example, a released bonding electron should weaken the bonds in a phenyl radical or strengthen the bonds in a *tert*-butyl radical.

Fortunately, it is not necessary to understand fully the origin of all reorganizational energies in order to recognize their role in bond dissociation and to make practical use of them. In particular, the series of values for hydrocarbon radicals can be especially helpful in explaining various aspects of hydrocarbon chemistry.

Registry No. Benzyl, 2154-56-5; allyl, 1981-80-2; *tert*-butyl, 1605-73-8; isopropyl, 2025-55-0; *n*-propyl, 2143-61-5; ethyl, 2025-56-1; methyl, 2229-07-4; vinyl, 2669-89-8; phenyl, 2396-01-2; phenoxy, 2122-46-5; nitro, 10102-44-0; acetyl, 3170-69-2; benzoyl, 2652-65-5; aldehyde, 2597-44-6; methyl sulfone, 4853-80-9; methoxy, 2143-68-2; phenylthio, 4985-62-0; ethoxy, 2154-50-9; carboxylic acid, 2564-86-5; acetate, 13799-69-4; hydroxymethyl, 2597-43-5; thiol, 13940-21-1; methylthio, 7175-75-9; hydroxyl, 3352-57-6; methylamino, 15622-51-2; amino, 13770-40-6; cyano, 2074-87-5; *n*-propyl fluoride, 460-13-9; 2,2′-difluorobiphenyl, 388-82-9; 2-chloro-2-methylbutane, 594-36-5; chlorobenzene, 108-90-7; 1-bromohexane, 111-25-1; benzyl bromide, 100-39-0; allyl iodide, 556-56-9; benzoyl bromide, 618-32-6; *sec*-butyl alcohol, 78-92-2; 2,5-dimethylphenol, 95-87-4; methyl *tert*-butyl ether, 1634-04-4; propanal, 123-38-6; ethyl phenyl ketone, 93-55-0; adipic acid, 124-04-9; isopropyl 3-pentenoate, 62030-41-5; cyclohexanethiol, 1569-69-3; methyl phenyl sulfide, 100-68-5; ethyl allyl sulfoxide, 34757-40-9; methyl phenyl sulfone, 3112-85-4; diphenylamine, 122-39-4; *p*-nitroaniline, 100-01-6; 3,5-dimethylpyridine, 591-22-0; acrylonitrile, 107-13-1; hexanamide, 628-02-4.

Thermolysis of Trialkylnitrosoureas: Formation of an Unusual Product

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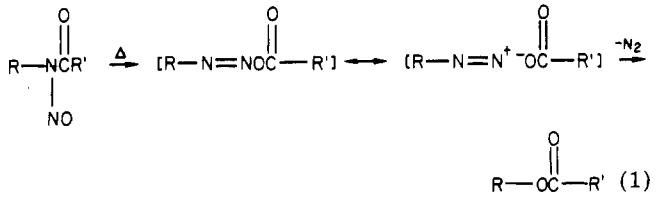
The thermolysis of four trialkylnitrosoureas, 1,1,3-trimethyl-1-nitrosourea (**1**), 3,3-diethyl-1-methyl-1-nitrosourea (**2**), 1-ethyl-3,3-dimethyl-1-nitrosourea (**3**), and 1,3,3-triethyl-1-nitrosourea (**4**), was carried out neat, in protic and aprotic solvents. When the thermolysis was run neat or in aprotic solvents, **4** gave as much as 70% of *N*,*N*-diethylalanine ethyl ester (**9**). Ethyl *N*,*N*-diethylcarbamate (**8**) (about 10%) was the only other product isolated. In protic solvent, however, **8** was the principal product. Neat thermolysis of **2** and **3** gave products analogous to those obtained from **4** but in much lower yields. Thermolysis of **1** did not give any product comparable to **9**. Tetramethylurea was a major product from the thermolyses of **1** and **3**. Decomposition of **3** was faster than any of the other three compounds studied, but **3** did not give high yields of products. Addition of CuCl to the reaction mixture caused the reaction products to change dramatically. The appropriate dialkylnitrosamine and the denitrosated urea were then the major products.

