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as-Triazine Chemistry. V. (1) The Oxidative Ring-opening of
5,6-Diphenyl-*as*-triazine-3(2*H*)-ones with Organic Peracids (2)

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The structures of the oxidation products of 5,6-diphenyl-*as*-triazine-3(2*H*)-ones (Ia-b) with organic peracids were chemically and spectroscopically reinvestigated and it was concluded that the products were 1,4-dibenzoyl semicarbazide (IIa) and the 2-methyl analogue (IIb).

Previously (3) we have reported the oxidation products of 5,6-diphenyl-*as*-triazine-3(2*H*)-one (Ia) and the 2-methyl analogue (Ib) with organic peracids. The products were assigned structures as the 5,6-diphenyl-*as*-triazine-3(2*H*)-one 1-oxide mono-hydrates (III).

At a later date, we revised their structures as covalently hydrated oxaziranes (IV) on the basis of further chemical and spectroscopic evidence (4). This revision was based mainly on the following facts: (1) The mass spectra of these oxidation products displayed neither (M-18) nor (M-16) cation peaks due to dehydration or deoxygenation, respectively, however, the (M-16) fragment peaks were observed without exception in the spectra of our substituted *as*-triazine-*N*-oxides (5). (2) Lithium aluminum hydride reduction of the oxidation product of Ib gave the known 2-methyl-5,6-diphenyl-4,5-dihydro-*as*-triazine-3(2*H*)-one (V) (6), indicating retention of the *as*-triazine skeleton in

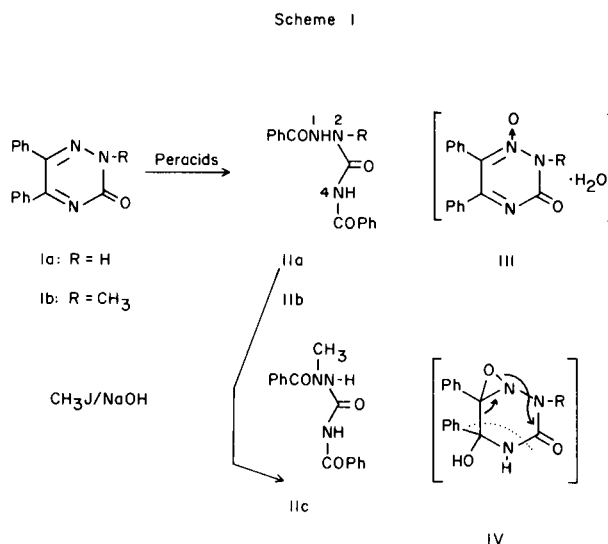


TABLE I

Ultraviolet Absorptions in Alcohol and Infrared Absorptions
in Potassium Bromide of IIa-c, VII, X, IX and XII

Compound No.	λ max $m\mu$ (log ϵ)	ν N-H (cm^{-1})	Absorptions in the Carbonyl Region (cm^{-1})
IIa	236(4.37), 275 (a) (3.57)	3200(s) (b)	1718, 1707, 1675
IIb	232(4.41), 272 (a) (3.44)	3243(s) (b)	1747, 1720, 1685, 1665
IIc	231(4.28), 266 (a) (2.15)	3240(s) (b)	1685, 1650
VII	262(4.05)	2800-3300	1723
X	265(4.87)	(c) 2800-3280	1727, 1638
IX	240 (a) (4.76), 271(4.90)	2800-3280	1716, 1630
XII	220 (a) (4.76), 260 (a) (3.70)	3300(s) (b)	1668, 1642

(a) Inflections. (b) Strong and sharp. (c) Medium to strong and broad.

TABLE II

NMR Spectra of IIa-c Measured at 60 MC (ppm) (a)

Compound No.	Solvent	1-NH	2-NH	4-NH	1-Me	2-Me
b) IIa	DMSO-d ₆	10.28	10.63	11.04	----	----
IIb	DMSO-d ₆	10.27	----	10.68	----	3.11
IIc	CDCl ₃	----	10.40	10.81	3.37	----

