of cupric bromide and 60 g. (0.50 mole) of potassium bromide in 200 ml. of water and the mixture was allowed to stand at room temperature for 65 hr. The crystalline product was collected by filtration, washed with concd. potassium bromide solution, and recrystallized from methanol-water to give 37.1 g. (85%) of 2-bromo-5,5-dimethylcyclohexane-1,3-dione (VII), m.p. 177–178°. The melting point was not depressed by admixture with VII prepared by the procedure of Vorländer.[5]

Acknowledgment. Financial support of this work from the Faculty Research Fund of the University of Kentucky is gratefully acknowledged.

LEXINGTON, KY.

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(5) D. Vorländer and M. Kohlmann, *Ann.*, **322**, 239 (1902).

[CONTRIBUTION FROM THE ROHM AND HAAS CO.]

Reactions of *N*-Alkylazomethines and Enamines with Isocyanates and Isothiocyanates

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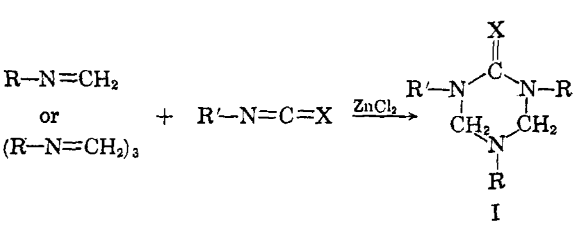
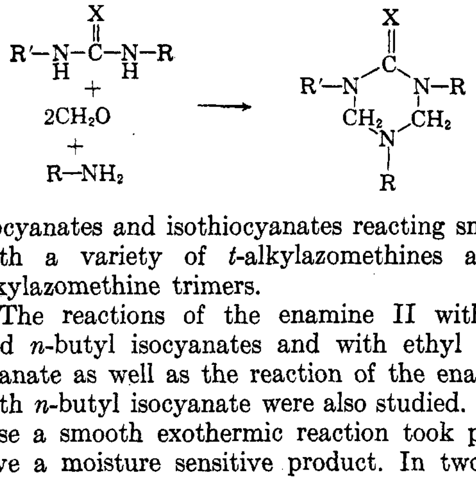
Isocyanates and isothiocyanates react with azomethines to yield triazones and thiotriazones and with enamines to produce substituted ureas.

The electrophilic character of isocyanates and isothiocyanates, as indicated by their ready reaction with a variety of electron rich species, is well known.[1] Enamines have been shown by Stork, *et al.*[2] to react by nucleophilic attack of their β-vinyl carbon atom upon some electrophilic substrate, the facile alkylation of the enamine II with methyl iodide being an excellent example of this situation. The nucleophilic nature of imines is also well known. These facts, coupled with our knowledge of the zinc chloride catalyzed reaction of ketene with *N*-*t*-alkylazomethines[3] have lead us to study the reactions of *N*-alkylazomethines and enamines with isocyanates and isothiocyanates.

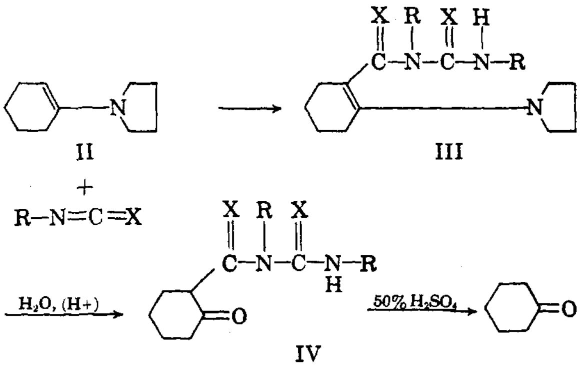
Isocyanates and isothiocyanates react smoothly with a variety of *N*-alkylazomethines to produce triazones or thiotriazones of the general structure, I. The physical properties and analytical data for the compounds are listed in Table I. The structure of two representatives of the series, If and Ii, was confirmed by independent synthesis from the corresponding urea or thiourea, formaldehyde, and the appropriate primary amine. The reaction is seen to be quite general with phenyl isocyanate (see Ig) and cyanic acid (see Ia) as well as alkyl isocyanates and isothiocyanates reacting smoothly with a variety of *t*-alkylazomethines and *N*-alkylazomethine trimers.

