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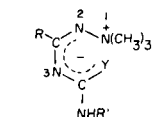
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N^3 -Acylamidrazone ylides **3** were synthesized by the reaction of 2-(iminophenylmethyl)-1,1,1-trimethylhydrazinium hydroxide, inner salt (**2a**) or 2-(1-iminoethyl)-1,1,1-trimethylhydrazinium hydroxide, inner salt (**2b**) with acyl chlorides or acetic anhydride. Thermolysis of **3** gave 3,5-disubstituted oxadiazoles **4** and trimethylamine.

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We recently reported (4) that trimethylamine and good yields of 1,2,4-thiadiazoles are obtained from the thermal decomposition of N^3 -thiocarbamoylamidrazone ylides **1a** (5). However, thermolysis of a N^3 -carbamoyl ylide **1b** afforded a mixture from which the anticipated 1,2,4-oxadiazole was not isolated.



1a, Y = S
1b, Y = O, R = C₆H₅; R' = *p*-tolyl

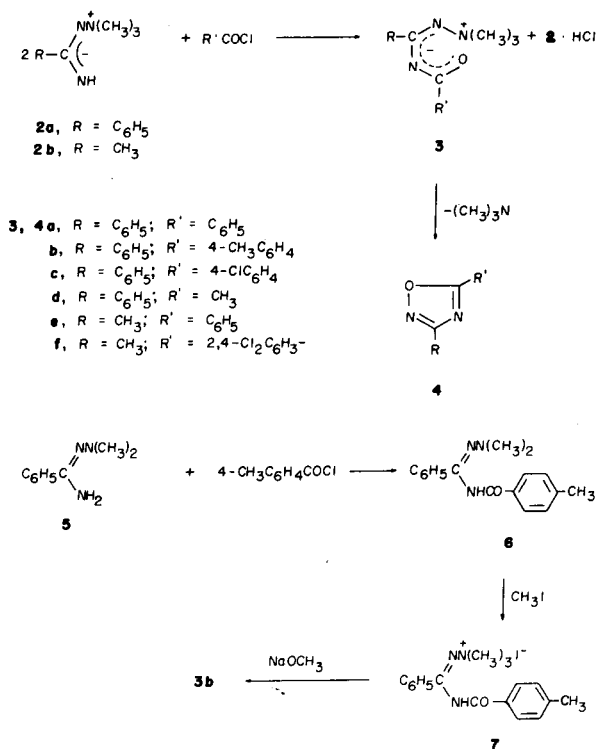
In this paper we report the results of our study of the preparation of N^3 -acylamidrazone ylides **3** and the synthesis of 1,2,4-oxadiazoles *via* the thermal decomposition of these compounds.

Addition of acyl chlorides to methylene chloride solutions containing two equivalents of 2-(iminophenylmethyl)-1,1,1-trimethylhydrazinium hydroxide, inner salt (**2a**) or 2-(1-iminoethyl)-1,1,1-trimethylhydrazinium hydroxide, inner salt, (**2b**) resulted in precipitation of the hydrochlorides of **2a** or **2b**. The acylated ylides **3a-f** were isolated from the filtrates in yields ranging from 41 to 97%. Acylation procedures employing equimolar quantities of acyl chlorides and **2a** in either pyridine, aqueous sodium hydroxide, or potassium carbonate-methylene chloride did not give satisfactory yields of **3**. The N^3 -acetylated ylide **3d** was also obtained in 42% yield by reaction of **2a** with acetic anhydride.

Thermolysis of the acylated ylides **3** gave trimethylamine and excellent yields of 3,5-disubstituted-1,2,4-oxadiazoles **4a-f**.

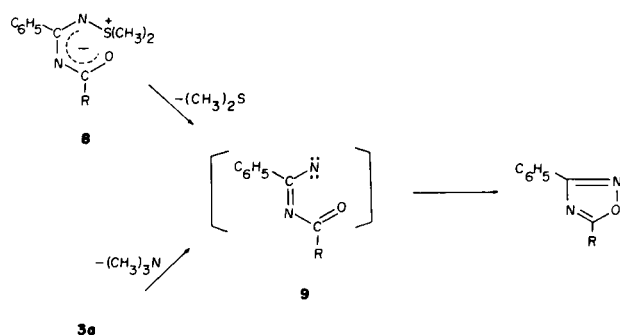
Ylide **3b** was also synthesized by a procedure which utilized benzamide dimethylhydrazone (**5**) as starting material. Acylation of **5** with *p*-tolyl chloride gave the N^3 -acylated amidrazone **6** in 93% yield. Reaction of **6** with methyl iodide gave the ylide conjugate acid **7** in 51% yield. Neutralization of **7** with methanolic sodium methoxide gave **3b**.

