

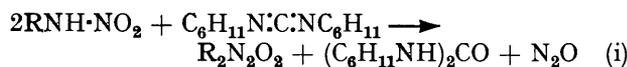
Nitramines and Nitramides. Part XVII.¹ Reactions with Dicyclohexylcarbodi-imide

By Alexander H. Lamberton,* Roger D. Porter, and Hafiz M. Yusuf, Department of Chemistry, The University of Sheffield, Sheffield S3 7HF

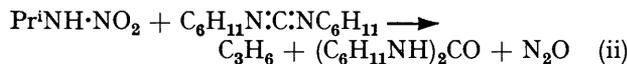
The reaction of dicyclohexylcarbodi-imide with aliphatic primary nitramines ($\text{RNH}\cdot\text{NO}_2$) yielded *NN'*-dicyclohexylurea and nitrous oxide, together with variable proportions of $\text{RN}\cdot\text{NO}_2\text{R}$, $\text{R}_2\text{N}\cdot\text{NO}_2$, and the olefin which might be derived from the alkyl group R. 2,4,6-Tribromophenylnitramine gave the urea and a tar, from which 1,3,5-tribromobenzene was obtained by sublimation.

Primary nitro-carbamates ($\text{RO}_2\text{C}\cdot\text{NH}\cdot\text{NO}_2$; R = Me or Et) yielded stable addition compounds which we formulate as $\text{C}_6\text{H}_{11}\text{N}(\text{CO}_2\text{R})\cdot\text{C}(\text{NH}\cdot\text{NO}_2)\cdot\text{NC}_6\text{H}_{11}$, and which could be hydrolysed to *NN'*-dicyclohexyl-*N''*-nitroguanidine; but concurrent reactions took place so that, in the case of nitrourethane (R = Et), the dicyclohexylurea, nitrous oxide, carbon dioxide, and ethylene were also identified as products. A few reactions with other nitramines and carbodi-imides are reported briefly.

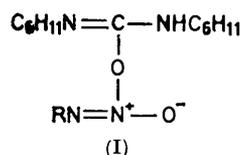
THE reaction between aliphatic nitramines and dicyclohexylcarbodi-imide was found to proceed at a convenient rate in dioxan or ether as solvent. *NN'*-Dicyclohexylurea separated from the solutions, and gas was evolved smoothly. The observed rate of gas evolution (between first and second order) did not help us to interpret the reaction. In the cases of methyl- and benzyl-nitramines the yield of the urea (based on the di-imide used) was nearly theoretical provided that a sufficient excess of the nitramine was present; otherwise (as in the case of 1:1 molecular proportions) the urea obtained did not exceed 0.5 mol per mol of nitramine. The yield of nitrous oxide (in the presence of sufficient di-imide) was 0.4–0.5 mol per mol of nitramine. We conclude that for these compounds the overall reaction may be formulated as in equation (i). Ethylnitramine



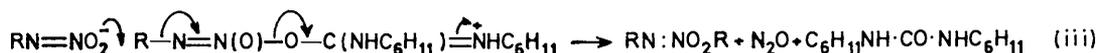
yielded some, and isopropylnitramine considerably more gas; in the latter case nitrous oxide and propene were produced in a ratio of ca. 55:45, and the yield of dialkyl-nitramines ($\text{R}_2\text{N}_2\text{O}_2$) was small. It appears that, for isopropylnitramine at least, a 1:1 overall reaction



[equation (ii)] is predominant. Later experiments on larger quantities showed that the crude dialkylnitramines



consisted mainly of the *NO*-variety, but were accompanied by some of the *NN*-isomer.



We consider that the first stage is the production of a transient intermediate which we formulate with the

¹ Part XVI, F. Dewhurst and A. H. Lamberton, *J. Chem. Soc. (B)*, 1971, 788.