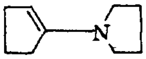


I



The reactions of the enamine II with ethyl and *n*-butyl isocyanates and with ethyl isothiocyanate as well as the reaction of the enamine V with *n*-butyl isocyanate were also studied. In each case a smooth exothermic reaction took place to give a moisture sensitive product. In two cases, (III, $R = -C_2H_5$, $X = O$; $R = -C_2H_5$, $X = S$), the products were solids and could be isolated and characterized. Analysis and neutral equivalent were in agreement with the proposed structures. All products of the type III were very readily hy-





V

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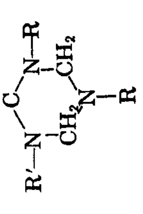
(1) R. G. Arnold, J. A. Nelson, and J. J. Verbanc, *Chem. Revs.*, **57**, 47 (1957).

(2) G. Stork, R. Terrell, and J. Szmuszkovitz, *J. Am. Chem. Soc.*, **76**, 2029 (1954).

(3) D. H. Clemens and W. D. Emmons, *J. Org. Chem.*, **26**, 949 (1961).

TABLE I. PROPERTIES OF THE TRIAZONES AND THIOTRIAZONES, I

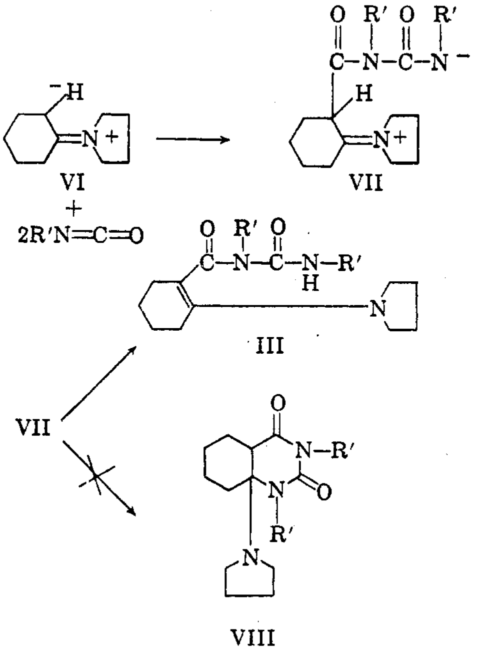


No.	R	R'	X	Yield, %	B.P. (mm.)	n_D^{25}	Formula	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
Ia	$—CH_3$	—H	O	47	113–116[a,b]		$C_5H_{11}N_3O$	46.49	8.59	32.53	46.49	8.73	32.25
Ib	$—C_2H_5$	$—C_2H_5$	O	49	107–110 (0.6)	1.4765	$C_9H_{19}N_3O$	58.35	10.34	22.68	57.98	10.30	22.60
Ic	$—CH_3$	—n-C_4H_9	O	43	111–113 (0.1)	1.4787	$C_9H_{19}N_3O$	58.35	10.34	22.68	58.78	10.69	22.39
Id	—t-C_4H_9	$—C_2H_5$	O	26	116–118 (0.25)	1.4749	$C_{13}H_{27}N_3O$	64.68	11.28	17.41	64.44	11.50	17.66
Ie	—t-C_4H_9	—n-C_4H_9	O	76	118–120 (0.25)	1.4741	$C_{15}H_{31}N_3O$	66.87	11.60	15.60	66.80	11.51	15.56
If	—n-C_4H_9	—n-C_4H_9	O	98	136–140 (0.3)	1.4691	$C_{15}H_{31}N_3O$	66.87	11.60	15.60	66.58	11.88	15.58
Ig	—n-C_4H_9	$—C_6H_5$	O	50	[c]	1.5340	$C_{17}H_{27}N_3O$	70.55	9.41	14.52	69.99	9.19	14.34
Ih	$—CH_3$	$—C_2H_5$	S	100	80–82[a,d]		$C_7H_{15}N_3S$	48.52	8.73	24.25	48.26	8.92	24.24[e]
Ii	$—C_2H_5$	$—C_2H_5$	S	86	57–59[a,f]		$C_9H_{19}N_3S$	53.69	9.51	20.87	53.80	9.69	20.81[g]

