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Dedicated to the memory of Professor Nicholas Alexandrou

The synthesis and lead tetraacetate oxidation of the title mono- and bis-arylhydrazones to the corresponding 5-acyl-4-aryl(alkyl)-2-aryl-1,2,3-triazole 1-oxides is described.

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As it happens with the vast majority of nitrogen heterocycles, two major pathways are generally available for obtaining 2-aryl-1,2,3-triazole 1-oxides *i.e.* (a) preparation from a preformed 2-aryl-1,2,3-triazole and, (b) oxidative cyclization of the appropriate *vic*-arylhydrazone oxime [1].

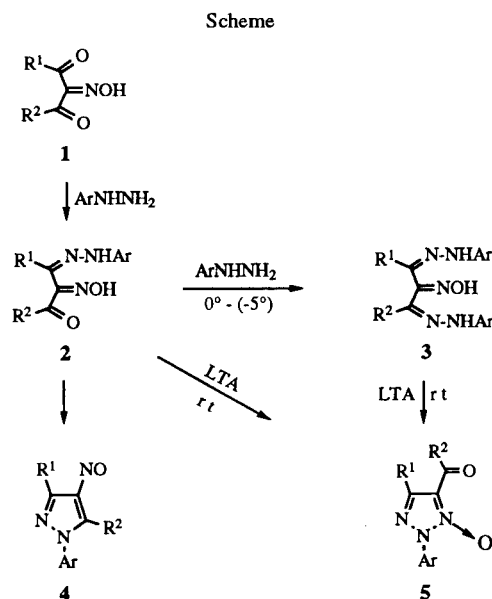
Of the two, the former has never been realized. In particular attempts to obtain 2-phenyl-1,2,3-triazole 1-oxide by oxidation of 2-phenyl-1,2,3-triazole with a variety of appropriate oxidants such as peracetic acid, *meta*-chloroperbenzoic acid, dichloropermaleic acid and others were of no avail [2].

On the other hand, oxidative cyclization of *vic*-arylhydrazones oximes readily provides the required *N*-oxides [2-8].

The synthesis of the title compounds *via* the aforementioned oxidative cyclization however, presupposes the synthesis of the appropriate monohydrazones of the α -hydroxyimino- β -diketones **2**. With respect to the last the bibliographical evidence is negative, since it is known that the addition of some arylhydrazine to 3-hydroxyiminopentane-2,4-dione (**1a**) yields nitrosopyrazoles **4** [9]. The latter are presumably obtained *via* the intramolecular cyclization of the intermediately formed *vic*-arylhydrazone oximes **2**.

In order to overcome the problem which is due to the participation of the free carbonyl in the intramolecular cyclization of **2**, we aimed at the synthesis of bishydrazone oximes **3**. Our efforts are summarized in the present paper.

We found that, when 2.2 moles of arylhydrazines per mole of oxime **1**, at low temperature ($\sim 0^\circ$) were used the bisarylhydrazones of α -hydroxyiminodiones **3** were separated (Table). Quite often the precipitate contained small-to-fair amounts of the monohydrazone **2** and, as far as the preparation of the 2-aryl-1,2,3-triazole 1-oxides **5** *via* the oxidative cyclization is concerned, this does not present any problems.