Introduction

The thermolysis of nitrosamides was studied carefully by White,[1] Streitweiser,[2] Huisgen,[3] and others[4] about 25 years ago. At that time, it was established that the major pathway for thermolysis of nitrosamides,[1] nitrosocarbamates,[5] and nitroamides[6] was via rearrangement to a diazo compound that subsequently lost N_2 (N_2O in the case of nitroamides) to give an ester (eq 1). This reaction

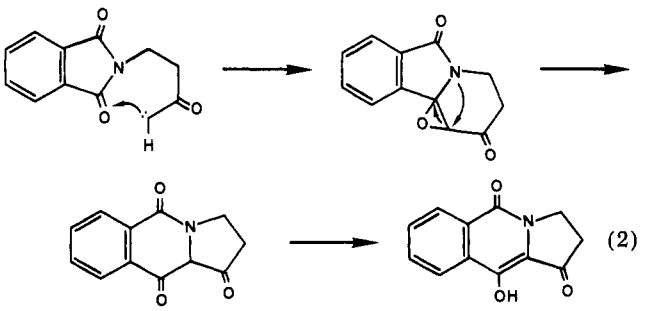


(1)

was shown to occur by way of a tight ion pair that had a lifetime sufficient for partial scrambling of O^{18} from specifically labeled carbonyl.[1]

At higher temperatures, free-radical processes competed with the diazo ester rearrangement, and olefinic products were observed when R contained a β-hydrogen.[3]

While the thermolyses of nitrosamides and nitrosocarbamates have been studied in some detail, nitrosoureas have received only minimal attention. Werner in 1919 demonstrated the thermal decomposition of methylnitrosourea to give nitrogen, methyl isocyanate, and water.[8] Boivin and Boivin later studied the decomposition of methylnitrosourea in boiling water and the products derived from the reaction of isocyanate produced with alkylamine.[9] However, neat thermolyses or thermolyses of substituted nitrosoureas in aprotic solvents do not appear to have been studied in any detail. The thermolysis reactions of four trialkylnitrosoureas produce carbamates, as expected, but the nitrosoureas also undergo an unusual insertion reaction that appears to be the result of a carbene insertion into an amide C–N bond. This is not a common reaction of carbene or carbenoid species, although a similar insertion was observed by Krauser and Watterson.[7] The carbene derived from 1-diazo-4-phthalimido-2-butanone gave 1,5,8-trioxobenz[*f*]indolizidine as the final product of a rearrangement that was initiated by insertion of the carbene across the imide carbonyl (eq 2).



(2)

(1) (a) White, E. H. *J. Am. Chem. Soc.* **1955**, *77*, 6011. (b) White, E. H.; Aufdermarsh, C. A., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1174.
(2) Streitweiser, A., Jr.; Schaeffer, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 2893.
(3) Huisgen, R.; Reimlinger, H. *Justus Liegibs Ann. Chem.* **1956**, *599*, 183.
(4) Lobl, T. J. *J. Chem. Educ.* **1972**, *49*, 730.
(5) Autsche, C. D.; Johnson, H. E. *J. Am.. Chem. Soc.* **1954**, *76*, 1776.
(6) Lijinsky, W.; Taylor, H. W. T. *Z. Krebsforsch.* **1975**, *83*, 315.
(7) Krauser, S. F.; Watterson, A. C., Jr. *J. Org. Chem.* **1978**, *43*, 2026.
(8) Werner, E. A. *J. Chem. Soc.* **1919**, *115*, 1093.
(9) Boivin, J. L.; Boivin, P.A. *Can. J. Chem.* **1951**, *29*, 478.

0022-3263/82/1947-3839$01.25/0

Table I. Thermolysis of Nitrosoureas at 83 °C (Neat)

no.	urea	yield,[a] % carbamate	insertion product	tetramethylurea	starting material[a]	corresponding urea[a]	rxn time, h
1	1-nitroso-1,3,3-trimethyl-	8.0		12	60	2	5
2	1-nitroso-1-methyl-3,3-diethyl-	8.6	15		76	0.5	4
3	1-nitroso-1-ethyl-3,3-dimethyl-	9.3	14	14	19	3	3
4	1-nitroso-1,3,3-triethyl-	5	40		24	1.6	4

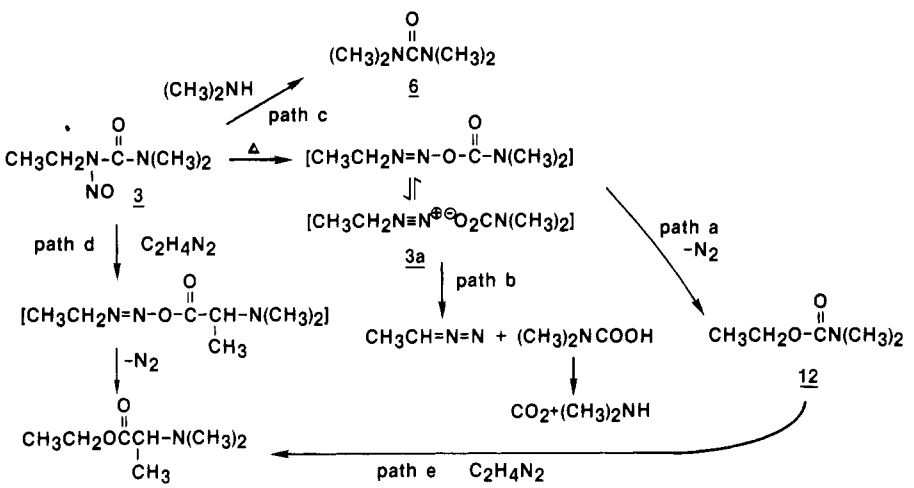
[a] Yields given are actual yields determined by GLC relative to *N*-nitrosodipropylamine internal standard.