² So presented for simplicity, and following H. G. Khorana (*Chem. Rev.*, 1953, **53**, 154); protonation (to yield the urea) might alternatively be the final rather than the initial step.

isonitramino-structure (I), since the formation of an N-C bond between the nitramine and the di-imide would lead to a guanidine rather than the urea. The protonated ² intermediate may be attacked by $\text{RN}^-\cdot\text{NO}_2 \rightleftharpoons \text{RN}:\text{NO}_2^-$ to give, by an extended *E2* type of elimination, the dialkylnitramines, nitrous oxide, and the dicyclohexylurea [equation (iii)]. Alternatively, when R is more electron donative, the protonated intermediate may decompose in *E1* fashion to give R^+ and hence the olefin, with relatively little alkylation of the surplus nitramine. In the case of ethylnitramine the *E2* route appears predominant, but with some contribution from the *E1*.

The production of *NO*-diethylnitramine from ethylnitramine and dicyclohexylcarbodi-imide seems to be more stereospecific than the alternative route from ethyl iodide and the silver salt of the nitramine. Material prepared by the first method showed kinetically homogenous behaviour on decomposition in aqueous potassium hydroxide, whereas crude samples prepared by the second method showed the kinetic anomaly which has been previously described.³ We conclude that preparation by use of the carbodi-imide leads almost wholly to the *trans*-Et/OEt form^{3,4} of *NO*-diethylnitramine. The rate of decomposition of the pure compound in dilute potassium hydroxide was consonant with the rates observed³ for other *NO*-dialkylnitramines.

Phenyl- and *p*-nitrophenyl-nitramines reacted more vigorously than the aliphatic nitramines with dicyclohexylcarbodi-imide, but were not investigated in detail. The more accessible 2,4,6-tribromophenylnitramine gave gas, the urea, and a tar which yielded, surprisingly, 1,3,5-tribromobenzene on sublimation *in vacuo*. This denitramination possibly occurs during the sublimation; and we can only comment that it does not appear to depend on a free-radical abstraction of hydrogen from

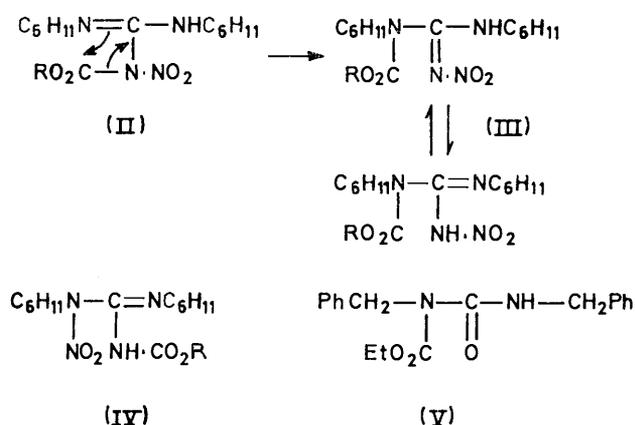
the solvent during the initial reaction, since similar results were obtained when carbon tetrachloride was used in place of ether. 2,6-Dibromo-4-methylphenyl-

³ A. H. Lamberton and G. Newton, *J. Chem. Soc.*, 1961, 1797.

⁴ A. H. Lamberton and H. M. Yusuf, *J. Chem. Soc. (C)*, 1969, 397.

nitramine behaved in the same fashion, but with a poorer yield of 3,5-dibromotoluene.

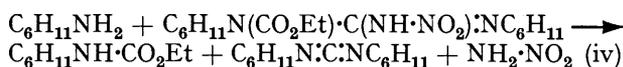
Nitrourethane reacted readily with dicyclohexylcarbodi-imide to give a stable 1:1 addition compound, together with *NN'*-dicyclohexylurea and a mixture of gases (nitrous oxide, carbon dioxide, and ethylene). The addition compound did not react further with fresh nitrourethane or carbodi-imide; nor did it react with ethylnitramine. The yields of addition compound, urea, and total gas were measured as accurately as possible over a wide range of molar ratios (nitrourethane/carbodi-imide, 0.25–4.0) in dioxan as solvent, and seem compatible with the following suggestions. First, nitrourethane reacts concurrently in two ways with dicyclohexylcarbodi-imide, to yield isonitramino- (I; R = EtO₂C) and nitramino- (II; R = Et) intermediates; the latter rearranges to the addition compound (III; R = Et) and takes no further part in the reactions. Secondly, the nitrourethane and carbodi-imide not used in the production of (III) react in 2:1 ratio to give the urea and gases, presumably by the action of a second molecule of nitrourethane on the isonitramino-intermediate.