Scheme 1



A similar oxadiazole synthesis has been reported by Fuchigami and Odo (6) who prepared acylated sulfilimines **8** from *N*-chlorobenzamidine and established that thermolysis of the latter compounds gives dimethylsulfide and 3-phenyl-5-aryl-1,2,4-oxadiazoles. Nitrene intermediates **9** have been proposed to account for the conversion of **8** to oxadiazoles. These intermediates may also be formed from **3** if the cyclization of these ylides occurs *via* a non-concerted pathway. Studies designed to distinguish between concerted and non-concerted processes in the cyclization of **8** and **3** have not been carried out.

Scheme 2



The oxadiazole synthesis described in this paper provides a novel route to 3-alkyl (or aryl)-5-alkyl (or aryl)-1,2,4-oxadiazoles. A survey of 1,2,4-oxadiazole syntheses may be found in a recent review (7).

EXPERIMENTAL

Melting points were determined with a Mel-temp apparatus and are uncorrected. The nmr spectra were determined with a Hitachi-Perkin Elmer R24B spectrometer utilizing hexamethyldisiloxane as the internal standard. Infrared spectra were determined with a Perkin-Elmer 710B instrument.

2-(Iminophenylmethyl)-1,1,1-trimethylhydrazinium Hydroxide, Inner Salt (2a).

Table 1

Analytical and Spectroscopic Data (3a-f)

Compound	Mp °C (dec)	Yield (a)	Molecular Formula	Analysis			IR (cm ⁻¹) (b)	NMR δ (c)
				Calcd.	(Found)			
				C	H	N		
3a	209-210 (d)	41	C ₁₇ H ₁₉ N ₃ O	72.57 (72.54)	6.80 (6.83)	14.93 (14.89)	1595	3.6 (s, 9H), 7.1-7.8 (m, 8H), 8.0-8.2 (m, 2H)
3b	207-208 (d)	86	C ₁₈ H ₂₁ N ₃ O	73.19 (73.17)	7.17 (7.17)	14.22 (14.19)	1595	2.5 (s, 3H), 3.6 (s, 9H), 7.0-7.5 (m, 7H), 8.0 (d, 2H)
3c	219-220 (d)	68	C ₁₇ H ₁₈ ClN ₃ O · ½H ₂ O	62.86 (62.86)	5.89 (5.87)	12.94 (12.94)	1570	(DMSO-d ₆) 3.5 (s, 9H), 7.2-7.5 (m, 7H), 7.9 (d, 2H), 3.3 (s, H ₂ O)
3d	186-188 (e)	48	C ₁₂ H ₁₇ N ₃ O	65.72 (65.68)	7.81 (7.81)	19.16 (19.11)	1595	(DMSO-d ₆) 2.0 (s, 3H), 3.5 (s, 9H), 7.1-7.7 (m, 5H)
3e	162-163 (e)	75	C ₁₂ H ₁₇ N ₃ O	65.72 (65.67)	7.81 (7.82)	19.16 (19.19)	1595	2.3 (s, 3H), 3.5 (s, 9H), 7.2-7.5 (m, 3H), 7.9-8.2 (m, 2H)
3f	153-155 (d)	97 (f)	C ₁₂ H ₁₅ Cl ₂ N ₃ O	50.01 (49.93)	5.25 (5.31)	14.58 (14.56)	1590	2.2 (s, 3H), 3.5 (s, 9H), 7.1-7.6 (m, 3H)

(a) Yield of recrystallized product. Yields are not optimized. (b) Potassium bromide pellets. (c) Unless otherwise specified, determined in deuteriochloroform. (d) Recrystallized from ethanol. (e) Recrystallized from ethanol-ether. (f) Unrecrystallized product, mp 120-127°.

Table 2

Properties of 1,2,4-Oxadiazoles (4)

Compound No.	Thermolysis Temperature °C (time, minutes)	Yield (a)	MP °C (b)	Literature MP °C	Reference	Molecular Formula	NMR (δ) (c)
4a	210 (5)	97	103-106	108	(6)	C ₁₄ H ₁₀ N ₂ O	7.3-7.6 (m, 6H), 7.9-8.3 (m, 4H)
4b	210 (10)	97	109-112	117-118	(8)	C ₁₅ H ₁₂ N ₂ O	2.3 (s, 3H), 7.2-7.6 (m, 5H), 7.8-8.4 (m, 4H)
4c	215 (15)	98	116-119	121-122	(8)	C ₁₄ H ₉ ClN ₂ O	7.3-7.6 (m, 5H), 8.0-8.3 (m, 4H)
4d	190 (5)	77 (d)	27-29	41	(9)	C ₉ H ₉ N ₂ O	2.5 (s, 3H), 7.1-7.5 (m, 3H), 7.8-8.1 (m, 2H)
4e	165 (15)	60 (d)	57-58	57	(9)	C ₉ H ₉ N ₂ O	2.5 (s, 3H), 7.3-7.7 (m, 3H), 8.0-8.2 (m, 2H)
4f	170 (30)	88	67-71 (e)	79-80	(10)	C ₉ H ₈ Cl ₂ N ₂ O	2.4 (s, 3H), 7.2-7.9 (m, 3H)

(a) Crude yield. (b) Mp of crude material. (c) Obtained in deuteriochloroform. (d) Some loss by sublimation during thermolysis. (e) Recrystallization from ethanol gave material with mp 80-82°.

