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Preparation and Properties of Novel Trisubstituted N-Nitrosoureas which Decompose to Afford Triazenes and Nitro Compounds under Mild Conditions[1)]

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3,3-Diethyl- (IIa, b) and 3-methyl-3-(3-pyridylmethyl)-1-nitroso-1-tolylureas (IIc, d) were prepared from the corresponding ureas (Ia—d). 3,3-Dialkyl-1-(2-tolyl)nitrosoureas (IIa, c) decomposed to produce 3,3-dialkyl-1-(2-tolyl)triazenes (IIIa, c) at room temperature. On the other hand, 3,3-dialkyl-1-(4-tolyl)ureas (IIb, d) gave mainly the corresponding triazenes (IIIb, d) in protic solvents, although IIb, d gave 3,3-dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d) and the denitrosated products (Ib, d) in chloroform or carbon tetrachloride.

Keywords——nitrosourea; triazene; 3,3-diethyl-1-nitroso-1-tolylurea; 3-methyl-3-(3-pyridylmethyl)-1-tolylurea; 3,3-dialkyl-1-(2-nitro-4-tolyl)urea; ^{1}H-NMR; ^{13}C-NMR

Some trialkyl N-nitrosoureas have been found to exhibit antitumor[2)] or strong carcinogenic[3)] activities in rats. Moreover, some of them show cytotoxic activity *in vivo*.[4)] However, the chemical and biological reactivities of 1-aryl-1-nitroso-3,3-dialkylureas are unknown. This paper describes the preparation and properties of novel trisubstituted N-nitrosoureas which decompose to afford triazenes and nitro compounds under mild conditions.

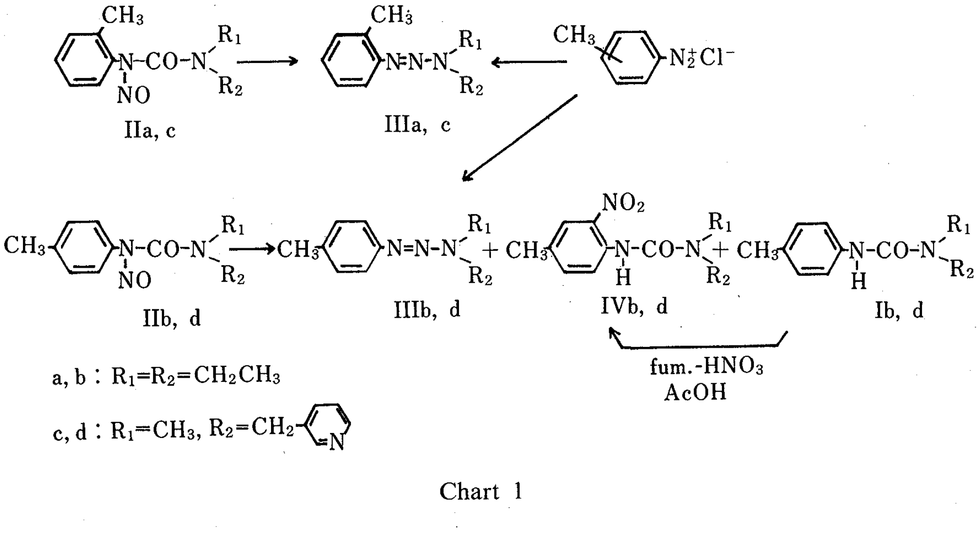

Chart 1

3,3-Dialkyl-1-tolylureas (Ia—d) were prepared in good yields by the reaction of tolyl isocyanates with dialkylamines in ether. Nitrosation of these ureas was carried out by using sodium nitrite in acidic solution at low temperature (Chart 1). As the obtained nitrosoureas (IIa—d) were unstable at room temperature, they were quickly purified by silica gel column chromatography under ice-cooling. The yields of IIa—d were 44—53%.

These trisubstituted nitrosoureas (IIa—d) decomposed to 3,3-dialkyl-1-tolyltriazenes

(IIIa—d) with evolution of carbon dioxide in chloroform[5] at room temperature. 3,3-Dialkyl-1-(2-tolyl)triazenes (IIIa, c) were obtained from 3,3-dialkyl-1-nitroso-1-(2-tolyl)ureas (IIa, c) in 46—52% yields, while 3,3-dialkyl-1-(4-tolyl)triazenes (IIIb, d) were produced from the corresponding (4-tolyl)nitrosoureas (IIb, d) in low yields (12—26%). The features of the decomposition of these nitrosoureas in chloroform at room temperature were observed by infrared (IR) spectroscopy. For example, the decomposition of IIb is shown in Fig. 1. The absorption at 2320 cm^{-1} due to carbon dioxide increased with the passage of time (Fig. 1, a—c), and disappeared when the solution was degassed (Fig. 1, d). The generated gas was trapped as precipitates of barium carbonate by passing it through 5% aqueous barium hydroxide.