[a] This number is a melting point. [b] Recrystallized from benzene. [c] This material was flash distilled at 240° and 0.1 mm. [d] Recrystallized from a benzene-iso-octane mixture. [e] Sulfur analysis. Calcd.: 18.50. Found: 18.70. [f] Recrystallized from methanol at −70°. [g] Sulfur analysis. Calcd.: 15.92. Found: 16.13.

drolyzed by dilute acid or even moist air to the corresponding ketones, IV. The ketones IV absorbed at 1705–1711 cm.$^{-1}$ in the infrared, a behavior characteristic of six-membered ring ketones. The corresponding ketone prepared from the five-membered ring enamine V absorbed at the higher frequency, 1750 cm.$^{-1}$ as would be expected for a five-membered ring ketone.[4] The ketone structure was further confirmed by the preparation of representative 2,4-dinitrophenylhydrazones. Finally, vigorous acid hydrolysis of IV (R = $—C_2H_5$, X = O) gave cyclohexanone, indicating for it a structure which would lead on hydrolysis to a β-keto acid. Only such a material would decarboxylate readily to cyclohexanone.

It is interesting to speculate on the mode of formation of III. The enamine, II, in the contributing form VI might be expected to react with two moles of isocyanate to yield a zwitterion of the type VII. This ion could easily stabilize itself in



two ways; by proton abstraction *via* a six-membered cyclic transition state to produce III or by cyclization to produce VIII. That the former course was the one followed is indicated by the ultraviolet spectrum of III, which absorbs at 295 mμ (ε 5250). Opitz, *et al.*[5] have established a range of 220–235 mμ (ε 3500–9960) for a large number of enamines and amide substitution as in III would be expected to shift the absorption to higher wave lengths. VIII would not be expected to have any ultraviolet absorption of high intensity.

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(4) *The Infrared Spectra of Complex Molecules*, L. Bellamy, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 148.

(5) G. Opitz, H. Hellmann, and H. W. Schubert, *Ann.*, 623, 112 (1959).

EXPERIMENTAL

1,5-Dimethyltriazone-2. Potassium cyanate (16.2 g., 0.2 mole) was dissolved in 20 ml. of water and 17.2 g. (0.13 mole) of 1,3,5-trimethyltriazine added. A white solid, probably potassium cyanate, crystallized. The slurry was stirred and cooled in ice while 20 g. of concd. hydrochloric acid was added dropwise. After stirring for 3 hr. the reaction mixture was extracted with methylene chloride, the methylene chloride layer dried and the solvent distilled under reduced pressure. There remained 4 g. (47%) of crude 1,5-dimethyltriazone-2. After recrystallization from benzene it melted at 113–116°.

Typical preparation of a triazone or thiotriazone of the Type I. To a stirred mixture of 0.3 mole of the *N*-alkylazomethine and 0.3 g. of zinc chloride was added slowly 0.15 mole of the alkyl isocyanate or isothiocyanate. The reaction was cooled in ice when necessary to keep it at 20–25°. After the initial exotherm was over the reaction mixture was heated 3 hr. on the steam bath and then distilled or recrystallized.

1,3,5-Tri-n-butyltriazone-2. A mixture of 34.4 g. (0.2 mole) of *N*,*N*′-di-*n*-butylurea, 14.6 g. (0.2 mole) of *n*-butylamine and 33.4 g. (0.4 mole) of 36% formaldehyde solution were heated on the steam bath overnight with stirring. The reaction mixture was extracted with methylene chloride and the organic layer dried and distilled to yield 30.4 g. (56.5%) of 1,3,5-tri-*n*-butyltriazone-2, b.p. 136–140° (0.3 mm.), n_D^{25} 1.4683. The infrared spectrum of this material was identical with that of 1,3,5-tri-*n*-butyltriazone-2, prepared from *n*-butyl isocyanate and 1,3,5-tri-*n*-butyltriazine.