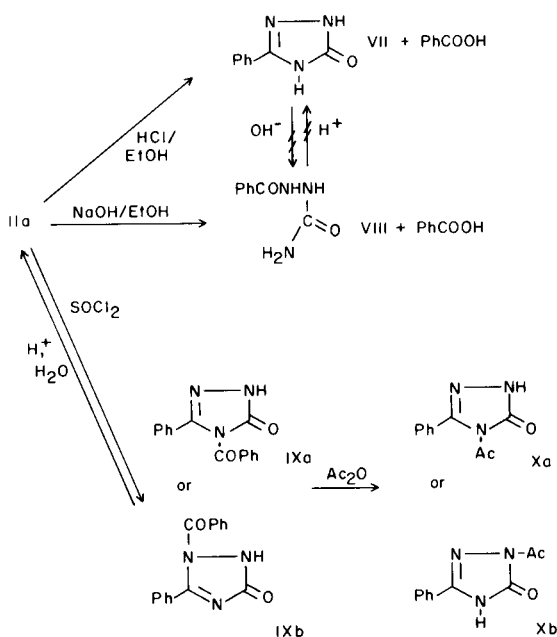
(a) All the signals are singlets. Intensity ratios of NH- to Me-protons are 1:3. (b) No clear-cut coupling between H¹ and H² was discernible.

the present oxidation products. (3) Alkali cleavage of the same oxidation product afforded the known oxadiazolone (VI) (7) (Scheme III) and benzamide. The ether oxygen atom in VI seemed to be rearranged from the oxazirane ring as shown by arrows with concomitant formation of benzamide (Scheme I). However, the formation of the dihydrotriazine (V) was proved to arise from the starting material (Ib) contaminated by the oxidation product (IIb). Thus, the structures of these oxidation products were reinvestigated and ultimately assigned the structures 1,4-dibenzoyl semicarbazide (IIa) (8) and the 2-methyl analogue (IIb).

This paper describes the process of the structural elucidation of these unusual reaction products.

Methylation of compound IIa gave a mono-methylated compound (IIc), which was different from IIb in every respect (melting point, mixture melting point and spectra). The NMR data of these substances are given in Table II, and their ultraviolet and infrared spectral data are summarized in Table I. It is evident from the UV and NMR spectra, that these products are of similar structure. The overall features of their infrared spectra were also similar but the absorption in the carbonyl region are complicated. The position of methylation in IIc is in question because the NMR data were measured in different solvents from those of IIa-b. Further investigation of the structure of IIc was not possible because of the low yield of IIc. We propose the two alternate structures, N¹- or N⁴-methyl-1,4-dibenzoyl semicarbazide.

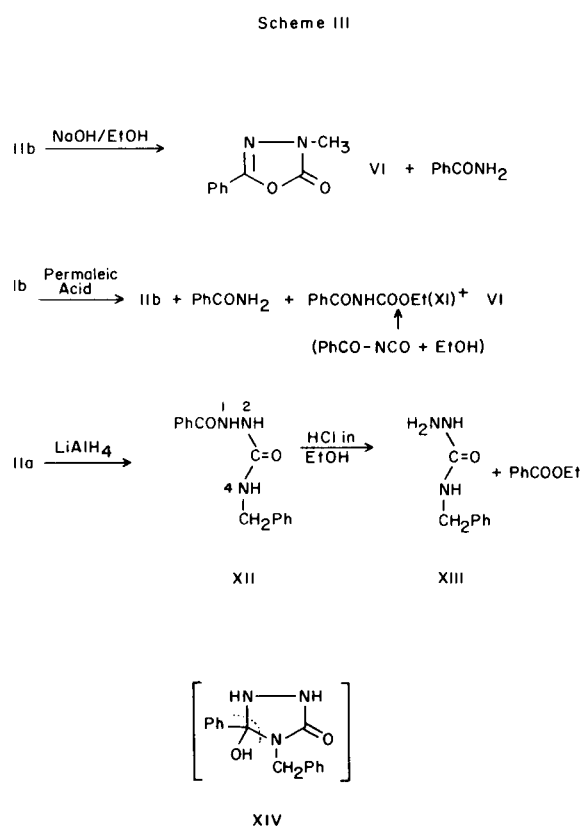
Scheme II



For the purpose of structure elucidation some chemical reactions on IIa and IIb were carried out. Acidic hydrolysis of IIa with alcoholic hydrochloric acid gave the known 3-hydroxy-5-phenyl-1,2,4-triazole (VII) (9) and benzoic acid, while basic degradation of IIa with alcoholic sodium hydroxide produced the known 1-benzoyl semicarbazide (VIII) (10) and benzoic acid. Compound VII and VIII were formed by independent routes, because the basic conditions, whereby compound VIII was formed, could not produce a change on compound VII and furthermore, compound VIII was not cyclized to compound VII under acidic conditions similar to those whereby compound VII was produced from IIa. Reaction of IIa with thionyl chloride in pyridine solution gave a dehydration product IX (a or b), whose reaction with acetic anhydride gave a mono-acetylated triazolone X (a or b) which appeared to be formed by acetylation after debenzoylation. As expected, the ultraviolet absorption spectrum of X was in agreement with that of VII (Table I). Compound IX could be so easily cleaved into the original oxidation product IIa, that at first it appeared as if an acid-catalyzed covalent hydration were involved.