Schemes for the production of the urea, nitrous oxide, carbon dioxide, and ethylene from the isonitramino-intermediate seem as yet too speculative to warrant publication, but the addition compound was identified as *NN'*-dicyclohexyl-*N*-ethoxycarbonyl-*N''*-nitroguanidine (III; R = Et) on the following grounds. It acted as a nitrating agent in sulphuric acid, and could be converted into *NN'*-dicyclohexyl-*N''*-nitroguanidine by mild hydrolysis; specimens of this nitroguanidine were also prepared by the action of nitramine (NH₂·NO₂) on dicyclohexylcarbodi-imide, and by the direct nitration of *NN'*-dicyclohexylguanidine. *NN'*-Dicyclohexyl-*N''*-nitroguanidine was more stable under alkaline conditions than the related nitramino-imidazolines investigated by McKay,⁵ but could be further hydrolysed to *NN'*-dicyclohexylurea by more drastic treatment. Addition compounds of type (III) might be of either tautomeric form, but the only real alternatives would

seem to be (II) and (IV), the latter produced by migration of NO₂ in place of CO₂R. These seem to us less likely by reason of the n.m.r. spectra. Compounds of type (II) might be expected to show a cyclohexyl CH₂ multiplet similar in shape to that from the symmetrical dicyclohexylcarbodi-imide, but the addition compounds which we prepared (III; R = Et or Me) gave a different spectrum in this respect. Again, hydrolysis of (IV) would give *NN'*-dicyclohexyl-*N*-nitroguanidine, in which the cyclohexyl groups are not identical; but our dicyclohexylnitroguanidine gave a multiplet whose shape closely resembled that from the symmetrical dicyclohexylcarbodi-imide, and was different from that shown by both the addition compounds.

Heating of (III; R = Et) in xylene with moist cyclohexylamine again removed the ethoxycarbonyl group to yield *NN'*-dicyclohexyl-*N''*-nitroguanidine, but under dry conditions *NN'*-dicyclohexylurea and *N*-cyclohexylurethane were produced. The formation of the cyclohexylurethane showed that the ethoxycarbonyl group was removed as a unit, and therefore the central guanidino carbon atom of the molecule (and not the C=O of the ethoxycarbonyl group) must become the C=O of the urea. The primary reaction thus appears to be equation (iv). The nitramine may be evolved not as



itself, but in the form of its decomposition products, N₂O + H₂O, and we think the source of the ultimate *NN'*-dicyclohexylurea to be carbodi-imide and water produced directly, or from NH₂·NO₂, at earlier stages. This general formulation is supported by (a) the presence of some dicyclohexylcarbodi-imide (i.r. and n.m.r. evidence) in the crude material before crystallisation of the cyclohexylurethane; and (b) the formation of dicyanohexylurea, but not of diphenylurea, when aniline was used in place of cyclohexylamine.

Di-*p*-tolylcarbodi-imide reacted with nitrourethane to give an addition compound which could not be adequately purified, but whose n.m.r. spectrum (in particular, two aromatic Me singlets) was consistent with an unsymmetrical structure. Hydrolysis gave *NN'*-di-*p*-tolylurea. The addition product from dibenzylcarbodi-imide and nitrourethane was apparently thermally unstable, losing nitrous oxide to yield *NN'*-dibenzyl-*N*-ethoxycarbonylurea (V) on heating.

EXPERIMENTAL

N.m.r. spectra were measured with a Varian A60 spectrometer (deuteriochloroform as solvent and tetramethylsilane as internal reference). Mass spectra were recorded with A.E.I. MS 9^o or MS 12 spectrometers. Dicyclohexylcarbodi-imide was prepared from *NN'*-dicyclohexylurea;⁶ the nitramines and nitro-carbamates used have all been described.⁷

⁵ A. F. McKay, *Chem. Rev.*, 1952, **51**, 329.

⁶ G. Amiard and R. Heymès, *Bull. Soc. chim. France*, 1956, 1360.

⁷ For a review of preparative methods see H. Söll, 'Methoden der Organischen Chemie (Houben-Weyl)', Georg Thieme Verlag, Stuttgart, 4th edn., 1958, vol. XI (2), p. 99.

