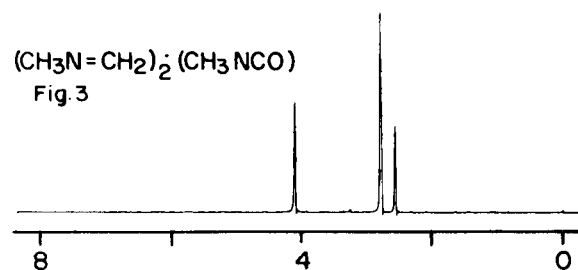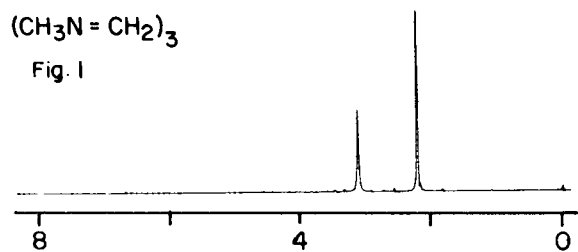The preparation of triazinone (I) from certain isocyanates and *N*-alkyl azomethines was found to proceed easily without catalyst, particularly in refluxing chlorobenzene. The physical and chemical properties, including n.m.r. spectra of the oily triazinones, are contrasted with the newly discovered solid adducts arising from low temperature reaction of azomethine and chlorophenyl isocyanates. From stoichiometry of the reaction, elemental analysis, molecular weight of the products, and spectral analyses, the new materials (II) were found to incorporate two isocyanate and three azomethine moieties in their molecular make-up. The relative merits are considered for assigning II a molecular structure arising from a complex between a four and six-membered ring (III, IV) versus a ten-membered ring system (V, VI, VIa).

Certain reversible reactions of isocyanates with various materials containing C=N unsaturation to form diverse heterocyclic systems have been investigated and reported. Thus isocyanates add to their own unsaturated systems to form, under certain conditions, the dimeric uretidinediones (1,2), and under other conditions the trimeric 1,3,5-triazinetriones. The uretidinedione is thermally unstable, and reverts to the isocyanate on heating. Carbodiimides have been found to give crystalline compounds with isocyanates (3), their structures formulated as 2-imino-4-oxo-1,3-diazetidines (4). These materials likewise are thermally unstable and regenerate carbodiimide and isocyanate on even mild heating (3). The reaction of isocyanates with imines yield a variety of compounds (1) including cycloaddition products, depending upon reaction conditions. These latter heterocyclic materials have usually been found to be six-membered triazinones (5) or triazinediones (6).

We wish to report here our experience with the reaction of trimeric *N*-methyl and *N*-ethyl azomethine (the formaldehyde imines of methyl and ethyl amine) with certain aryl isocyanates. Clemens and Emmons (5) reported that azomethines (or their trimeric hexahydrotriazines) react with isocyanates in ratios of 2:1 in the presence of zinc chloride to give stable six-membered ring triazinones. We had occasion to prepare some of these materials by their method, where the aryl group was substituted with *meta* and/or *para* chlorine. The latter triazinones had previously been prepared as viscous oils by reactions of 3-alkyl-1-aryl

urea with formaldehyde and alkyl amine (7). We found, utilizing the method of Clemens and Emmons, that triazinone formation occurred easily when chlorophenyl

Eq. 1

Eq. 2

Alternative structure for (II)

$(CH_3N = CH_2)_3$

Fig. I

$(CH_3N = CH_2)_2^-(OCN-\langle\bigcirc\rangle-Cl)$
$\qquad\qquad\qquad\qquad\qquad Cl$

Fig. 2

$(CH_3N = CH_2)_2^-(CH_3NCO)$

Fig. 3

$(CH_3N= CH_2)_3^-(OCN-\langle\bigcirc\rangle-Cl)_2$
$\qquad\qquad\qquad\qquad\qquad Cl$

Fig. 4

$(C_2H_5N= CH_2)_3^-(OCN-\langle\bigcirc\rangle-Cl)_2$
$\qquad\qquad\qquad\qquad\qquad Cl$

Fig. 5

$(C_2H_5N = CH_2)_2^-(OCN-\langle\bigcirc\rangle-Cl)$
$\qquad\qquad\qquad\qquad\qquad Cl$