Pure, anhydrous samples of **2a** were required for the acylation reactions. Crude material which was prepared as previously described (11) was not conveniently purified by recrystallization. Purification was accomplished by neutralization of the hydroiodide (11) which was obtained either by addition of hydroiodic acid to a 10% ethanolic solution of crude **2a** or by the following procedure.

A solution containing 1.6 g of benzamide dimethylhydrazone (**5**) (1) and 1.6 ml of methyl iodide in 10 ml of acetonitrile was kept at room temperature for 24 hours. After ice cooling 1.6 g (62%) of 2-(imino-phenylmethyl)-1,1,1-trimethylhydrazinium iodide (**2a·HI**) was filtered off, mp 202-204°, lit mp 212-213 (11).

The ylide was obtained by stirring a 10% suspension of the salt in methanolic sodium methoxide (1.1 equivalent) for 1.5 hours. The solvent was removed *in vacuo* (40°) and the ylide separated from inorganic material by several extractions with warm benzene. Evaporation of the benzene extracts *in vacuo* (40°) gave a quantitative yield of the solid, hygroscopic product which was placed in a nitrogen atmosphere and immediately used for acylation experiments.

2-(1-Iminoethyl)-1,1,1-trimethylhydrazinium Hydroxide, Inner Salt (**2a**).

Pure, anhydrous samples of the ylide were obtained by neutralization of the hydrochloride (11) by the procedure described above. The hydrochloride was precipitated by passing anhydrous hydrogen chloride into the solution of crude **2b** (11) in ethanol.

Oxadiazoles (**4a-f**).

Conditions for the thermal decomposition of **4a-f** are given in Table 2. The unrecrystallized products were found to be homogeneous by tlc (silica gel, 1:1 methylene chloride/cyclohexane). The products have all been previously reported and their nmr spectra were compatible with the assigned structures. The nmr spectra of **4a** and **4d** were identical with those obtained from authentic samples.

2-(Acetylamino)phenylmethylene]-1,1,1-trimethylhydrazinium Hydroxide Inner Salt (**3d**).

A mixture consisting of **2a** (2.0 g), acetic anhydride (1.3 ml), anhydrous sodium carbonate (0.74 g) and methylene chloride (15 ml) was vigorously stirred for 1 hour. Water (10 ml) was added to dissolve the inorganic material. The aqueous layer was saturated with sodium carbonate and extracted with methylene chloride. Evaporation of the combined, dried (magnesium sulfate) extracts gave 1.0 g of crude **3d**, mp 169-170°.

1,1-Dimethyl-2-[(4-methylbenzoylamino)phenylmethylene]hydrazine (**6**).

p-Toluy chloride (1.9 g) was added to a stirred solution containing benzamide dimethylhydrazone (2.0 g) (1) and triethylamine (1.2 ml) in 20 ml of methylene chloride. After 12 hours the reaction mixture was diluted with 50 ml of methylene chloride and treated with 15 ml of water. The aqueous layer was extracted with methylene chloride. Evaporation of the combined, dried (magnesium sulfate) extracts gave 3.1 g (93%) of

product, mp 154-159°. Recrystallization from ethanol gave yellow crystals, mp 163-165°; nmr (deuteriochloroform): δ 2.4 (s, 3H), 2.5 (s, 6H), 7.0-7.9 (m, 10H); ir (potassium bromide): 1680 and 3350 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}$: C, 72.57; H, 6.81; N, 14.93. Found: C, 72.70; H, 6.86; N, 14.88.

2-[(4-Methylbenzoylamino)phenylmethylene]-1,1,1-trimethylhydrazinium Iodide (**7**).

A solution containing **6** (3.8 g) and methyl iodide (6 ml) in 100 ml of acetonitrile was heated under reflux for 6 hours. The solvent was removed *in vacuo* and the product recrystallized from ethanol-ether to give 2.8 g (51%) of hygroscopic yellow crystals, mp 98-104°. Recrystallization from ethanol gave yellow crystals, mp 109-110°; nmr (deuteriochloroform): δ 2.4 (s, 3H), 3.8 (s, 9H), 7.1-7.4 (m, 6H), 7.7-7.9 (m, 2H), 8.2 (d, 2H).

Anal. Calcd. for $\text{C}_{17}\text{H}_{22}\text{I}\text{N}_3\text{O}$: C, 51.08; H, 5.24; N, 9.93. Found: C, 51.13; H, 5.72; N, 9.63.

Neutralization of the salt by the procedure employed for the conversion of **2a·HI** to **2a** afforded a 45% yield of **3b**, mp 190-194° dec.

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