Moreover, (2-tolyl)nitrosoureas (IIa, c) gave mainly (2-tolyl)triazenes (IIIa, c) even in well-dried chloroform,[5] though (4-tolyl)nitrosoureas (IIb, d) afforded 3,3-dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d) and the denitrosated products (Ib, d) in this solvent. The identities of these products were confirmed by comparing their spectral data with those of authentic samples which were prepared by the methods shown in Chart 1.

Next, the decomposition of 3,3-diethyl-1-nitroso-1-(2-tolyl)urea (IIa) and the 4-tolyl isomer (IIb) were investigated in various solvents at room temperature; the product yields estimated by high performance liquid chromatography (HPLC) are shown in Table I. It can be seen from these data that (2-tolyl)nitrosourea (IIa) gave chiefly the triazene (IIIa) regardless of the solvent properties. On the other hand, the 4-tolyl isomer (IIb) afforded predominantly the nitro compound (IVb) and the urea (Ib) in carbon halides such as chloroform and carbon tetrachloride, although the triazene (IIIb) was produced in protic or polar solvents as shown in Table I.

We examined the structures of the nitrosoureas by nuclear magnetic resonance (NMR) spectroscopy, since the structural difference between the two nitrosoureas (IIa and IIb) in

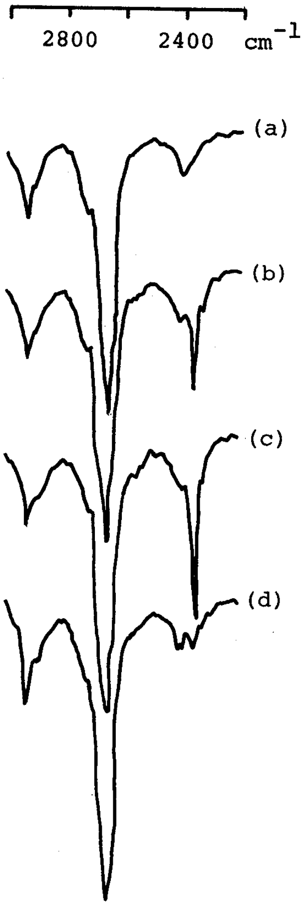

Fig. 1. IR Spectra of IIb in $CHCl_3$

Appearance of the CO_2 absorption at 2320 cm^{-1} with the passage of time (a, 5 min; b, 3 h; c, 5 h) and disappearance after degassing (d).

TABLE I. Product Yields Obtained by the Decomposition of IIa, b in Various Solvents[a]

Nitrosoureas	Solvents	Product yields (%)				
		IIIa	IIIb	IVb	Ia	Ib
IIa	EtOH[c]	57			Trace[b]	
IIa	$CHCl_3$[c]	67			6	
IIa	CCl_4[d]	58			15	
IIb	DMSO[d]		71	3		5
IIb	EtOH[c]		57	11		18
IIb	MeOH[c]		53	19		14
IIb	EtOH–$CHCl_3$ (1 : 1)		48	9		19
IIb	EtOH–$CHCl_3$ (1 : 9)		27	20		47
IIb	$CHCl_3$-contain. H_2O		14	31		23
IIb	$CHCl_3$[c]		Trace[b]	46		42
IIb	CCl_4[c]		Trace[b]	74		17

a) Product yields were determined by HPLC, under the operating conditions described in Experimental.
b) The products were identified by thin layer chromatography (TLC) using silica gel, but their yields could not be determined by HPLC.
c) They were dried over Molecular Sieves 3 Å after distillation.
d) Special reagent grade obtained commercially.

carbon halides seems to be reflected in the nature of the decomposition products formed. The spectral data for the nitrosoureas (IIa—d) and related compounds in chloroform-d_1 are listed in Tables II and III.

In the proton nuclear magnetic resonance (^{1}H-NMR) spectra, the signals of N^3-alkyl groups of IIa—d are broad at room temperature, and those of the 4-tolyl derivatives (IIb, d) are broader than those of the 2-tolyl isomers (IIa, c). Moreover, in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra, the resonance peak for the alkyl moiety bound to the N^3-nitrogen in each of IIa—d appears as a broad singlet or broad doublet at low temperature. For instance, the peaks of these alkyl groups change from broad doublets to sharp singlets with rise of temperature, as illustrated for IIa in Fig. 2. The signals of ethyl groups attached to the N^3-nitrogen in IIa are two sharp singlets at 20 °C, but they are still doublets in IIb at that temperature. These results can be interpreted in terms of a rotation barrier of the CO–N^3 bond arising as the result of partial double bond character.[6] The extent of the barrier seems to be greater in IIb than in IIa.