Table II. Effect of Temperature and Solvent on Thermolysis of 1,3,3-Triethyl-1-nitrosourea (4)

temp, °C	t, h	solvent	yield,[a] % triethyl carbamate	*N,N*-diethylalanine (9)	4	triethylurea
83	5	hexadecane	1	14	79	trace
96	1.5	hexadecane	6	46	57	trace
105	1	hexadecane	5	60	25	trace
85	2	EtOH	44	2	18	trace
85	2	*n*-PrOH	40	2	29	trace

[a] Yields given are actual yields determined by GLC relative to *N*-nitrosodipropylamine internal standard.

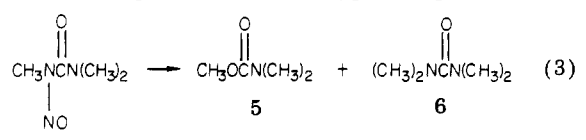
Scheme I



Results

The four trialkylnitrosoureas studied were 1,3,3-trimethyl-1-nitrosourea (**1**, TMNU), 3,3-diethyl-1-methyl-1-nitrosourea (**2**, MDENU), 1-ethyl-3,3-dimethyl-1-nitrosourea (**3**, EDMNU), and 1,3,3-triethyl-1-nitrosourea (**4**, TENU). Reactions of **1–3** were carried out neat, while those of **4** were also studied in hexadecane, 1-propanol, and ethanol.

1,3,3-Trimethyl-1-nitrosourea (**1**) decomposed most slowly of the four compounds studied. The major prodcts were methyl *N,N*-dimethylcarbamate (**5**) and tetramethylurea (**6**) (eq 3). Yields for a typical experiment are

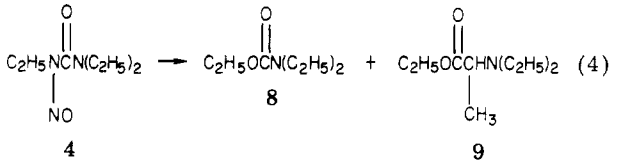


(3)

given in Table I.

Tetramethylurea can arise from the reaction of dimethylamine with **1**.[8] The dimethylamine must arise from a decomposition of *N,N*-dimethylcarbamic acid that could form from the diazo ester intermediate before it goes on to **5** (see Scheme I).

Triethylnitrosourea (**4**) was thermolyzed neat or in hexadecane at 83, 96, and 105 °C. Two major reaction products were found, *N,N*-diethylethyl carbamate (**8**) and *N,N*-diethylalanine ethyl ester (**9**). The major product was **9**, with yields as high as 70% being observed (eq 4). The



(4)

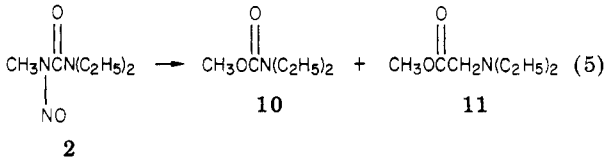
alanine ester **9** could be formed by a diazoethane insertion into the C–N bond of **8** or by attack of diazoethane on the $C–N_3$ bond in **4** followed by rearrangement and elimination of N_2. Denitrosation is apparently not an important pathway. A trace of triethylurea was present throughout the course of the reaction, but the concentration did not increase with time (see Table II).

When the thermolysis was carried out in a protic solvent (ethanol or 1-propanol), the only product observed was **8** (40–44%). The absence of propyl esters when the thermolysis was carried out in 1-propanol suggests that the loss of nitrogen by the intermediate diazo ester and subsequent recombination of the fragments occurs rapidly in a solvent cage. This is in agreement with the results of White[1] on diazo ester decompositions.