In preliminary experiments the reagents (0.5—2.0 mmol) were separately loaded into a conical flask (25 ml) whose base had been indented to form a dividing ridge, and diluted with adequate dioxan (0.1—0.5 ml). The flask was attached to a manometer for the measurement of gas evolution at constant pressure, and set in the thermostat. The reaction was initiated by tilting the flask; on conclusion ether was added and the insoluble *NN'*-dicyclohexylurea collected. Typical results for four nitramines are included in the Table. Experiments on a larger scale were carried out by heating the nitramine (*ca.* 5 g) with dicyclohexylcarbodi-imide (0.5 mol. equiv.) overnight under reflux in dry ether (*ca.* 20 ml). After collection of the precipitate of *NN'*-dicyclohexylurea the filtrate was washed with aqueous sodium hydrogen carbonate, dried, and fractionated by distillation *in vacuo*; the results are included in the Table.

(characterised as the 2,4-dinitrophenylhydrazone). Addition of ether to the residue promoted crystallisation of *NN-bis-4-nitrobenzyl-nitramine* as needles, m.p. 155° (from moist ethanol) (Found: C, 50.7; H, 3.8; N, 17.2. $C_{14}H_{13}N_4O_6$ requires C, 50.6; H, 3.6; N, 16.9%), whose structure was confirmed by the following synthesis of purer material. *Bis-4-nitrobenzylamine hydrochloride*¹⁰ (3.3 g) was added with stirring and cooling (ice) to a mixture of acetic anhydride (12 ml) and colourless fuming nitric acid (2 ml). The white slurry thus formed was heated to 85° (evolution of nitrogen oxides), maintained above 60° for 30 min, and poured into water (40 ml). The precipitate (2.9 g) gave *NN-bis-4-nitrobenzyl-nitramine*, needles, m.p. 156—158° (from ethanol) (Found: C, 50.3; H, 3.6%).

NN-Bis-4-nitrobenzyl-nitramine was also obtained by treatment of the potassium salt of 4-nitrobenzyl-nitramine with 4-nitrobenzyl chloride in ethanol at 20°; this product,

Conditions Molar ratio, nitramine : di-imide	Yields in reactions of $RNH \cdot NO_2$ with $C_6H_{11}N:C:NC_6H_{11}$						
	In dioxan at 25°				In ether at 35°		
	1 : 1	2 : 1	1 : 1	2 : 1	2 : 1	2 : 1	2 : 1
Products	Gas (%) ^a		$(C_6H_{11}NH)_2CO$ (%) ^b		$(C_6H_{11}NH)_2CO$ (%) ^b	$RN:NO_2R$ (%) ^c	$R_2N \cdot NO_2$ (%) ^c
R = Me	45	42	46	94	90	14	6
Et	59	57	37	68	91	45	15
Pr ^l	98	71	61	82	81	Trace	Trace
PhCH ₂	52	44	43	84	87	<i>d</i>	<i>d</i>

^a Calc. as mol per mol of initial nitramine. ^b Calc. as mol per mol of initial di-imide. ^c Calc. as mol per 2 mol of initial nitramine. ^d Crude mixture decomposed on distillation; see text.

Stereospecificity of the Reaction.—A sample of *NO*-diethylnitramine prepared by the silver salt method⁸ showed a fall as the reaction proceeded (10^{3k} from 24.9 to 6.8 min⁻¹) in the apparent first-order rate constant of decomposition in 0.243M-potassium hydroxide at 70°. This anomaly was removed by partial decomposition and recovery.³ Material prepared by use of the di-imide, and purified only by distillation, showed no such anomaly. Fully purified *NO*-diethylnitramine prepared by either method gave a second-order rate constant of decomposition (k_{OH^-} of 0.035 l mol⁻¹ min⁻¹ for 0.05M-*NO*-diethylnitramine in 0.243M-potassium hydroxide at 70°). Methods of measurement have been described^{9,10} and the rate is given in terms of min⁻¹ to facilitate comparison with earlier results.³

Dibenzyl- and Bis-4-nitrobenzyl-nitramines.—We failed to isolate pure *NO*-dibenzyl-nitramine by vacuum distillation of crude material prepared by either the silver salt or the carbodi-imide method. Vigorous decomposition occurred at temperatures >70°, with the production of benzaldehyde (characterised as the semicarbazone). Evaporation (40° and 0.1 mmHg) of volatile constituents without attempting distillation left crude liquid samples with closely similar i.r. spectra, which were presumably mainly *NO*-dibenzyl-nitramine (Found, for sample prepared from benzyl chloride and the silver salt of benzyl-nitramine: C, 68.9; H, 5.9; N, 11.1. Calc. for $C_{14}H_{14}N_2O_2$: C, 69.4; H, 5.8; N, 11.6%).