Fig. 6

-PPM

- PPM
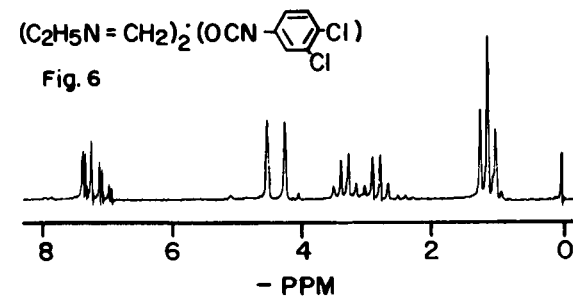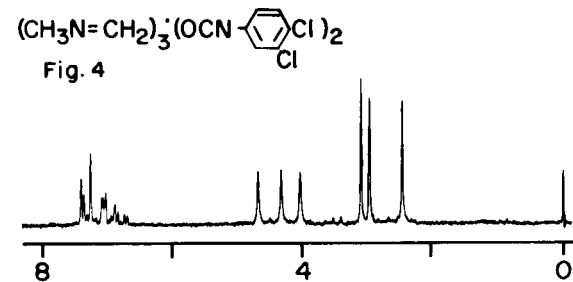
isocyanates and azomethine were heated in refluxing chlorobenzene; no catalyst was necessary (Eq. 1).

N.m.r. was particularly reliable in confirming structure. The spectrum (Fig. 1) of the trimeric N-methyl azomethine (one singlet each for methyl and methylene in a ratio of 3:2) was quite different from the spectrum (Fig. 2) after heating the former with 3,4-dichlorophenyl isocyanate (two N-CH₃ and two CH₂ groups). The spectrum (Fig. 3) of the more symmetrical triazinone from N-methyl azomethine and methyl isocyanate gave the expected two N-CH₃ singlets (2:1) and single methylene absorption. When isocyanate was allowed to react with trimeric N-ethyl azomethine, the n.m.r. spectrum (Fig. 6) also clearly indicated the different methylene groups.

We noticed an exotherm on mixing N-methyl azomethine and 3,4-dichlorophenyl isocyanate (azomethine: isocyanate=2:1) at room temperature, and the infrared spectrum prior to chlorobenzene reflux indicated that all of the isocyanate had reacted (disappearance of NCO band at 4.5 μ), although the n.m.r. spectrum indicated no triazinone and a small amount of unreacted N-methyl azomethine still present. Conversely, when a 1:1 molar ratio of the two reactants was mixed at room temperature, the infrared spectrum revealed some unreacted isocyanate,

while the n.m.r. showed no evidence of starting azomethine. The reaction, preferably carried out in pentane, with a 3:2 ratio of azomethine to isocyanate, gave insoluble solid on standing at room temperature and a minimum of unreacted isocyanate and azomethine. The solid material was soluble in benzene or chlorobenzene, but insoluble in ether, while thermal treatment in the former solvents quickly converted the material to triazinone and isocyanate (Eq. 2). The vapor phase osomometric method (at 38°) gave values consistent with molecular weights of two isocyanates combined with three monomeric azomethine units (II). The infrared spectrum of the solid (II) showed no isocyanate band, but did evidence a strong carbonyl band between 6-6.1 μ. The n.m.r. spectrum (Fig. 4) displayed six singlets (2:2:2:3:3:3) for the three methylene and three N-CH₃ groups, while the aromatic hydrogens integrate for six protons, indicating two aromatic rings present. From stoichiometry of the reaction, elemental analysis, molecular weights of the product, and spectral analyses, the solid incorporates two 3,4-dichlorophenyl isocyanates and three N-methyl azomethine moieties in its molecular make-up (II). Solid adducts derived from other chlorophenyl isocyanates or N-alkyl azomethine are also consistent (see Fig. 5 and Table for examples).