The carbamate ester obtained from **4** is analogous to that obtained from **1** and was the expected product from

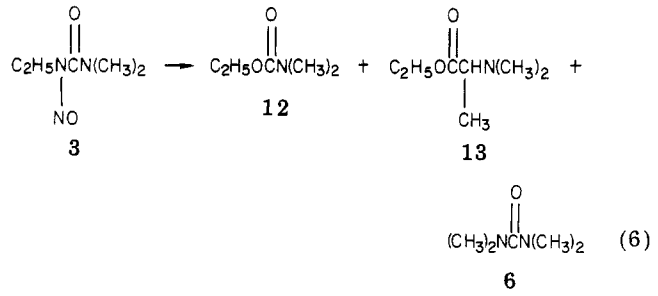
the diazo ester intermediate. There was no tetraethylurea formed in the thermolysis of 4, and the major product was the alanine derivative 9 (eq 4). The structure of 9 has been established by measurement of the high-resolution GC/MS (m/e 173.1318, $C_9H_{19}NO_2$), by its characteristic NMR spectrum, as well as by synthesis from ethyl 2-bromopropionate and diethylamine.

The two "mixed" trialkylureas (2 and 3) gave the results anticipated on the basis of the reactions of 1 and 4. 3,3-Diethyl-1-methyl-1-nitrosourea (2) reacted somewhat more rapidly than 1 but more slowly than either of the 1-ethyl compounds (3 and 4). The major reaction products were methyl *N,N*-diethylcarbamate (10) and a glycine derivative, *N,N*-diethylglycine methyl ester (11). Both products were formed in approximately equal amounts (8–15% yield) (eq 5).



2 10 11 (5)

The other "mixed" nitrosourea, 1-ethyl-3,3-dimethyl-1-nitrosourea (3) gave three products on thermolysis and reacted the most rapidly of the four nitrosoureas studied. The products were ethyl *N,N*-dimethylcarbamate (12, 9.3%), *N,N*-dimethylalanine ethyl ester (13, 14%), and tetramethylurea (6, 14%)(eq 6).



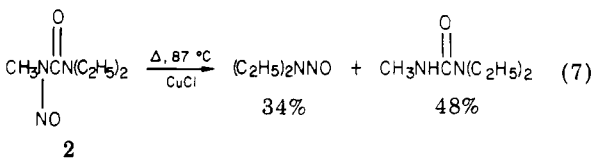
3 12 13 6 (6)

A comparison of the yields obtained from each nitrosourea studied is given in Table I. Because there is a considerable disparity in reaction rates for the four compounds, a comparison at exactly the same reaction time is difficult. For example, 3 will have reacted considerably by t = 60 min, while 1 would not have reacted at all.

The mass spectra of the possible insertion products from the four trialkylnitrosoureas are similar and are summarized in Table III. The anticipated insertion products from 1 could not be identified in thermolysis reaction mixtures.

Tetraethylurea was synthesized by treating 2 (3,3-diethyl-1-methyl-1-nitrosourea) with diethylamine by the method of Boivin and Boivin.[9] The desired product was formed in small amounts (ca. 1%), and its structure was confirmed by GC/MS. No tetraethylurea is present in *thermolysis* mixtures of 2 or 4 (both of which bear diethylamino groups).

Cuprous chloride is known to have a strong catalytic effect on reactions of diazomethane, particularly those thought to proceed through carbene intermediates.[10] The effect of CuCl on the thermolysis of trialkylnitrosoureas was profound. Carbamates and "insertion" products (9, 11, 13) were absent, and the major products were the appropriate dialkylnitrosamine and the denitrosated urea (eq 7), neither of which is a product of thermolyses without



2 34% 48% (7)

CuCl. Results are given in Table IV.

Discussion

The four nitrosoureas studied all underwent the expected diazo ester rearrangement leading to the alkyl *N,N*-dialkylcarbamate. Old samples of all the trialkylnitrosoureas are likely to be contaminated with carbamate, even when they have been stored at 0 °C. Samples of the 1-ethyl-1-nitroso compounds (3 and 4) that were over 6 months old contained more carbamate than nitrosourea, and 4 contained a significant amount of the alanine derivative as well, although at 0 °C the carbamate is the major product.

The results obtained on thermolysis of compounds 1–4 can be explained in terms of a general reaction mechanism shown in Scheme I for 3. (Compound 3 is used as the example because it alone forms all the possible types of products found in these reactions.)

There is no information in the literature on thermolysis of trialkylnitrosoureas. It appears, however, that ester formation proceeds via the same mechanism for the ureas as it does for nitrosoamides, etc. The expected product from the thermolysis of a trialkylnitrosourea is an alkyl *N,N*-dialkylcarbamate, such as 12.