Further, the carbonyl resonances of nitrosoureas (IIa, b, d) at low temperature appear as two distinct signals at 151.6—153.3 ppm and 154.2—155.7 ppm. In the case of IIc, only one carbonyl is observed at -20 °C, at 155.4 ppm. Each signal is ascribed to an individual isomer with distinct orientations of the nitroso group. The major conformational isomer of IIa shows a carbonyl signal at 154.2 ppm and that of IIb shows a signal at 151.6 ppm at -40 °C. The minor isomers of IIa and IIb show signals at 151.7 ppm and 154.5 ppm, respectively.

These spectral data show that the *syn–anti* isomer based on the orientation of the nitroso group is present in IIa—d. We assume that the preferred conformation generated by an interlocked steric interaction among the N^3-substituents, the methyl group at the *ortho*-position of the phenyl ring and the N-nitroso group is a significant factor determining the direction of reaction in the 2-tolyl derivatives and the 4-tolyl isomers.

The mechanism proposed for the decomposition of the trisubstituted nitrosoureas (IIa—d) which give the trisubstituted triazenes (IIIa—d) and the 2-nitroaryl compounds (IVb, d) is illustrated in Chart 2. The first step in the thermal decomposition is the production of a diazoester intermediate (V) or an ion pair (VI), as in the recently reported thermolysis of

Table II. IR, UV and ^{1}H-NMR Spectral Data[a] for 3,3-Dialkyl-1-tolylureas (Ia—d), 3,3-Dialkyl-1-nitroso-1-tolylureas (IIa—d), 3,3-Dialkyl-1-tolyltriazenes (IIIa—d) and 3,3-Dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d)

Compd.	IR ν_{max} cm^{-1} CO	UV λ_{max} nm (log ε)					^{1}H-NMR, δ[11]				
							CH_3–Ph[c]	CH_3–C[d]	CH_3–N[c]	–CH_2–N	NH[b]
Ia	1650	243	273	282			2.22	1.20	—	3.37[e]	6.15
		(4.02)	(3.00)	(sh)							
Ib	1650	246	282				2.25	1.15	—	3.32[e]	6.37
		(4.07)	(3.03)								
Ic	1653	243	262	270	280		2.15	—	2.97	4.52[c]	6.40
		(4.09)	(sh)	(sh)	(sh)						
Id	1655	243	270	290			2.30	—	2.98	4.60[c]	6.52
		(4.23)	(sh)	(sh)							
IIa	1680	242	260	394			2.05	1.18	—	3.50[e]	—
		(3.70)	(sh)	(2.06)							
IIb	1700	242	288	395			2.35	1.15[b]	—	3.40[b]	—
		(3.80)	(3.67)	(sh)							
IIc	1680	243	255	261	394		2.05	—	3.10	4.75[c]	—
		(4.13)	(4.15)	(4.17)	(2.07)						
IId	1700	293	262	267	280	391	2.38	—	2.88[b]	4.67[b]	—
		(4.13)	(4.13)	(4.13)	(sh)	(2.32)					
IIIa	—	239	288	315			2.40	1.23	—	3.73[e]	—
		(3.94)	(4.15)	(4.14)							
IIIb	—	239	287	318			2.32	1.23	—	3.73[e]	—
		(3.75)	(4.12)	(4.09)							
IIIc	—	238	284	312			2.39	—	3.20	4.94[c]	—
		(3.93)	(4.10)	(sh)							
IIId	—	238	287	297	315		2.32	—	3.15	4.93[c]	—
		(3.94)	(4.13)	(sh)	(4.13)						
IVb	1658	244	285	395			2.35	1.25	—	3.45[e]	10.05
		(4.27)	(3.77)	(3.65)							
IVd	1660	246	268	289	389		2.34	—	3.10	4.65[c]	10.12
		(4.28)	(3.79)	(sh)	(3.59)						

a) IR and UV spectra were measured in $CHCl_3$, and ^{1}H-NMR spectra in $CDCl_3$.
b) Broad signals. *c)* Singlet. *d)* Triplet, $J=7$ Hz. *e)* Quartet, $J=7$ Hz.

trialkylnitrosoureas,[7] and the second step is the decomposition of these intermediates to afford aryltriazenes and carbon dioxide.

On the other hand, the mechanism of formation of 2-nitro-4-tolylureas (IVb, d) can be explained by a free radical process.[8] The initial step is denitrosation by elimination of a nitroso radical, and the next step is oxidation of the nitroso radical to a nitro radical. The final step is nitration of the phenyl ring by the active species. This pathway is similar to the process described for the nitration of 2,3-dehydropiperidine, which is obtained from the nitroso enamine.[9] Another possible mechanism for the conversion of N-nitrosoureas to C-nitro compounds involves the formation and oxidation of an intermediate (2-nitrosoaryl)urea produced by rearrangement of a nitroso group. Further studies on the decomposition of IIa, b are in progress, in relation to the conformations of these molecules.