4-Nitrobenzyl-nitramine (3.30 g) and dicyclohexylcarbodi-imide (1.73 g) were heated to reflux in dioxan (20 ml) for 36 h, and *NN'*-dicyclohexylurea (1.50 g, 80%) was collected after cooling. Vacuum distillation of the filtrate was ineffective, yielding at 100° some 4-nitrobenzaldehyde

⁸ P. Bruck and A. H. Lamberton, *J. Chem. Soc.*, 1955, 3997; 1957, 4198.

and the di-imide preparation, were slightly coloured but otherwise identical with the material produced by direct nitration.

The silver salt of 4-nitrobenzyl-nitramine (7.3 g) was refluxed in dry ether for 36 h with 4-nitrobenzyl bromide (5.2 g). Removal of the silver bromide and partial evaporation gave a solid, which yielded *NO-bis-4-nitrobenzyl-nitramine* as pale yellow needles, m.p. 120—122° (from ethanol) (Found: C, 50.7; H, 3.6. $C_{14}H_{12}N_4O_6$ requires C, 50.6; H, 3.6%).

Reaction of 2,4,6-Tribromophenyl-nitramine.—A vigorous reaction occurred when the nitramine (3.75 g, 10 mmol) was mixed with dicyclohexylcarbodi-imide (2.06 g, 10 mmol) in ether (40 ml). After warming for 1 h, *NN'*-dicyclohexylurea (1.72 g, 77%) was collected. The filtrate was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to yield a tar, from which 1,3,5-tribromobenzene (0.78 g) was isolated by vacuum sublimation. Similar results were obtained when benzene or carbon tetrachloride was used as solvent.

Preparation of 1 : 1 Addition Compounds (III; R = Et or Me) with *N*-Nitrocarbarnates.—Nitrourethane (ethyl *N*-nitrocarbarnate) (6.7 g, 50 mmol) was heated overnight under reflux with dicyclohexylcarbodi-imide (5.2 g, 25 mmol) in dry ether (50 ml), and the precipitate of *NN'*-dicyclohexylurea (2.3 g, 40%) was collected. The filtrate was washed with aqueous sodium hydrogen carbonate and evaporated to yield an oil, which was dissolved in 75% acetic acid and set aside in a refrigerator. *NN'-Dicyclohexyl-N-ethoxycarbonyl-N'-nitroguanidine* (4.2 g, 50%)

⁹ J. Barrott, I. N. Denton, and A. H. Lamberton, *J. Chem. Soc.*, 1953, 1998.

¹⁰ H. R. Snyder and J. R. Demuth, *J. Amer. Chem. Soc.*, 1956, 78, 1981.

separated from the solution to give finally prisms of m.p. 92–93° (from AcOH–H₂O, 3 : 1 v/v) (Found: C, 57.0; H, 8.1; N, 16.2%; *m/e* 294. C₁₆H₂₆N₄O₄ requires C, 56.5; H, 8.3; N, 16.4%; *M* – NO₂, 294); ν_{\max} (KBr) 1700 (C=O) and 1590 (NO₂) cm⁻¹; τ 7.8–9.0 (m, with max. at 8.20, 20H, cyclohexyl CH₂), 5.95–6.65 (2H, m, cyclohexyl CH), 5.78 (q) and 8.72 (t) (5H, Et, *J* 7 Hz), and –0.55 to 0.35 (1H, NH).