The first step in the thermolysis is probably the formation of the diazoester or the corresponding ion pair 3a. Similar intermediates have been postulated for the thermolysis of nitrosamides and nitroamides by Streitweiser,[2] Huisgen[3], White,[1] and others.[4] Efforts to isolate intermediates such as 3a have not been successful. For nitrosamides, the next step in the thermolysis (path b) proceeds via a tight ion pair with a finite lifetime—long enough to permit *partial* scrambling of ^{18}O when the carbonyl is labeled in the starting material[2].

The ion pair may proceed directly to the carbamate ester 12 or may disproportionate to give the diazoalkane and *N,N*-dimethylcarbamic acid. The latter can decompose to give CO_2 and dimethylamine (path b). Path a, a concerted loss of N_2 from the diazo ester to form 12, is plausible but should be considered less likely than path b in view of the work of Streitweiser,[2] Huisgen,[3] and White.[3] The presence in our reaction mixtures of products that can only come from carbenoid precursors in one case and dimethylamine in the other (6 and 13) also indicates that much, if not all, of the thermolysis must proceed through path b. The existence of 3a as a tight ion pair is supported by the observation that no *n*-propyl *N,N*-diethylcarbamate was formed when 4 was thermolyzed in propanol.

Tetramethylurea (6) probably arises by the reaction of dimethylamine (from the decomposition of *N,N*-dimethylcarbamic acid) with the starting material (EDMNU, 3). A similar reaction has previously been shown to occur in aqueous systems with *N*-methyl-*N*-nitrosourea and *sym*-dimethylnitrosourea.[9] Boivin and Boivin[9] heated aqueous solution of 1-methyl-1-nitrosourea with various amines to obtain the *asym*-ureas. They believed the reaction proceeded via thermolysis of 1-methyl-1-nitrosourea to form isocyanic acid, which reacts with the added amine to give the corresponding urea. A modification of this mechanism would be necessary for trialkylnitrosourea, for the corresponding isocyanate would be a charged species (eq 8). The ion pair from the diazo ester can be written

(10) Cowell, G. W.; Ledwith, A. *Q. Rev., Chem. Soc.*, **1970**, *24*, 119.

Table III. Principle Fragments in Mass Spectra of Insertion Product

no.	urea	insertion product	M^+	100%
1	1-nitroso-1,3,3-trimethyl	$CH_3OC(=O)CH_2N(CH_3)_2$ [a]	117	58 $(CH_3)_2NCH_2^+$
2	1-nitroso-1-methyl-3,3-diethyl-	$CH_3OC(=O)CH_2N(C_2H_5)_2$	145	86 $(C_2H_5)_2NCH_2^+$
3	1-nitroso-1-ethyl-3,3-dimethyl-	$C_2H_5OC(=O)CH(CH_3)N(CH_3)_2$	145	72 $(CH_3)_2NCHCH_3^+$
4	1-nitroso-1,3,3-triethyl-	$C_2H_5OC(=O)CH(C_2H_5)_2$ (9)	173	100 $(C_2H_5)_2NCHCH_3^+$

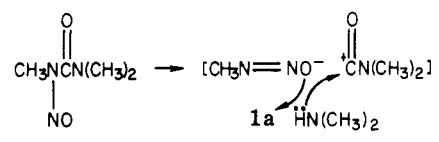
[a] This product would be expected from 1 but is not found. It has been synthesized and characterized.

Table IV. Effect of CuCl Catalysis on Trialkylnitrosourea Thermolysis at 87 °C

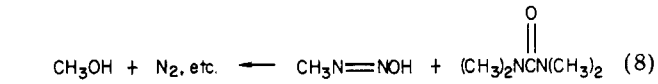
			yield, %						
no.	urea	CuCl, mmol	methyl *N,N*-dimethyl-carbamate (5)	tetra-methyl-urea (6)	dimethyl-nitrosamine	trimethyl-nitroso-urea (1)	trimethyl-urea	total % of theor	*t*, h
1	trimethyl-nitroso-, 0.3 mmol	0	10	22	0	4	3	39	17
		0.035	<1		18	1	80	99	17

			yield, %						
	urea	CuCl, mmol	methyl *N,N*-diethyl-carbamate (10)	*N,N*-diethyl-glycine methyl ester (11)	diethyl nitros-amine	3,3-diethyl-1-methyl-1-nitrosourea (2)	3,3-diethyl-1-methylurea	total % of theor	*t*, h
2	3,3-diethyl-1-methyl-1-nitroso-, 0.3 mmol	0	8.1	8.4		6	tr	23	17
		0.04	0.5		34	1	48	84	17

			yield, %						
	urea	CuCl, mmol	*N,N*-diethyl-carbamate (8)	*N,N*-diethyl-alanine ethyl ester (9)	diethyl-nitrosamine	triethyl-nitrosourea (4)	triethyl-urea	total % of theor	*t*, h
4	triethyl-nitroso-, 0.3 mmol	0	1	2.4		62	0.8	73.4	0.5
		0.045	0.7		3.7	47	16	67.4	0.5
		0	3.3	29.5		40	2.0	74.8	2
		0.045	1.4		15	1	74	91	2
		0	5	18	0.5	14	5	43	3
		0.032	1.5		22	1	26	50	3