- a, $\text{R}^1 = \text{R}^2 = \text{CH}_3$, $\text{Ar} = \text{C}_6\text{H}_5$
b, $\text{R}^1 = \text{R}^2 = \text{CH}_3$, $\text{Ar} = 4\text{-CH}_3\text{C}_6\text{H}_4$
c, $\text{R}^1 = \text{R}^2 = \text{CH}_3$, $\text{Ar} = 4\text{-ClC}_6\text{H}_4$
d, $\text{R}^1 = \text{R}^2 = \text{CH}_3$, $\text{Ar} = 4\text{-NO}_2\text{C}_6\text{H}_4$
e, $\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{Ar} = \text{C}_6\text{H}_5$
f, $\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{C}_6\text{H}_5$, $\text{Ar} = 4\text{-CH}_3\text{C}_6\text{H}_4$
g, $\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{C}_6\text{H}_5$, $\text{Ar} = 4\text{-ClC}_6\text{H}_4$
h, $\text{R}^1 = \text{CH}_3$, $\text{R}^2 = \text{C}_6\text{H}_5$, $\text{Ar} = 4\text{-NO}_2\text{C}_6\text{H}_4$
i, $\text{R}^1 = \text{R}^2 = \text{Ar} = \text{C}_6\text{H}_5$
j, $\text{R}^1, \text{R}^2 = \begin{array}{c} \text{H}_3\text{C} \\ | \\ \text{C} \\ | \\ \text{H}_3\text{C} \end{array}$, $\text{Ar} = \text{C}_6\text{H}_5$

Table

Preparation and Lead Tetraacetate Oxidation [a] of
 α -Hydroxyiminohydrazones **2** and **3** to 5-Acyl-4-aryl(alkyl)-2-aryl-
1,2,3-triazole 1-Oxides **5**

Code	Isolated yields (%)		
	Monohydrazone 2	Bishydrazone 3	1,2,3-Triazole 1-Oxide 5
a	-	56	70
b	70	-	45
c	-	67	78
d	-	46	23
e	-	65	68
f	80	-	72
g	-	80	98
h	-	72	79
i	-	68	86
j	-	31	94

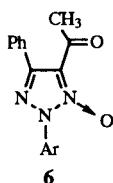
[a] Solvent methylene chloride at room temperature.

It is worth noting at this stage that when *p*-tolylhydrazine was used with both α -hydroxyiminodiketones **1a** and **1e** monohydrazones **2a** and **2e** were isolated.

When compounds **2** or **3** were oxidized with lead tetraacetate in methylene chloride, fair-to-excellent yields of 5-acyl-2-aryl-1,2,3-triazole 1-oxides **5** were obtained (Table).

Structure proof for the new compounds is provided by their elemental analyses and spectroscopic characteristics.

In the case of the 1-oxides **5e-f** in particular, the choice between the two possible isomers i.e. **5e** and its isomer 4-acyl-2,5-diphenyl-1,2,3-triazole 1-oxide (**6**), was made on the basis of the low (when compared to, say, **5a**) ir carbonyl absorption of 1638 cm^{-1} . The appearance of an abundant peak at m/z 105 in the mass spectra of **5a-f** points out to the same direction. Similar reasoning applies to structure **2f**.



In conclusion, the title reaction which could be viewed as involving, besides the oxidative cyclization, a protection - oxidative deprotection sequence for one of the carbonyls in **2**, provides a useful entry to the 5-acyl-2-aryl-1,2,3-triazole 1-oxide **5** system.

EXPERIMENTAL

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Infrared spectra were recorded as nujol mulls on a Perkin-Elmer 297 or 257 spectrometer calibrated with the 1602 cm^{-1} absorption of polystyrene. Proton nmr spectra were obtained in deuteriochloroform solution with tetramethyl silane as internal standard, using a Bruker AW 80 instrument. The mass spectra were recorded with a VG TS-250 spectrometer and elemental microanalyses were performed with a Perkin-Elmer 240B analyzer. The reactions were monitored by tlc using pre-coated 0.25 mm Merck silica gel 60 F₂₅₄ plates and the spots were visualized under uv light. All solvents were purchased from Fluka and were purified according to established procedures [10].

Preparation of Bisphenylhydrazones of 3-Hydroxyiminopentane-2,4-diones (**3**). General Procedure.

To an ice cooled solution (1 mmole) of 3-hydroxyiminopentane-2,4-dione (**1**) in methanol-water (1:1) (5 ml), a solution of phenylhydrazine (2.2 mmoles) in the same solvent (5 ml) and glacial acetic acid (2-3 drops) was added dropwise over a few minutes. The light yellow product was usually separated after 20 to 30 minutes. The solid, which was obtained by filtration, in addition to **3**, usually carried a small quantity of the corresponding monohydrazone **2**. The latter was removed by repeated washings with a mixture of methylene chloride-petroleum ether.