TABLE

Cyclic Adducts from Isocyanates and Azomethines

Structure R' or Ar	R	Type	m.p. °C	Formula	Calcd.	Found	IRμ	Spectra (a) N.M.R. NCH₂N (c)	NCH₃ (d)	NCH₂CH₃ (e)	NCH₂CH₃ (f)
CH₃	CH₃	I	49-51	$C_6H_{13}N_3O$	N 29.35 MW 143	29.25 141	6.2	4.1 (g,h)	2.55 (g,i) 2.78	—	—
3,4-(Cl)₂C₆H₃	CH₃	I	viscous oil	$C_{11}H_{13}Cl_2N_3O$	C 48.19 H 4.78 Cl 25.87 N 15.33	48.31 4.82 26.05 15.33	6.05	4.12 (g) 4.44	2.62 (g) 2.83	—	—
3,4-(Cl)₂C₆H₃	CH₃	II	101-112 (b)	$C_{20}H_{21}Cl_4N_5O_2$	MW 274 C 47.54 H 4.19 Cl 28.07 N 13.86 MW 505	271 (1) 47.50 4.37 28.02 13.92 510 (j)	6.0	4.01 4.30 4.67	2.42 2.95 3.08	—	—
3,4-(Cl)₂C₆H₃	CH₃CH₂	I	viscous oil	$C_{13}H_{17}Cl_2N_3O$	C 51.66 H 5.67 Cl 23.46 N 13.90 MW 302	51.66 5.55 23.50 13.84 308 (1)	6.08	4.28 4.54	—	2.88 3.36	1.15 1.15 (k)
3,4-(Cl)₂C₆H₃	CH₃CH₂	II	109-112.5 (b)	$C_{23}H_{27}Cl_4N_5O_2$	Cl 25.91 N 12.80 MW 547	25.94 12.57 538 (1)	6.0- 6.1	4.02 4.41 4.67	—	2.70 3.50 3.62	1.08 1.19 1.24
3(Cl)C₆H₄	CH₃	I	viscous oil	$C_{11}H_{14}ClN_3O$	Cl 14.79 N 17.53 MW 240	14.94 17.42 240	6.1	4.13 4.45	2.60 2.85	—	—
3(Cl)C₆H₄	CH₃	II	97-104 (b)	$C_{20}H_{23}Cl_2N_5O_2$	Cl 16.25 N 16.05 MW 436	16.20 15.84 436 (1)	6.0- 6.05	4.02 4.32 4.69	2.43 2.96 3.09	—	—

(a) Chloroform (deuteriochloroform) solvent unless otherwise noted. (b) With decomposition. (c) Singlet, 2H ea. (d) Singlet, 3H ea. (e) Quartet, 2H ea. (f) Triplet, 3H ea. (g) Carbon tetrachloride solvent. (h) Singlet, 4H. (i) Two singlets, 3H:6H respectively. (j) Osmometric determination in benzene. (k) Two triplets of equal intensity apparent in benzene. (l) Osmometric determination in chloroform.

In the absence of definite structure proof the data allows several alternatives to be considered for the molecular structure of II. Molecular complexes, although rare, have been reported in the chemistry of isocyanate adducts (8), and thus can be considered here. A complex between a six-membered trimeric azomethine and four-membered uretidinedione (III) would seem unlikely. III would be expected to show symmetry and hence equivalence of the N-alkyl and methylene units. Uretidinediones consistently display a carbonyl absorption at considerably shorter wavelengths (ca. 5.7 μ) than evidenced by II. Furthermore, when the high-melting uretidinedione from 3,4-dichlorophenyl isocyanate was separately prepared, it reacted only slowly with N-methyl azomethine; nor was formation of II from isocyanate and azomethine hastened by employing the specific catalyst dibutylphenylphosphine for uretidinedione formation (2).

Uretidinones, the four-membered ring system in the complex IV are rare. The only examples from azomethine are its reported formation by Senier (9) from phenyl or naphthyl isocyanate and N-phenyl azomethine. Compound IV does fulfill the requirement for having dissimilar N-alkyl and methylene groups.

If crystalline II is not a complex, but is covalently bonded, the non-equivalence of the methylene and N-alkyl groups, and the ease with which the solid material is converted to triazinone (I) and isocyanate suggest that the structure consists of an alternating carbon-nitrogen ten-membered heterocyclic adduct. There are two possibilities (V and VI) if it is assumed that no deep-seated structural changes have taken place; a reasonable assumption because the products obtained on heating are themselves identical or little changed in structural similarity to reactant azomethine and isocyanate.

However, it is hard to visualize ether insoluble, relatively high melting II (see Table) having structures V or VI, while the more stable, and perhaps more symmetrical six-membered triazinones (I) are ether soluble and oils. Therefore it is tempting to assign II structural symmetry and ionic charge, two properties usually associated with high melting point and ether insolubility. This can be done by formulating a coordinate-covalent bond resulting in charged, fused six-membered rings. The latter transannular phenomenon has been demonstrated to occur in eight and ten-membered amino- and thioketones (10). One such alternative, VIa, would result from attack of amino nitrogen on a carbonyl carbon.