1



6 (8)

in the form **1a**, which could give tetramethylurea on reaction with dimethylamine. It is of interest to note that only **1** and **3** (which can form dimethylamine) formed a tetraalkylurea. Compounds **2** and **4** (which could form diethylamine) did *not* give rise to tetraethylurea, although we know that **2** and **4** must decompose to some extent to give diethylamine, since the other products of that decomposition have been identified (i.e., CO_2 and products that come from carbenoid reactions). Apparently, diethylamine is not reactive under the thermolysis conditions, since a large excess of diethylamine was necessary to obtain a very small amount of tetraethylurea when the method of Boivin and Boivin was used.[9] (Most of **2** was recovered unchanged.)

Cuprous chloride is known to catalyze certain diazoalkane reactions, in particular cyclopropanation reactions. The latter are often called carbenoid reactions but probably do not proceed via free carbenes, which tend to give insertion products.[10] It was of interest to determine the effect of cuprous chloride on the thermolysis of trialkylnitrosoureas, since a diazoalkane or carbene insertion is postulated as one of the reaction pathways. Suprisingly cuprous chloride completely changed the nature of the products obtained (eq 7). When **1**, **2**, or **4** was thermolyzed in the presence of CuCl, the appropriate dialkylnitrosamine was obtained in ca. 20% yield, and the denitrosated urea was obtained in 70–80% yield. Neither of these was normally a major product in the nitrosourea thermolysis. It is clear that some decomposition via path b occurred to produce the free dialkylamine, but CuCl also seems to catalyze a denitrosation of the nitrosourea and nitrosation of the dialkylamine. (No more than trace quantities of dialkylnitrosamines are normally observed in these processes.) There are reports in the literature of nitrosation by metal nitrosyls or metal nitrito complexes.[11]

The decompositions in the presence of cuprous chloride result in better material balances than the neat thermolyses. This can be attributed to the formation of the urea as the major reaction product. The urea is stable and nonvolatile at reaction temperatures and, hence, is easily recovered. In the thermolyses, most of the products of decomposition are very low boiling volatiles (CO_2, dialkylamine, N_2) and are not as readily quantitated.

It is apparent that the thermolytic behavior of trialkylnitrosoureas is strongly dependent on solvent (since polar solvents, such as propanol, shut down the insertion pathway). In addition, one-electron transfer agents, such as CuCl, also have a profound effect on the reaction and change its course dramatically.

Conclusions

We have reported a novel insertion reaction of trialkylnitrosoureas that involves two molecules of the starting material and yet proceeds in quite high yields for certain compounds (triethylnitrosourea). Even such simple compounds as the four trialkylnitrosoureas discussed in this study are capable of some rather exotic chemistry.

Experimental Section

Caution: Nitrosoureas are known to be carcinogenic in laboratory animals and should be handled only with appropriate precautions.

Materials. Organic chemicals were generally supplied by Aldrich or Tridom Fluka and were used without further purification. Inorganic chemicals were Fisher or Mallinckrodt ACS Reagent Grade. Solvents were Burdick and Jackson "Distilled in Glass".

The trialkylnitrosoureas were synthesized by literature methods[6,12,13] and purified by column chromatography on silica gel with hexane–ethyl acetate as eluant. The last traces of solvent were removed from the pure compounds at the vacuum pump (0.3 mmHg), but the compounds were not distilled. Purity was assayed by GLC [Ultrabond 20M (Ultrascientific Corp.) 10 ft × 2 mm, 100–120 mesh, 4 min at 70 °C, 16/min program to 140 °C, 20 mL/min He] with a Perkin-Elmer 3920 GC equipped with flame ionization and nitrogen detectors. Quantitation was based on the nitrogen detector output and was accomplished with the use of a Hewlett Packard 3354a chromatographic computer. An injector temperature of 150 °C was necessary to prevent thermal decomposition of the nitrosoureas. (The nitrosoureas could be quantitated at injector temperatures above 200 °C.) Although the nitrosoureas are thermally unstable even below 150 °C, little decomposition is seen in the GC traces. Use of an internal standard (dipropylnitrosamine) in all analyses made quantitation of the amount of nitrosourea present in any injection possible by standard analysis techniques. Analyses of trimethylnitrosourea were also carried out on an Ultrabond PEGS (Ultrascientific Corp., 6 ft × 2 mm column, 100–120 mesh, 4 min at 80 °C 16 °C/min to 140 °C 20 mL/min He). This column does not separate the carbamate **5** from *O,N,N*-trimethylglycine but is suitable for analyses of thermolysis mixtures of **1**, since the glycine ester is not a product.