Experimental

All melting points are uncorrected. IR spectra were measured on a JASCO A-102 spectrometer and ultraviolet (UV) spectra on a Shimadzu UV-240 spectrophotometer. HPLC was done on a JASCO TWINCLE chromatograph with UV absorbance detector (Toyo Soda UV-8) operating at 254 nm and a 4×300 mm i.d. column packed with

TABLE III. ^{13}C-Chemical Shifts[12] of 3,3-Dialkyl-1-tolylureas (Ia—d), 3,3-Dialkyl-1-nitroso-1-tolylureas (IIa—d), 3,3-Dialkyl-1-tolyltriazenes (IIIa—d) and 3,3-Dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d)

Compd.	CO	Phenyl ring						N–CH$_2$	N–CH$_3$	C–CH$_3$	Pyridine nucleus				
		C-1	C-2	C-3	C-4	C-5	C-6				C′-2	C′-3	C′-4	C′-5	C′-6
Ia	154.9	137.6	128.9	130.1	123.6	126.5	123.1	41.6		17.1, 13.9					
Ib	154.8	136.9	120.2	128.9	131.8	128.9	120.2	41.2		20.5, 13.7					
Ic	155.9	136.9	129.4	130.3	124.4	126.7	123.4	50.0	34.6	17.7	149.0	133.5	135.4	123.7	149.0
Id	156.1	136.6	120.8	129.1	132.6	129.1	120.8	49.8	34.4	20.7	149.0	133.6	135.4	123.5	148.1
IIa[d]	154.2	134.0	136.4	130.9	127.3	129.9	126.7	42.2 44.1		18.0, 12.2 13.7					
	151.7	[b]	136.8	132.0	126.9	129.1	124.7	[b]		18.6 [b]					
IIb[d]	151.6	135.3	117.6	130.3	137.6	130.3	117.6	41.4 42.8		21.0, 12.4 13.7					
	154.5	131.4	126.6	129.9	139.7	129.9	126.6	[b]		21.2 [b]					
IIc	155.4	133.5[c]	136.4	130.9	127.5	130.1	126.8	51.3[a]	37.0[a]	17.9	149.2	131.6[c]	135.8[a]	123.8	149.2
IId[d]	153.3	134.7[c]	118.3	130.3	137.8	130.3	118.3	49.9[a]	34.4[a]	21.0	149.3	130.8[c]	135.7	123.9	149.0
	155.7	131.6[c]	126.9	130.0	139.6	130.0	126.9	51.2[a]	33.7[a]	[b]	149.8	131.0[c]	135.4	123.6	149.0
IIIa		149.1	132.4	130.5	125.0	126.2	116.5	44.9[a]		17.7, 12.7[a]					
IIIb		149.1	120.4	129.3	134.5	129.3	120.4	44.5[a]		20.9, 12.9[a]					
IIIc		148.2	132.5[c]	130.6	125.8	126.2	116.7	54.5[a]	36.2[a]	17.6	149.3	132.8[c]	135.5	123.5	149.0
IIId		148.5	120.6	129.4	135.5	129.4	120.6	54.7[a]	35.6[a]	20.9	149.4	132.5	135.4	123.5	149.0
IVb	153.7	131.0	135.3	125.1	135.5	136.9	121.4	42.0		20.3, 13.7					
IVd	154.7	131.7	135.7	125.2	134.7	136.8	121.4	49.9	34.4	20.3	149.2	133.0	135.4	123.6	149.1

a) Broad signal. *b*) Not observable under the experimental conditions used.
c) Assignments may be reversed.
d) The signals are classified as being due to two conformational isomers on the basis of their intensities.