On the other hand, all the attempts of similar chemical

reactions on IIb resulted in intractable mixtures of oils or tars, except the one described below.



Treatment of IIb with alcoholic sodium hydroxide and careful separation of the reaction mixture by column chromatography gave the known 2-phenyl-4-methyl-1,3,4-oxadiazolone-5 (VI) (7) and benzamide. Compound VI was also obtained as a by-product of IIb with benzamide and *N*-benzoyl ethylurethane (XI) (11). The last com-

TABLE III

The NMR Spectrum of Compound XII
in DMSO- d_6 (ppm)

4.26 (2H, doublet, $J = 6$ cps) (a)	-----	CH ₂
7.02 (1H, triplet, $J = 6$ cps) (b)	-----	4-NH
7.28 (5H, singlet)		
7.4-7.6 (2H, multiplet)	-----	2 Phenyl
7.8-8.0 (4H, multiplet)		
10.15 (1H, singlet) (b)	-----	1- or 2-NH

(a) Became singlet by deuterium oxide addition. (b) Disappeared by deuterium oxide addition.

pound (XI) must have been formed by reaction of the alcohol with benzoyl isocyanate which resulted by degradation of IIb.

Lithium aluminum hydride reduction of IIa gave the benzyl compound (XII), which furnished the final evidence that the oxidation products (IIa, IIb and IIc) possessed a second benzoyl group at the N^4 and an open-chain structure. It is noteworthy that only the benzoyl group at N^4 was specifically reduced even with a large excess of lithium aluminum hydride. Cleavage of XII with alcoholic hydrochloric acid afforded the known 4-benzyl semicarbazide (XIII) (12) and ethyl benzoate. The ultraviolet absorptions and some of the IR-data of compound XII are given in Table I. The IR bands at $3200-3300\text{ cm}^{-1}$ of IIa-c and XII are so strong and sharp that at first we were deluded to consider them as typical hydroxyl absorptions and envisaged, for a while, a covalently hydrated triazolone XIV for this reduction product. The NMR spectrum of XII was assigned as shown in Table III. The presence of a doublet at 4.26 ppm and a triplet at 7.02 ppm required a structure containing a Ph-CH₂-NH- unit, precluding the structure XIV in bracket. The multiplet signal at 7.8-8.0 ppm corresponds to four protons, one of which is due to 1-NH or 2-NH. The low-field signal at 10.15 ppm may be ascribed to a bonded NH but the conclusive assignment is difficult to make from the present data, because both the N^1 - and the N^2 -proton can bond with one of the two carbonyl groups with equal ease. Thus, the precursor of compound XII must be 1,4-dibenzoyl semicarbazide (IIa), which was spectroscopically identical with an authentic sample prepared from benzoyl hydrazide and benzoyl isocyanate.