1,3,5-Triethylthiotriazone-2. A mixture of 18 g. (0.13 mole) of *N*,*N*′-diethylthiourea, 22 g. (0.26 mole) of 36.6% formaldehyde and 8.1 g. (0.13 mole) of 72% ethylamine was stirred and heated on the steam bath overnight. The mixture was extracted with methylene chloride, the extract dried and the methylene chloride removed by distillation, leaving 15.6 g. (60%) of 1,3,5-triethylthiotriazone-2 melting at 50–55°. After two recrystallizations from methanol at −70° it melted at 57–59° and gave no depression on admixture and melting with a sample of the material prepared from 1,3,5-triethyltriazine and ethyl isothiocyanate. The infrared spectra of the two samples were also identical.

N-1-Pyrrolidinocyclohexene-2-oyl-N,N′-diethylurea. To a mixture of 7.1 g. of ethyl isocyanate and 20 ml. of chloroform was added 7.5 g. of 1-pyrrolidinocyclohexene and the mixture stirred at room temperature for 3 hr. Isooctane was added to incipient cloudiness and the *N*-1-pyrrolidinocyclohexene-2-oyl-*N*,*N*′-diethylurea allowed to crystallize. After drying 1.5 hr. at 70° (0.5 mm.) it melted at 162–164°, λ_{max} 295 mμ (ϵ 5250).

Anal. Calcd. for $C_{16}H_{27}N_3O_2$: C, 65.49; H, 9.28; N, 14.33; neut. equiv. 293.4. Found: C, 65.82; H, 9.59; N, 14.13; neut. equiv. 296.0.[6]

N-2-Ketocyclohexanoyl-N,N′-diethylurea. To a stirred mixture of 7.1 g. (0.1 mole) of ethyl isocyanate and 25 ml. of iso-octane was added dropwise 7.5 g. (0.05 mole) of 1-pyrrolidinocyclohexene. The reaction became quite warm and after about 10 min. a white solid product was filtered off, washed with iso-octane, and air dried. It weighed 11.1 g. and melted at 143–165° after standing overnight exposed to the air. An 8.5-g. sample of this material was treated with an excess of dilute hydrochloric acid and filtered to give 5.2 g. (equivalent to 57% yield) of *N*-2-keto-cyclohexanoyl-*N*,*N*′-diethylurea, m.p. 200–202°. After recrystallization from methanol it melted at 203–205°.

Anal. Calcd. for $C_{12}H_{20}N_2O_3$: C, 59.98; H, 8.39; N, 11.66. Found: C, 59.92; H, 8.55; N, 11.50.

The 2,4-dinitrophenylhydrazone[7] of *N*-2-ketocyclohexanoyl-*N*,*N*′-diethylurea after recrystallization from methanol melted at 193–195°.

Anal. Calcd. for $C_{18}H_{24}N_6O_6$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.12; H, 5.95; N, 19.99.

N-2-Ketocyclohexanoyl-N,N′-di-n-butylurea. To a stirred mixture of 19.8 g. (0.2 mole) of *n*-butyl isocyanate and 50 cc. of iso-octane was added dropwise 15.1 g. (0.1 mole) of 1-pyrrolidinocyclohexene. After about 1 hr. an excess of 1*N* hydrochloric acid was added, the mixture stirred for a few minutes and then filtered to yield 22.7 g. (77%) of *N*-2-ketocyclohexanoyl-*N*,*N*′-di-*n*-butylurea. After recrystallization from ethanol it melted at 206–208°.

Anal. Calcd. for $C_{16}H_{28}N_2O_3$: C, 64.83; H, 9.52; N, 9.45. Found: C, 64.83; H, 9.68; N, 9.40.