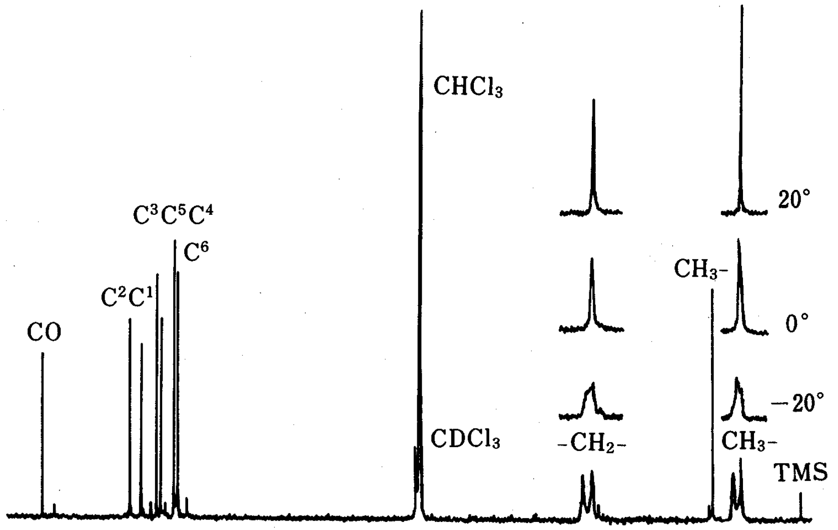

Fig. 2. ^{13}C-NMR Spectrum of IIa in $CDCl_3$ (−40 °C)

The weak and intense signals represent conformentional isomers. $CHCl_3$ was placed in an external tube.

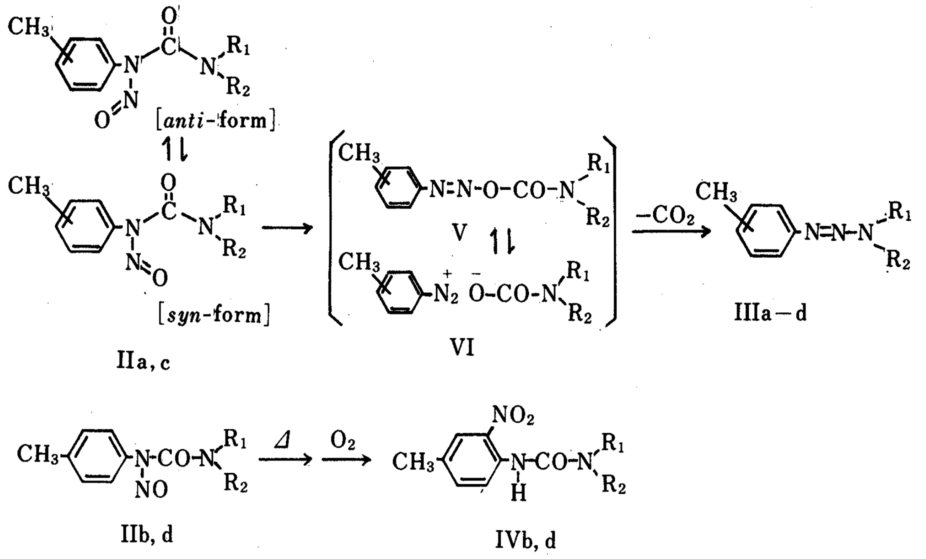

Chart 2

TSK-Gel LS310K (Toyo Soda). Eluent, *n*-hexane–ethyl acetate (4:1); flow rate, 2 ml/min. Peak areas were determined with a Shimadzu C-E1B chromatopack. ^{1}H-NMR spectra were measured with a Varian EM 360A and ^{13}C-NMR spectra were measured with a JEOL FX-200 spectrometer with tetramethylsilane as an internal standard. The abbreviations are as follows: s, singlet; d, doublet; t, triplet; Ph, phenyl ring; Py, pyridine ring; sh, shoulder. IR, UV and NMR spectral data and analytical data for the ureas (Ia—d), the nitrosoureas (IIa—d), the triazenes (IIIa—d) and the nitro compounds (IVb, d) are shown in Tables II, III and IV, respectively.

1-Aryl-3,3-dialkylureas (Ia—d)——A typical experiment is described here for Ia.

3,3-Diethyl-1-(2-tolyl)urea (Ia): 2-Tolyl isocyanate (5.5 g, 0.075 mol) was added to a solution of diethylamine (10 g, 0.075 mol) in ether (300 ml) at −5 °C with stirring. The resulting crystals (after concentration of the mixture, if necessary) were filtered off, and recrystallized from a mixture of ether and *n*-hexane. Colorless needles, mp 82—83 °C. Yield, 14.5 g (94%). Other ureas (Ib—d) were prepared from suitable isocyanates and amines by the same method.

3,3-Diethyl-1-(4-tolyl)urea (Ib): Colorless plates (from a mixture of ether and *n*-hexane), mp 69.5—70.5 °C. Yield, 86%.

3-Methyl-3-(3-pyridylmethyl)-1-(2-tolyl)urea (Ic): Colorless prisms (from a mixture of ether and $CHCl_3$), mp 92—93 °C. Yield, 82%.