Mass spectra were run on a Finnegan 1015C or a VG-Micromass ZAB2F mass spectrometer, and NMR spectra were taken on a Varian XL-100 spectrometer equipped with a Nicolet 1080 FT computer.

Thermolysis Reactions. Thermolyses were carried out in 1-mL reaction vials equipped with pressure caps. Triethylnitrosourea was soluble in hexadecane, and this was used as the solvent for the thermolysis so that aliquots could be taken for time points. The other three nitrosoureas were not soluble in hexadecane, and their thermolyses were studied neat. Triethylnitrosourea was studied neat, in hexadecane, and in 1-propanol. Reactions were carried out at temperatures ranging from 60 to 105 °C. Reaction conditions: neat reactions; 20 mg of compound was weighed into the vial and heated at the given temperature for either 0.5 to 3 h (**3** and **4**) or 17 h (**1** and **2**). To prepare samples for analysis, the reaction vials were cooled in liquid nitrogen, opened, and allowed to warm to room temperature. The contents were then dissolved in 10 mL of methanol with internal standard added (dipropylnitrosamine) and analyzed by GLC. Results are given in Tables I and II. Reactions run in 1-propanol were treated in the same manner as neat reactions. Triethylnitrosourea reactions in hexadecane were either treated the same as the neat reactions or aliquots were taken at given time points and diluted in suitable amounts of methanol for analysis.

Gas evolution was followed at 97 °C by running the reaction in Wheaton Micro-Kit glassware set up as if for distillation with gas collection in an inverted water-filled buret. Some of the effluent gas was trapped in $Ba(OH)_2$, giving the white precipitate of $BaCO_3$. With each of compounds **1–4**, somewhat more than a mole equivalent of gas was produced. The initial rates of gas evolution were as follows: **1**, 0.21, **2**, 0.17; **3**, 0.72; **4**, 0.73 mL/min.

Thermolyses with CuCl. All reactions were studied neat. In a typical reaction, 0.30 mmol of the nitrosourea and 1–7 mg of CuCl (0.01 to 0.07 mmol) were placed in a reaction vial and heated at 87 °C for an appropriate time (30 min to 3 h for **4**; 17

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h for 1 or 2). The reaction mixtures were cooled, taken up in methanol, and filtered to remove copper salts. Internal standard (*N*-nitrosodipropylamine) was added, and the solutions were made up to volume for GC analysis. Products were identified by GLC/MS and positive spike experiments. Results are given in Table IV.

Carbamates were synthesized by literature methods.[15] Boiling points for all compounds were in reasonable agreement with those in the literature. Identity with carbamates found in thermolysis reaction mixtures was established by GC/MS and positive spike experiments.

Methyl *N*,*N*-dimethylcarbamate (5): bp 126–128 °C (lit.[16] bp 131 °C); NMR ($CDCl_3$) δ 2.90 (s, 6 H, N-CH_3), 3.68 (s, 3 H, OCH_3).

Methyl *N*,*N*-Diethylcarbamate (10): bp 156–157 °C (lit.[16] 155 °C) NMR ($CDCl_3$) 1.07 (t, 6 H, NCH_2CH_3), 3.15 (q, 4 H, NCH_2CH_3), 3.61 (s, 3 H, OCH_3).

Ethyl *N*,*N*-dimethylcarbamate (12): bp 145–147 °C (lit.[16] bp 147 °C); NMR ($CDCl_3$) δ 1.13 (t, 3 H, CH_2CH_3), 2.97 (s, 6 H, NCH_3), 4.06 (q, 2 H, CH_2CH_3).

Ethyl *N*,*N*-diethylcarbamate (8): bp 164–167 °C (lit.[16] bp 169–172 °C); NMR ($CDCl_3$) δ 1.15 (overlapping triplets, 9 H, OCH_2CH_3 and NCH_2CH_3), 3.28 (q, 4 H, NCH_2CH_3), 4.15 (q, 2 H, OCH_2CH_3).

N,N-Disubstituted alanine and glycine esters were synthesized by standard literature procedures from the appropriate bromo esters and dialkylamines. Boiling points were comparable to those reported in the literature, and appropriate NMR and mass spectral data were obtained. Identity with the alanine and glycine derivatives found in thermolysis reaction mixtures was established by GLC/MS and positive spike experiments.