Methyl *N*-nitrocarbamate (2.4 g, 20 mmol) was heated overnight under reflux with dicyclohexylcarbodi-imide (2.06 g, 10 mmol) in dry ether (40 ml) and the mixture was worked up as described above to give *NN'*-dicyclohexylurea (0.74 g, 33%) and *NN'*-dicyclohexyl-*N*-methoxycarbonyl-*N'*-nitroguanidine (1.7 g, 52%) as prisms, m.p. 120–121° (Found: C, 55.3; H, 7.8; N, 17.4%; *m/e*, 280. C₁₅H₂₆N₄O₄ requires C, 55.2; H, 8.0; N, 17.2%; *M* – NO₂, 280); ν_{\max} (KBr) 1700 (C=O) and 1580 (NO₂) cm⁻¹; τ 7.8–9.0 (m with max. at 8.20, 20H, cyclohexyl CH₂), 6.0–6.6 (2H, m, cyclohexyl CH), 6.24 (3H, s, Me), and –0.4 to 0.3 (1H, NH).

NN'-Dicyclohexyl-*N'*-nitroguanidine.—This compound was prepared by five distinct routes. Spectral (i.r. and n.m.r.) and analytical results left no doubt regarding the essential identity of these products, but m.p. determinations (Kofler hot-stage microscope) suggested that complete purification was only achieved in the preparations from dicyclohexylguanidine. Mass spectra suggested the presence of traces of the addition compounds in samples prepared therefrom.

(a) *From dicyclohexylguanidine.* *NN'*-Dicyclohexylguanidine¹¹ was first converted into its *nitrate*, needles, m.p. 222–223°, by means of nitric acid in aqueous ethanol (Found: C, 54.4; H, 8.8; N, 19.5. C₁₃H₂₆N₄O₃ requires C, 54.5; H, 9.1; N, 19.6%). The nitrate (1.4 g) was dissolved in sulphuric acid (87% w/w; 25 ml), set aside for 45 min at 25°, and poured into ice-water (100 ml). The precipitate yielded *NN'*-dicyclohexyl-*N'*-nitroguanidine (0.7 g, 53%) as plates from aqueous ethanol (charcoal), m.p. 151–152° (Found: C, 58.4; H, 8.9; N, 21.4%; *M*⁺, 268. C₁₃H₂₄N₄O₂ requires C, 58.2; H, 9.0; N, 20.9%; *M*, 268); ν_{\max} (KBr) 1580 cm⁻¹ (NO₂); τ 7.8–9.1 (m, with max. at 8.6, 20H, cyclohexyl CH₂) and 6.1–6.7 (2H, m, cyclohexyl CH). The nitroguanidine was also obtained (40% yield) by treatment of the base (2.3 g) with a sulphuric acid (87% w/w; 50 ml)–fuming nitric acid (0.4 ml) mixture.

(b) *From nitramine.* Dicyclohexylcarbodi-imide (1.71 g, 8.3 mmol) and nitramine¹² (1.03 g, 16.6 mmol) were dissolved in dioxan (10 ml) and set aside overnight at 25°. Addition of ether (25 ml), removal of *NN'*-dicyclohexylurea (87 mg), and evaporation gave crude material (0.6 g) which ultimately yielded the nitroguanidine, m.p. 152° (partial from ca. 140°) on crystallisation (Found: C, 58.5; H, 8.7; N, 20.9%; *M*⁺, 268).

(c) *From the 'addition compounds' (III).* *NN'*-Dicyclohexyl-*N*-ethoxycarbonyl-*N'*-nitroguanidine (III; R = Et) (1.7 g) was heated under reflux for 2 h with ethanol (50 ml) and aqueous 2*M*-sodium hydroxide (5 ml). After collection of the precipitated sodium carbonate (0.51 g, 97%) the filtrate was concentrated (ca. $\frac{1}{2}$ volume), acidified with dilute hydrochloric acid, and set aside at room temperature for evaporation. Plates of the nitroguanidine (1.0 g, 75%) separated; m.p. 150–152° (partial from 138–140°) (Found: C, 58.2; H, 8.5; N, 21.1%; *M*⁺, 268). Alter-

¹¹ S. I. Burmistrov and Y. V. Sukhoruchkin, *J. Gen. Chem. (U.S.S.R.)*, 1963, **33**, 1202.

natively, the addition compound (III; R = Et) (0.34 g) was heated under reflux for 20 h with xylene (2 ml), cyclohexylamine (0.35 g), and water (0.25 ml). Acidification (dil. HCl) and crystallisation (EtOH–H₂O) gave the nitroguanidine in 40% yield (Found: C, 58.4; H, 9.1%).