3-Methyl-3-(3-pyridylmethyl)-1-(4-tolyl)urea (Id): Colorless pillars (from a mixture of ether and $CHCl_3$), mp

TABLE IV. Analytical Data for 3,3-Dialkyl-1-tolylureas (Ia—d), 3,3-Dialkyl-1-nitroso-1-tolylureas (IIa—d), 3,3-Dialkyl-1-tolyltriazenes (IIIa, c, d) and 3,3-Dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d)

Compd.	Formula	Analysis (%)					
		Calcd			Found		
		C	H	N	C	H	N
Ia	$C_{12}H_{18}N_2O$	69.87	8.80	13.58	69.60	8.87	13.35
Ib	$C_{12}H_{18}N_2O$	69.87	8.80	13.58	69.97	8.70	13.43
Ic	$C_{15}H_{17}N_3O \cdot H_2O$	65.91	7.01	15.37	65.98	6.88	15.34
Id	$C_{15}H_{17}N_3O$	70.56	6.71	16.46	70.68	6.74	16.51
IIa	$C_{12}H_{17}N_3O_2$	61.25	7.28	17.86	61.35	7.31	18.08
IIb	$C_{12}H_{17}N_3O_2$	61.25	7.28	17.86	61.37	7.31	17.94
IIc[a]	$C_{15}H_{16}N_4O_2 \cdot 1/4H_2O$	62.38	5.76	19.40	62.44	5.58	19.42
IId[a]	$C_{15}H_{16}N_4O_2 \cdot 1/5H_2O$	62.57	5.74	19.46	62.60	5.61	19.53
IIIa	$C_{11}H_{17}N_3$	69.07	8.96	21.97	68.53	8.89	22.25
IIIc	$C_{14}H_{16}N_4$	69.97	6.71	23.32	69.63	6.74	23.14
IIId	$C_{14}H_{16}N_4$	69.97	6.71	23.32	69.61	6.69	23.22
IVb	$C_{12}H_{17}N_3O_3$	57.35	6.82	16.72	57.47	6.89	16.58
IVd[a]	$C_{15}H_{16}N_4O_3 \cdot 1/4H_2O$	59.10	5.46	18.38	59.37	5.31	18.29

a) Hygroscopic.

135—136 °C. Yield, 80%.

1-Aryl-3,3-dialkyl-1-nitrosoureas (IIa—d)——3,3-Diethyl-1-nitroso-1-(2-tolyl)urea (IIa): A solution of sodium nitrite (1.6 g, 0.023 mol) in water (8 ml) was added in small portions to a solution of Ia (3.0 g, 0.015 mol) in formic acid (20 ml) under ice-water cooling. The reaction mixture was stirred for 30 min below 0 °C. Then cold water (20 ml) was added to the solution, and the mixture was neutralized with sodium bicarbonate and extracted with CH_2Cl_2. The CH_2Cl_2 layer was filtered through a silicone treated filter paper (1 ps phase separators, Whatman Ltd.) and evaporated under reduced pressure in an ice-water bath. The residue was chromatographed on a column of silica gel with a mixture of ether and *n*-hexane, using a Liebig condenser instead of an ordinary column tube and circulating cold water. IIa was a pale yellow oily product at room temperature, but solidified in a refrigerator. Yield, 1.5 g (44%).

3,3-Diethyl-1-nitroso-1-(4-tolyl)urea (IIb): This compound was prepared in the same way as described for IIa. A yellow oily product (solid in a refrigerator). Yield, 53%.

3-Methyl-3-(3-pyridylmethyl)-1-nitroso-1-(2-tolyl)urea (IIc): A solution of sodium nitrite (1.4 g, 0.02 mol) in water (5 ml) was added dropwise to a solution of Ic (2.6 g, 0.01 mol) in 10% HCl (20 ml) at −5 °C with stirring, and the mixture was further stirred for 30 min at −5 °C. The reaction mixture was neutralized with sodium bicarbonate, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was treated as described in the case of IIa. A mixture of ether and $CHCl_3$ was used as an eluting solvent in column chromatography. IIc was a pale yellow oily product.

3-Methyl-3-(3-pyridylmethyl)-1-nitroso-1-(4-tolyl)urea (IId): This compound was prepared in the same way as described for IIc. A yellow oily product (solid in a refrigerator). Yield, 46%.

1-Aryl-3,3-dialkyltriazenes (IIIa—d)——A typical experiment is described.

3,3-Diethyl-1-(2-tolyl)-triazene (IIIa): A solution of sodium nitrite (1.4 g, 0.02 mol) in water (7 ml) was added to a solution of 2-toluidine (2.14 g, 0.02 mol) in a mixture of 36% HCl (3.4 ml) and water (20 ml) at 0 °C with stirring, and the mixture was further stirred for 30 min. The reaction mixture was added to a solution of diethylamine (1.46 g, 0.04 mol) in water (50 ml) at 0—5 °C with stirring. After being stirred for 2 h, the reaction mixture was extracted with CH_2Cl_2, and the CH_2Cl_2 layer was dried over anhyd. Na_2SO_4. The solvent was evaporated off and the residue was chromatographed on a column of silica gel with a mixture of ether and CH_2Cl_2 as an eluting solvent. The oily product obtained was distilled, bp 103 °C (4 mmHg).[10] Yield, 1.3 g, (34%).