N-2-Ketocyclopentanoyl-N,N′-di-n-butylurea. To a stirred mixture of 19.8 g. (0.2 mole) of *n*-butyl isocyanate and 25 ml. of iso-octane was added 13.7 g. (0.1 mole) of 1-pyrrolidinocyclopentene. After stirring for 3 hr. the reaction mixture had separated into two layers. An excess of 1*N* hydrochloric acid was added and the layers separated. On standing overnight the aqueous layer precipitated 19.5 g. (69%) of *N*-2-ketocyclopentanoyl-*N*,*N*′-di-*n*-butylurea. After recrystallization from ethyl acetate it melted at 130–132°.

Anal. Calcd. for $C_{15}H_{26}N_2O_3$: C, 63.70; H, 6.54; N, 18.17. Found: C, 64.04; H, 6.61; N, 18.29.

The *2,4-dinitrophenylhydrazone*[7] of *N*-2-ketocyclopentanoyl-*N*,*N*′-di-*n*-butylurea after recrystallization from methanol decomposed at 200°.

Anal. Calcd. for $C_{21}H_{30}N_6O_6$: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.24; H, 6.61; N, 18.29.

N-2-Pyrrolidinocyclohexene-1-thioyl-N,N′-diethylthiourea. To a stirred mixture of 17.4 g. (0.2 mole) of ethyl isothiocyanate and 30 ml. of iso-octane was added 15.1 g. (0.1 mole) of 1-pyrrolidinocyclohexene. During 4 hr. at room temperature there crystallized 11.3 g. of *N*-2-pyrrolidinocyclohexene-1-thioyl-*N*,*N*′-diethylthiourea, m.p. 110–119°. After recrystallization from ethyl acetate it melted at 124–126°.

Anal. Calcd. for $C_{16}H_{27}N_3S_2$: C, 59.02; H, 8.36: N, 12.91; S, 19.70. Found: C, 59.10; H, 8.66; N, 12.98; S, 19.69.

N-Cyclohexanone-2-thioyl-N,N′-diethylthiourea. A 5-g. sample of crude *N*-2-pyrrolidinocyclohexene-1-thioyl-*N*,*N*′-diethylthiourea was heated on the steam bath for 1 hr. with 20 ml. of dilute hydrochloric acid. The aqueous layer was decanted from 3.6 g. of oily crystals and a 1.0 g. sample of these crystals chromatographed on G. F. Smith 50–200 mesh Silica. Elution with methylene chloride and 5% ethyl acetate in methylene chloride removed a small amount of oil. Elution with 5% methanol in methylene chloride gave 0.9 g. of *N*-cyclohexanone-2-thioyl-*N*,*N*′-diethylthiourea. After recrystallization from ethyl acetate it melted at 118–121°.

Anal. Calcd. for $C_{12}H_{20}N_2S_2O$: C, 52.90; H, 7.40; N, 10.29; S, 23.54. Found: C, 52.59; H, 7.65; N, 10.29; S, 23.46.

Cyclohexanone 2,4-dinitrophenylhydrazone. A mixture of 1.5 g. of *N*-2-ketocyclohexanoyl-*N*,*N*′-diethylurea and 20 cc. of 50% sulfuric acid were heated under reflux for 8 hr. An excess of 2,4-dinitrophenylhydrazine reagent[7] was added and the mixture heated on the steam bath for 10 min. On cooling there crystallized 0.70 g. of cyclohexanone 2,4-dinitrophenylhydrazone, m.p. 152–155°. After recrystallization from an ethanol–ethyl acetate mixture it melted at 157–159° and gave no depression on admixture and melting with an authentic sample of cyclohexanone 2,4-dinitrophenylhydrazone.

PHILADELPHIA 37, PA.

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[6] The neutralization equivalent was determined by potentiometric titration with 0.1*N* perchloric acid in acetic acid.

[7] *The Systematic Identification of Organic Compounds*, R. Shriner, R. Fuson, and D. Curtin, Fourth Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 219.