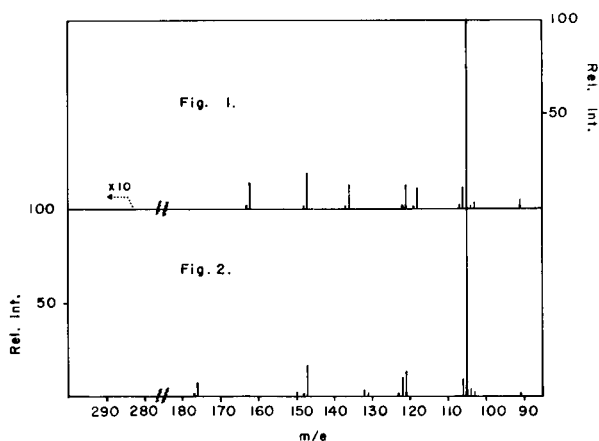
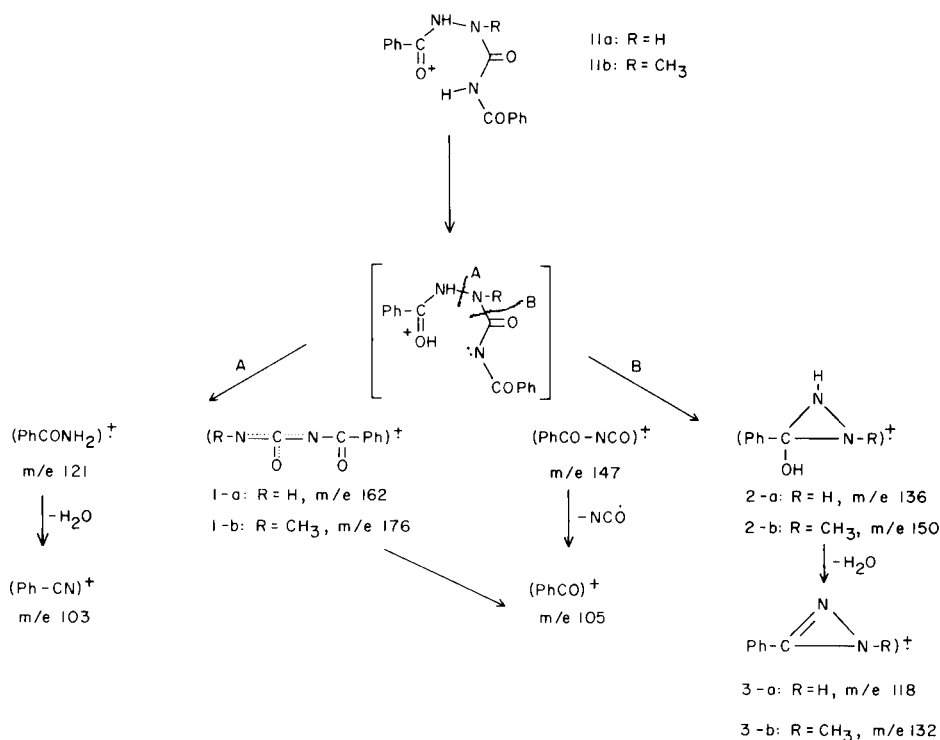


Fig. 1. Mass Spectrum of IIa.

Fig. 2. Mass Spectrum of IIb.

The mass spectra of the oxidation products IIa and IIb are presented in Figures 1 and 2. Their fragmentation patterns are given in Scheme IV. These simple patterns show some common peaks at mass 147, 121, 105 and 103,

Scheme IV



of which the *m/e* 105 ion appears as a base peak in both cases. These and other ion peaks could be interpreted by A and B type-cleavage. It is interesting to note that the formation of the benzamide and the benzoyl isocyanate cation is in harmony with the results obtained above in the chemical degradations.

The mechanisms of formation of IIa and IIb from Ia and Ib are now under investigation.

EXPERIMENTAL (13)

Methylation of 1,4-Dibenzoyl Semicarbazide (IIa).

Powdered IIa (1.2 g.), methyl iodide (1.2 g.) and a solution of sodium hydroxide (0.34 g.) in ethanol (10 ml.) were combined in a pressure tube and the mixture was heated in a water bath at 95°. The solid sodium salt of IIa went into solution within 1 hour. After further heating for 0.5 hour, the reaction mixture was evaporated *in vacuo* and extracted with chloroform (100 ml.) in the presence of water. The chloroform extract was eluted through a 1.5 cm. x 30 cm. alumina column (200-300 mesh) with chloroform. The last fraction was combined and the residue was recrystallized from methanol to give 0.2 g. of colourless prisms (IIc), *m.p.* 193-194°. A mixture melting point with IIb was depressed.

Anal. Calcd. for C₁₆H₁₅N₃O₃: C, 64.63; H, 5.09; N, 14.14. Found: C, 65.07; H, 5.14; N, 14.43.

Acidic Cleavage of IIa.

A mixture of IIa (1.0 g.), ethanol (100 ml.) and concentrated hydrochloric acid (10 ml.) was refluxed on a boiling water bath

for 4 hours and evaporated *in vacuo* to give a solid residue with a small amount of fine needles sublimed on the wall of the distilling column, which was identified as benzoic acid. The solid residue, which had the odor of ethyl benzoate, was recrystallized from ethanol to afford 0.3 g. (57%) of VII as colourless powder, *m.p.* above 300°.