3,3-Diethyl-1-(4-tolyl)triazene (IIIb): A yellow oily product, bp 110 °C (4 mmHg).[10] Yield, 27%.

3-Methyl-3-(3-pyridylmethyl)-1-(2-tolyl)triazene (IIIc): A pale yellow oily product, bp 168 °C (1 mmHg). Yield, 83%.

3-Methyl-3-(3-pyridylmethyl)-1-(4-tolyl)triazene (IIId): A yellow hygroscopic oil, bp 153 °C (2 mmHg). Yield, 75%.

3,3-Diethyl-1-(2-nitro-4-tolyl)urea (IVb)——Fuming nitric acid (*d*: 1.52, 2 ml) was added to a solution of Ib

(1.5 g, 0.007 mol) in acetic acid (10 ml) at 0—5 °C with stirring and the mixture was stirred for 30 min at room temperature. The reaction mixture was poured onto crushed ice and extracted with ether. The ether layer was washed with saturated sodium bicarbonate solution and dried over anhyd. Na_2SO_4. The solvent was evaporated off and the residue was recrystallized from *n*-hexane. Yellow prisms, mp 45—46 °C. Yield, 0.95 g (52%).

3-Methyl-3-(3-pyridylmethyl)-1-(2-nitro-4-tolyl)urea (IVd)——Fuming nitric acid (*d*: 1.52, 3 ml) was added to a solution of Id (1.3 g, 0.005 mol) in acetic acid (8 ml) with stirring and the mixture was stirred for 30 min at room temperature. The reaction mixture was poured onto crushed ice and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water several times and dried over anhyd. Na_2SO_4. The solvent was evaporated off and the residue was extracted with hot ether. The ether was evaporated off and the residue was chromatographed on a column with silica gel. The fraction eluted with $CHCl_3$ gave IVd. Yellow needles (from a mixture of ether and *n*-hexane), mp 76—77 °C. Yield, 0.65 g (42%).

Formation of 3,3-Dialkyl-1-(2-tolyl)triazenes (IIIa, c) by the Decomposition of 3,3-Dialkyl-1-nitroso-1-(2-tolyl)ureas (IIa, c)——Decomposition of IIa: 3,3-Diethyl-1-nitroso-1-(2-tolyl)urea (IIa) (470 mg, 0.002 mol) was dissolved in 2 ml of $CHCl_3$,⁵⁾ and allowed to stand for 2 d at room temperature. The solvent was evaporated off under reduced pressure, and the residue was chromatographed on a column of silica gel. The fraction eluted with *n*-hexane gave 3,3-diethyl-1-(2-tolyl)triazene, which was identical (IR and NMR spectra) with the authentic IIIa obtained above. Yield, 200 mg (52%).

Decomposition of IIc: (i) 3-Methyl-3-(3-pyridylmethyl)-1-nitroso-1-(2-tolyl)urea (IIc) (1.42 g, 0.005 mol) was dissolved in 5 ml of $CHCl_3$,⁵⁾ and the solution was treated as described for the decomposition of IIa. The fraction eluted with ether gave 3-methyl-3-(3-pyridylmethyl)triazene in 39% (0.47 g) yield. This compound was identical (IR and NMR spectra) with the authentic IIIc obtained above.

(ii) A solution of Ic (2.55 g, 0.01 mol) in 10% HCl (20 ml) was treated with sodium nitrite (1.4 g, 0.02 mol) as described in the case of nitrosation of Ic. The obtained crude nitrosourea (IIc) was dissolved in 10 ml of $CHCl_3$,⁵⁾ and the solution was warmed at 55 °C for 3.5 h. Then, the solvent was evaporated off and the residue was chromatographed on a column of silica gel. The fraction eluted with ether gave IIIc. Yield, 1.1 g (46%).

Formation of 3,3-Dialkyl-1-(4-tolyl)triazenes (IIIb, d), 3,3-Dialkyl-1-(2-nitro-4-tolyl)ureas (IVb, d) and 3,3-Dialkyl-1-(4-tolyl)ureas (Ib, d) by the Decomposition of 3,3-Dialkyl-1-nitroso-1-(4-tolyl)ureas (IIb, d)——Decomposition of IIb: 3,3-Diethyl-1-nitroso-1-(4-tolyl)urea (IIb) (470 mg, 0.002 mol) was dissolved in 2 ml of $CHCl_3$,⁵⁾ and the solution was treated as described for the decomposition of IIa. The first fraction eluted with *n*-hexane gave 3,3-diethyl-1-(4-tolyl)triazene (IIIb) as a yellow oil. Yield, 0.1 g (26%). The second fraction eluted with a mixture of *n*-hexane and ether gave 3,3-diethyl-1-(2-nitro-4-tolyl)urea (IVb), yellow needles, mp 44—45 °C. Yield, 98 mg (20%). The third fraction eluted with ether provided 3,3-diethyl-1-(4-tolyl)urea (Ib), colorless plates, mp 70 °C. Yield, 40 mg (10%). These products were identical (IR and NMR spectra) with the authentic samples mentioned above.