Methyl *N*,*N*-dimethylglycine: bp 94–96 °C [kut,[17] bp 50–53 °C (30 mmHg)]; NMR ($CDCl_3$) δ 2.35 (s, 6H, NCH_3), 3.18 (s, 2 H, CH_2), 3.73 (s, 3 H, OCH_3).

Methyl *N*,*N*-diethylglycine (11): bp 122–123 °C [lit.[17] bp 84.5–85.5 °C (57 mmHg)]; NMR ($CDCl_3$) δ 1.05 (t, 6 H, CH_2CH_3), 2.65 (q, 4 H, CH_2CH_3), 3.33 (s, 2 H, CH_2), 3.70 (s, 3 H, OCH_3).

Ethyl *N*,*N*-dimethylalanine (13): bp 70–72 °C (500 mmHg) (lit.[14] bp 154–157 °C); NMR ($CDCl_3$) δ 1.35 (overlapping triplets, 6 H, CH_2CH_3 and $CHCH_3$), 2.36 (s, 6 H, NCH_3), 3.25 (q, 1 H, $CHCH_3$), 4.23 (q, 2 H, CH_2CH_3).

Ethyl *N*,*N*-diethylalanine (9): bp 93-96 °C (500 mmHg) (lit.[18] bp 172–477 °C); NMR ($CDCl_3$) δ 1.05 and 1.30 (overlapping triplets, 12 H, CH_2CH_3 and $CHCH_3$), 2.62 (overlapping quartets, 4 H, NCH_2CH_3), 3.54 (q, 1 H, $CHCH_3$), 4.18 (q, 2 H, OCH_2CH_3).

Isolation of Ethyl *N*,*N*-Diethylalanine from a Large-Scale Thermolysis Reaction Mixture. Triethylnitrosourea (0.54 g) was heated at 95 °C under a water-cooled condenser. A vigorous evolution of gas was observed. The reaction mixture was heated for 17 h, and the yellow-brown oil remaining in the reaction vial was analyzed by GLC (Ultrabond 20 M, ft 10 × 2 mm, 20 mL/min He, 4 min at 80 °C, 8 °C/min to 130 °C). The pot residue contained **9** and **8** in a 4:1 ratio, accounting for 80% of the starting material. Column chromatography of the pot residue on silica gel with hexane/ethyl acetate (0–10%) as eluant gave a sample of **9** that was identical by IR, NMR, and mass spectrum with that synthesized (vide supra).

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Regioselective Aluminum Chloride Catalyzed Reactions of Unsaturated Electrophiles with Thiazoles

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Aluminum chloride promotes reactions of α,β-unsaturated esters and nitriles with 1,3-thiazoles to give 1:1 and 2:1 adducts, the nature and distribution of which depend on the substituent R at C_2 of the heterocycle and the nucleophile QN employed as a quencher of the reaction mixture. With 2-bromothiazole, ethyl propiolate, and dimethyl acetylenedicarboxylate give substituted (*E*)- and (*Z*)-*N*-vinylthiazolin-2-ones (QN, aqueous sodium bicarbonate) and 2-imino-*N*-vinylthiazolines (QN, benzylamine), while ethyl acrylate and acrylonitrile afford substituted *N*-propanoylthiazolin-2-ones (QN, aqueous sodium bicarbonate). With 1,3-thiazole and 2-ethylthiazole, ethyl propiolate gives (QN, aqueous sodium bicarbonate) *N*-formyl- and *N*-propanoylthiazolines, respectively, together with 2:1 open-chain adducts containing 2 mol of acetylene and 1 mol of thiazole. A plausible scheme accounting for the formation of the observed products involves a regioselective attack by C_β of the multiple bond of the ester or nitrile coordinated with $AlCl_3$ on the nitrogen of the thiazole ring to give a zwitterion with allenic structure which by action of the QN undergoes C_2–R (R = Br) or C_2–S (R = H, C_2H_5) bond fission and forms the observed products.

The functionalization of the 1,3-thiazole ring through reactions with unsaturated electrophiles, viz., π systems activated by electron-withdrawing groups, constitutes an attractive entry to direct synthesis of derivatives of this important heterocyclic system, the core of numerous natural and synthetic compounds with biological activity.[1] Unfortunately, because of its aza-aromatic character, the thiazole ring is little inclined to react with π acceptors,[2] and thus very few reactions of that type have been so far described. For instance, thiazoles have been reported to react with dimethyl acetylenedicarboxylate[3] to give various cycloadducts from secondary processes, thus considerably

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