Anal. Calcd. for C₈H₇N₃O: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.27; H, 4.30; N, 26.23.

The identity with an authentic sample (9) was confirmed by infrared and ultraviolet spectra.

Basic Cleavage of IIa.

A mixture of IIa (1.2 g.) and a solution of sodium hydroxide (0.35 g.) in ethanol (10 ml.) was refluxed for 5.5 hours and chilled. The mixture was then neutralized with acetic acid and evaporated *in vacuo*, when some sublimation of benzoic acid was observed on the wall of the distilling column. Water was added to the residue and the insoluble part was filtered, dried and after washing with 20 ml. of chloroform, once recrystallized from ethanol to afford 0.5 g. (80%) of VIII as colourless powders: *m.p.* 235-236° (Lit. (10) 225°); ν_{\max} (potassium bromide), 3450, 3235, 3018 (N-H), 1701, 1681, 1648 (C=O); 1612 (δ N-H) cm⁻¹.

The infrared spectrum of this product was superimposable on that of an authentic sample (10).

The aqueous filtrate from VIII was extracted with 50 ml. of chloroform and the chloroform layer was combined with the chloroform washings obtained above, dried and evaporated to a small bulk and chromatographed on a 1.5 cm. x 30 cm. alumina column (200-300 mesh) by using chloroform as eluent. Evaporation of the main fraction (30 ml.) gave 0.2 g. (50%) of benzoic acid, *m.p.* 120-122°, identified with an authentic sample by a

comparison of the infrared spectra.

Reaction of IIa with Thionyl Chloride.

To a stirred solution of IIa (2.2 g.) in anhydrous pyridine (20 ml.) was added dropwise a solution of thionyl chloride (1.1 g.) in benzene (8 ml.) at 7-10°. After the addition, the reaction mixture was stirred for 1.5 hours at room temperature, and then evaporated at 45° under reduced pressure. The residue was dissolved in chloroform (50 ml.) and washed with water. The chloroform extract was concentrated and the residue was repeatedly recrystallized from a mixture of chloroform and acetone to give 0.8 g. of IX as fine colourless needles, m.p. 209-210°.

Anal. Calcd. for $C_{15}H_{11}N_3O_2$: C, 67.91; H, 4.18; N, 15.84. Found: C, 68.10; H, 4.28; N, 15.75.

To a solution of IX (0.5 g.) in dioxane (10 ml.) was added concentrated hydrochloric acid (0.3 ml.) and the mixture was allowed to stand overnight. The separated crystals (80 mg.) were filtered and identified with the starting material (IX). The filtrate was evaporated *in vacuo* below 45° and the residual solid was crystallized once from ethanol to give practically pure IIa (0.4 g.).

Monoacetyl Derivative of VII (X).

A mixture of IX (0.3 g.), acetic anhydride (3 ml.) and anhydrous pyridine (2 ml.) was heated on a boiling water bath for 2 hours. After the solvent was evaporated off, the residual solid was triturated with water, filtered by suction and recrystallized from acetone to afford 0.2 g. of microcrystalline needles (X), m.p. 230-231°.

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.10; H, 4.46; N, 20.68. Found: C, 59.35; H, 4.49; N, 20.89.

Basic Cleavage of IIb. Formation of 2-Phenyl-4-methyl-1,3,4-oxadiazolone-(5) (VI) and Benzamide.

A mixture of IIb (0.5 g.) and a solution of sodium hydroxide (0.068 g.) in ethanol (5 ml.) was heated in a pressure tube on a boiling water bath for 1.5 hours. The solvent was evaporated and the residue was extracted with chloroform (50 ml.). The chloroform extract was chromatographed through a 1.5 cm. x 30 cm. alumina column (200-300 mesh) by using a mixed solvent, chloroform-ethanol (4:1), as eluent. The first oily fraction was again purified by silica gel column chromatography (1.0 cm. x 20 cm., 100 mesh) using chloroform as eluent to give a colourless solid, which was crystallized from a mixture of ether and petroleum ether, affording 0.15 g. of VI in the form of fine leaflets: m.p. 103-104° (Lit. (7) 100-101°); ν max (potassium bromide), C=O 1760, 1725 (shoulder) cm^{-1} ; λ max (ethanol), 263 $m\mu$ ($\log \epsilon = 4.84$).

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.21; H, 4.49; N, 16.13.