Hydrolysis of the methoxycarbonyl addition compound (III; R = Me) under the conditions used for (III; R = Et) again gave a nearly theoretical yield of sodium carbonate, and a 65% yield of the nitroguanidine.

All the above samples of *NN'*-dicyclohexyl-*N'*-nitroguanidine gave apparently identical i.r. and n.m.r. spectra; the shape of the n.m.r. trace closely resembled that given by dicyclohexylcarbodi-imide [τ 7.8–9.0 (m, with max. at 8.68) and 6.5–7.1 (m)].

Further Reactions of NN'-Dicyclohexyl-N-ethoxycarbonyl-N'-nitroguanidine (III; R = Et).—Treatment with acetanilide in sulphuric acid (95% w/w), as previously described,¹³ gave *p*-nitroacetanilide in 20% yield.

Heating of (III; R = Et) (0.34 g) under reflux for 24 h with ethanol (5 ml) and 2*M*-sodium hydroxide (1 ml) gave a mixture of *NN'*-dicyclohexyl-*N'*-nitroguanidine and *NN'*-dicyclohexylurea; when the same volume of 4*M*-sodium hydroxide was used a nearly quantitative yield of the urea was obtained.

Heating of (III; R = Et) (1.7 g) under reflux for 22 h with xylene (5 ml) and dry cyclohexylamine (0.52 g) gave *NN'*-dicyclohexylurea (0.83 g) on cooling and dilution with ether. Evaporation of the filtrate (finally *in vacuo*) gave a residue (1.1 g) which apparently contained some dicyclohexylcarbodi-imide [ν_{\max} (CHCl₃) 2130 cm⁻¹] but yielded *N*-cyclohexylurethane on crystallisation from ethanol. The use of aniline in place of cyclohexylamine again gave *NN'*-dicyclohexylurea (though in poorer yield), and not *NN'*-diphenylurea.

Determination of the Yields of Addition Compound, NN'-Dicyclohexylurea, and Total Gas from the Interaction of Dicyclohexylcarbodi-imide and Nitrourethane in Various Proportions.—Two series of experiments were performed in dry dioxan as solvent at 25° and with the following concentrations: carbodi-imide 0.25*M* with nitrourethane 0.25 and 0.5*M*; carbodi-imide 0.5*M* with nitrourethane 0.125, 0.375, 0.75, and 1.0*M*; carbodi-imide 1.0*M* with nitrourethane 1.0, 2.0, 3.0, and 4.0*M*. Experiments in the first series were worked up in standardised fashion to isolate the addition compound and *NN'*-dicyclohexylurea; when necessary, any residual excess of carbodi-imide was converted during the process into the urea, by use of 75% acetic acid. The presumed yields of addition compound, after correction for solubility losses, were 53 ± 10% when based on the minor reactant, and were not noticeably affected by an excess of either reagent. A materials balance (carbodi-imide → addition compound + total dicyclohexylurea) gave a useful check on the reliability of the experiments (Found: 87–104% of theory for all 34 experiments).

The second series of experiments was carried out under the same conditions, but the reactions were worked up to determine the yield of *NN'*-dicyclohexylurea without any contribution from surplus carbodi-imide; an apparatus was used which permitted (a) flushing with an inert gas, (b) measurement (by volume at constant pressure and temperature) of the gas evolved, and (c) sampling of the

¹² C. A. Marlies, V. K. La Mer, and J. Greenspan, *Inorg. Synth.*, 1939, **1**, 68.

¹³ C. Holstead and A. H. Lamberton, *J. Chem. Soc.*, 1952, 1886.

gas through a serum cap seal. The presumed yield of the 1:1 addition compound (obtained from the first series of experiments) was used to calculate the residual nitrourethane and carbodi-imide available for the formation of the urea and gas, and on this basis the observed yield of the urea was high (0.7—0.95 mol per mol of carbodi-imide) only when the nitrourethane/carbodi-imide ratio was >2. The gas evolved (*ca.* 2.7 mol per mol of the urea formed) was analysed (g.l.c.) by comparison with synthetic mixtures; it consisted of carbon dioxide and nitrous oxide (molecular ratio 9:10), together with ethylene (quantitative comparison not possible with the equipment available).