Decomposition of IId: A solution of 3-methyl-3-(3-pyridylmethyl)-1-(4-tolyl)urea (IId) (1.42 g, 0.005 mol) in 5 ml of $CHCl_3$⁵⁾ was treated as described for the decomposition of IIa. The first fraction eluted with a mixture of *n*-hexane and ether gave 3-methyl-3-(3-pyridylmethyl)-1-(4-tolyl)triazene (IIId). Yield, 0.14 g (12%). The second fraction eluted with $CHCl_3$ gave 3-methyl-3-(3-pyridylmethyl)-1-(2-nitro-4-tolyl)urea (IVd), yellow needles, mp 77 °C. Yield, 0.3 g (20%). The third fraction eluted with the same solvent gave 3-methyl-3-(3-pyridylmethyl)urea (Id), colorless pillars, mp 135 °C. Yield, 94 mg (7%). These products were identical (IR and NMR spectra) with the authentic samples mentioned above.

Decomposition of 3,3-Diethyl-1-nitroso-1-tolylureas (IIa, b) in Various Solvents——Each of IIa, b (6 mg) was dissolved in 1 ml of various solvents as described in Table I. Each solution was allowed to stand for 2 d at room temperature, then $CHCl_3$ was added to the solution to give 10 ml total volume. The solution was measured by HPLC with 4-acetamide-2-nitrotoluene as an internal standard (mp 94.5 °C, lit.,¹³⁾ mp 95 °C). Operating condition were as described above. The yields of decomposition products (Ia, b, IIIa, b and IVb) are indicated in Table I.

Trapping of Carbon Dioxide——A solution of IIc (0.56 g, 0.002 mol) in 10 ml of $CHCl_3$⁵⁾ was warmed at 45 °C for 4 h. The solution began bubbling after about 10 min, and the evolved gas was passed through 5% $Ba(OH)_2$ solution (15 ml). The $BaCO_3$ formed was filtered off and dried at 110 °C. Yield, 138 mg (36%). IId (0.5 g, 0.0017 mol) was treated as described for IIc. Yield, 33 mg (9.5%).

References and Notes

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5) The presence of a small amount of water contained in chloroform influences the yields of triazenes. Thus,

"chloroform" and "well-dried chloroform" in this paper imply "a distilled chloroform" and "chloroform which was dried over Molecular Sieves 3 Å after distillation," respectively.

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11) The observable aromatic protons are as follows: Ib: 7.00, 7.22 (4H, a pair of d, $J=8.5$ Hz, Ph-$C_{3,5}$ and $C_{2,6}$). Id: 7.05, 7.25 (4H, a pair of d, $J=8$ Hz, Ph-$C_{3,5}$ and $C_{2,6}$), 7.68 (1H, td, $J=2$ and 7.5 Hz, Py-C_4). IIIb: 7.10, 7.33 (4H, a pair of d, $J=8.5$ Hz, Ph-$C_{3,5}$ and $C_{2,6}$). IIId: 7.15, 7.40 (4H, a pair of d, $J=8.5$ Hz, Ph-$C_{3,5}$ and $C_{2,6}$). IVb: 7.38 (1H, dd, $J=2$ and 8.5 Hz, Ph-C_5), 7.97 (1H, d, $J=2$ Hz, Ph-C_3), 8.58 (1H, d, $J=8.5$ Hz, Ph-C_6). IVd: 7.40 (1H, dd, $J=2$ and 9 Hz, Ph-C_5), 7.95 (1H, d, $J=2$ Hz, Ph-C_3), 8.56 (1H, d, $J=9$ Hz, Ph-C_6), 7.68 (1H, td, $J=2$ and 8 Hz, Py-C_4).

12) The spectra were measured under the following conditions: nucleus ^{13}C at a frequency of 50.10 MHz with a spectral width of 10000 Hz; pulse width of 6 μs ($\theta=36°$); acquisition time of 0.8192 s; number of data points of 16384; temperature of *ca.* 30 °C except for IIa, b at -40 °C and IIc, d at -20 °C. Chemical shifts are relative to Me_4Si and are accurate to ± 0.05 ppm. Concentrations were 0.1—1.0 mmol/ml.

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