The identity with an authentic specimen (7) was confirmed by infrared and ultraviolet spectra.

On the other hand, the second fraction of the alumina chromatography gave 70 mg. of solid (m.p. 128-130°) whose IR-spectrum was identical with that of an authentic sample of benzamide.

Permalleic Acid Oxidation of Ib. Isolation of VI, Benzamide and Benzoyl Urethane (XI).

Compound Ib (8.2 g.) was oxidized with permalleic acid and the reaction mixture was worked up according to the previously described procedure (3). Thus, the chloroform extract freed from maleic acid was dried with sodium sulfate and evaporated to a brown paste. Fractional crystallization from ethanol gave 3.0 g. of IIb. The mother liquor of IIb was concentrated to a paste (ca.

2 g.) which was chromatographed on a 1.5 cm. x 30 cm. alumina column (200-300 mesh) by using chloroform as the eluent. The initial impure fraction (a sticky oil) was again chromatographed through an alumina column (1.5 cm. x 30 cm., 200-300 mesh) with chloroform to give 0.3 g. of VI (m.p. 101-103°) after evaporation of chloroform from the first eluate. The next fraction after removal of chloroform gave an oil which solidified on standing overnight. Repeated crystallization from ether gave 0.37 g. of benzoyl urethane (XI) as colourless needles, m.p. 110-112° (Lit. (11) 110°); ν max (potassium bromide), 3250 (N-H), 1767 and 1747 cm^{-1} (C=O); λ max (ethanol), 230 $m\mu$ ($\log \epsilon = 4.96$) and 270 $m\mu$ ($\log \epsilon = 4.40$).

On the other hand, from the second eluate of the original alumina chromatogram was obtained 0.2 g. of benzamide (m.p. 130-131°) after sublimation at 120°/4 mm.

All the above products were identified with authentic samples by infrared and/or ultraviolet spectroscopy.

1-Benzoyl-4-Benzyl Semicarbazide (XII).

Compound IIa (2.5 g.) was dissolved in anhydrous dioxane (110 ml.) by warming at 45°. To this solution was added under stirring 1.0 g. of lithium aluminum hydride in three portions, followed by an addition of anhydrous tetrahydrofuran (20 ml.). After the first violent reaction subsided, further lithium aluminum hydride (0.5 g.) and tetrahydrofuran (10 ml.) were added, and the mixture was stirred at 45° for 3.5 hours. After standing overnight at room temperature, the mixture was treated with saturated ammonium chloride solution and then with water. The resulting slurry was extracted with chloroform (5 x 70 ml.). The combined chloroform washings were dried with sodium sulfate and evaporated *in vacuo* to dryness.

Recrystallization of the residue from methanol gave 1.7 g. of XII in the form of star-like congregated needles, m.p. 183-184°.

Anal. Calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.61. Found: C, 66.42; H, 5.53; N, 15.27.

Acidic Cleavage of XII.

A mixture of XII (1.8 g.), ethanol (90 ml.) and concentrated hydrochloric acid (9 ml.) was refluxed for 3 hours and evaporated *in vacuo* to a solid residue (1.2 g.), which was washed with ether and dissolved in water (10 ml.). The aqueous solution to which chloroform had been added was made basic with 30% sodium hydroxide solution. After shaking, the organic layer was separated, dried and evaporated to give a solid (0.8 g.), which was recrystallized from a small amount of ethanol to give 0.6 g. of XIII as fine colourless needles, m.p. 111.5-112.5° (Lit. (12) 112°); ν max (potassium bromide), 3366, 3321, 3223, 3069 (N-H) and 1659 cm^{-1} (C=O).

Anal. Calcd. for $C_8H_{11}N_3O$: C, 58.16; H, 6.71; N, 25.44. Found: C, 57.84; H, 6.75; N, 25.58.

The infrared spectrum of this substance was perfectly superimposable on that of an authentic sample (12).

Hydrochloride.

This compound had a melting point of 237-239° (methanol); ν max (potassium bromide), 3282, 3204, 2964, 2654 and 1675 cm^{-1} .

Anal. Calcd. for $C_8H_{12}ClN_3O$: C, 47.65; H, 6.00; N, 20.84. Found: C, 47.74; H, 5.93; N, 20.70.

The above ether washings were evaporated to a brown oil, which was purified through a silica gel column with chloroform to give a small amount of a colourless mobil oil. This was identified as ethyl benzoate by IR spectroscopy.

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