Mechanistically, the formation of II can be visualized as arising from kinetic control. On heating, regardless of its molecular structure, certain of the alternating nitrogen-carbon atoms dissociate and reorganize to the thermodynamically stable I and isocyanate. The facile cleavage of such bonds in certain nitrogen heterocyclics is not

uncommon; the thermal dissociation of trimeric azomethine to monomer or uretidinedione to isocyanate are but two examples.

The scope of the low temperature reaction is quite narrow. We found only phenyl isocyanates substituted with deactivating groups would give solid products at room temperature. Of these, only halophenyl isocyanates substituted in either the *meta* or *para* position or both gave interpretable spectra. We did obtain solid products from *p*-nitrophenyl isocyanate and 2,4,5-trichlorophenyl isocyanate, but the n.m.r. spectra contained multiple absorptions, perhaps indicating a mixture. The narrow scope of the low temperature reaction is reminiscent of that found for the reaction of isothiocyanates with carbodiimides. The latter gives 2-imino-4-thiono-1,3-diazetidiones in quantitative yield only with isothiocyanates containing strong electron-withdrawing substituents (11).

EXPERIMENTAL

Melting points (uncorrected) were determined on a Fisher-Johns apparatus. Infrared spectra were determined on a Beckmann IR Va and n.m.r. spectra on a Varian Model A-60 spectrometer with chemical shifts reported in -ppm from tetramethyl silane as an internal standard. All microanalytical work reported here was performed by the Galbraith Laboratories, Knoxville, Tennessee.

Starting Materials.

1,3,5-trimethylhexahydrotriazine (N-methyl azomethine) and 1,3,5-triethylhexahydrotriazine (N-ethyl azomethine) were prepared from formaldehyde and the respective amines (12).

Triazinones.

The methods for the preparation of triazinones from azomethine and isocyanate are illustrated by the following two procedures:

Tetrahydro-1,3,5-trimethyl-*s*-triazin-2(1H)-one.

N-Methyl azomethine trimer (0.15 mole, 19.35 g.) in benzene was mixed with methyl isocyanate (0.225 mole, 12.8 g.). Successive infrared spectra of the mixture indicated only slow diminuation of isocyanate concentration; hence the mixture was heated at 50° for several hours, then allowed to stand at room temperature for three days, after which virtually all the isocyanate had reacted. The material on standing crystallized; the m.p. of this highly deliquescent material was taken in an oil bath after sealing the capillary in a drybox.

1-(3,4-Dichlorophenyl)tetrahydro-3,5-dimethyl-*s*-triazin-2(1H)-one.

To the trimer of N-methyl azomethine (0.0993 mole) was added 0.149 mole of 3,4-dichlorophenyl isocyanate. An exothermic reaction occurred, with disappearance of the isocyanate band (IR), but n.m.r. indicated that the desired triazinone had not been formed. The reaction mixture was then heated in refluxing chlorobenzene for approximately two hours; the solvent was removed under vacuum to give the product as a viscous amber oil. Although essentially pure triazinone at this stage, an analytical sample was obtained by flash distilling a small portion of the oil at 130-160° (0.2 mm).

Low Temperature Reaction Products II.

Several ratios of isocyanate:azomethine were used to help determine the stoichiometry of the low temperature reaction. The procedure given below for one of the products represents fairly optimum conditions, and may serve as the general method for preparing materials listed in the Table.

Trimeric N-ethyl azomethine (0.0367 mole, 6.27 g.), dissolved in approximately 50 ml. of dry pentane, was added to a clear filtered solution of 3,4-dichlorophenyl isocyanate (0.0734 mole, 13.8 g.) dissolved in 100 ml. of pentane contained in a 250 ml. erlenmeyer flask. The stoppered flask was allowed to stand several (2-4) days, the pentane solution was decanted, and the residue pulverized to a fine white powder (16.2 g.). The material was further triturated with 50 ml. of ether, then vacuum treated at room temperature to give 13.3 g. of dry white solid product.

The preparation was less effective when carried out in benzene or ether, as these latter solvents were difficult to completely remove at room temperature from the solid product.

Acknowledgment.

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