The invariant yields of the addition compound (particularly in the presence of excess of nitrourethane), and the need for the residual nitrourethane and carbodi-imide to be in the ratio of 2:1 to give high yields of the urea, suggested to us that the sequence of reactions must be of the type $a + b \rightarrow c$ or d , followed by rearrangement of c and reaction of d with a second molecule of b , rather than by passage through a single intermediate ($a + b \rightarrow c$; c then either rearranges or reacts with a second molecule of b). Some of the gas probably remains dissolved in the solvent, and we feel that the formation of each molecule of urea gives rise (though not necessarily in one reaction stage) to one molecule each of nitrous oxide, carbon dioxide, and ethylene.

*Reactions of Nitrourethane with Bis-*p*-tolylcarbodi-imide and with Dibenzylcarbodi-imide.*—Nitrourethane (4.0 g) was heated in dioxan (30 ml) for 24 h at 30° with bis-*p*-tolyl carbodi-imide (3.3 g) (lit.,¹⁴ but we used the method already cited⁶ with satisfactory results).

Removal of most of the solvent *in vacuo* and addition of ether (25 ml) gave *NN'*-di-*p*-tolylurea (0.3 g, 8%). The filtrate was washed with sodium hydrogen carbonate and evaporated to yield a gum (5 g) which could not be crystallised from aqueous acetic acid but gave an n.m.r. spectrum consonant with the production of *N*-ethoxycarbonyl-*N'*-

nitro-*NN'*-di-*p*-tolylguanidine: τ 2.8—3.0 (8H, m, ArH), 7.68 (s) and 7.71 (s) (6H, ArCH₃), 5.85 (q) and 8.82 (t) (5H, Et, *J* 7 Hz). For comparison, di-*p*-tolylcarbodi-imide gave τ 2.91 (8H, s, ArH) and 7.70 (6H, s, ArCH₃).

Hydrolysis of the above crude gum (0.55 g) by heating to reflux for 3 h with 2*M*-sodium hydroxide (0.5 ml) in ethanol (95%; 20 ml) gave *NN'*-di-*p*-tolylurea (0.35 g), m.p. 260—263° (lit.,¹⁵ 264°) on work-up.

Nitrourethane (2.7 or 5.4 g) was heated in dioxan (10 or 20 ml) overnight under reflux with dibenzylcarbodi-imide¹⁶ (4.5 g). Removal of most of the solvent *in vacuo* and addition of ether (25 ml) gave *NN'*-dibenzylurea (0.6 or 0.3 g). The filtrates from these experiments were combined, washed with sodium hydrogen carbonate, dried, and distilled, finally under reduced pressure. Gas was evolved, and the main fraction (5.5 g; b.p. 180—184° at 0.5 mmHg) appeared to be *NN'*-dibenzyl-*N*-ethoxycarbonylurea (Found: C, 69.5; H, 6.7; N, 8.8%; *M*⁺, 312. C₁₈H₂₀N₂O₃ requires C, 69.2; H, 6.5; N, 9.0%; *M*, 312); ν_{\max} (CHCl₃) 1700 and 1660 cm⁻¹ (different C=O groups); τ 2.70 (10H, s, ArH), 5.02 [2H, s, N(CO₂Et)CH₂], 5.49 (2H, d, NH·CH₂, *J* 5.5 Hz), 5.86 (q) and 8.81 (t) (5H, Et, *J* 7 Hz), and 0.7—1.2 (1H, NH). For comparison, dibenzylcarbodi-imide gave τ 2.77 (10H, ArH) and 5.75 (4H, CH₂).

Hydrolysis of a portion (0.72 g) of the above main fraction by refluxing for 2 h in ethanol (25 ml) with 2*M*-sodium hydroxide (2 ml) gave almost theoretical yields of sodium carbonate (0.21 g) and of *NN'*-dibenzylurea (0.42 g), m.p. 166—167° (lit.,¹⁷ 167°) on work-up. The evidence for the identity of *NN'*-dibenzyl-*N*-ethoxycarbonylurea (V) appears conclusive, but we remain suspicious of its characterisation as a liquid at room temperature.

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