The above general procedure was applied for the synthesis of all mono- and bishydrazones **2** and **3**. The solutions of those of the substituted phenylhydrazines, which are commercially avail-

able as hydrochloric acid salts, were neutralized first using a slight excess of potassium hydroxide and then were acidified by the addition of a few drops of glacial acetic acid. Product yields are reported in the Table.

Bisphenylhydrazone of 3-Hydroxyiminopentane-2,4-dione (**3a**).

This compound was obtained as a yellow solid mp 141-142°; ir (nujol): 3368, 3164, 1598, 1503, 1321, 935, 756 cm^{-1} ; ms: m/z 201 (98) [M^+ -PhNHNH₂], 143 (49), 130 (30), 118 (60), 103 (18), 91 (12), 77 (100).

Anal. Calcd. for C₁₇H₁₉N₅O: C, 66.00; H, 6.19; N, 22.64. Found: C, 65.88; H 6.11; N, 22.49.

4-Methylphenylhydrazone of 3-Hydroxyiminopentane-2,4-dione (**2b**).

This compound was obtained as a light-yellow solid mp 116-118°; ir (nujol): 3268, 1703, 1568, 1249, 1168, 956, 808 cm^{-1} ; ms: m/z 233 (48) [M^+], 215 (11), 173 (12), 106 (100), 91 (41), 79 (27), 43 (63).

Anal. Calcd. for C₁₂H₁₅N₃O₂: C, 61.78; H, 6.48; N, 18.02. Found: C, 61.61; H 6.38; N, 17.88.

Bis-4-chlorophenylhydrazone of 3-Hydroxyiminopentane-2,4-dione (**3c**).

This compound was obtained as a yellow solid mp 97-99°; ir (nujol): 3280, 3162, 1595, 1492, 1073, 979, 829 cm^{-1} ; ms: m/z 235 (100) [M^+ -4-ClC₆H₄NHNH₂], 200 (14), 177 (16), 152 (41), 129 (75), 111 (36), 75 (24).

Anal. Calcd. for C₁₇H₁₇N₅OCl₂: C, 53.98; H, 4.53; N, 18.52. Found: C, 53.67; H 4.41; N, 18.32.

Bis-(4-nitrophenyl)hydrazone of 3-Hydroxyiminopentane-2,4-dione (**3d**).

This compound was obtained as a yellow solid mp 198-199°; ir (nujol): 3290, 3180, 1598, 1268, 1105, 985, 845 cm^{-1} ; ms: m/z 263 (8) [M^+ -PhNHNH₂], 245 (8), 142 (8), 100 (54), 90 (12), 76 (23), 43 (100).

Anal. Calcd. for C₁₇H₁₇N₇O₅: C, 51.12; H, 4.29; N, 24.55. Found: C, 51.00; H 4.09; N, 24.38.

Bisphenylhydrazone of 2-Hydroxyimino-1-phenylbutane-1,3-dione (**3e**).

This compound was obtained as a yellow solid mp 164-165°; ir (nujol): 3223, 1546, 1500, 1313, 1170, 986, 768 cm^{-1} ; ms: m/z 263 (85) [M^+ -PhNHNH₂], 221 (25), 205 (29), 193 (13), 180 (49), 91 (11), 77 (100).

Anal. Calcd. for C₂₂H₂₁N₅O: C, 71.14; H, 5.70; N, 18.86. Found: C, 71.00; H 5.48; N, 18.68.

2-(4-Methylphenyl)hydrazone of 3-Hydroxyiminopentane-2,4-dione (**2f**).

This compound was obtained as a light-yellow solid mp 113-115°; ir (nujol): 3172, 1668, 1610, 1510, 992, 813, 756 cm^{-1} ; ms: m/z 295 (M^+ , 15), 277 (7), 105 (100), 91 (30).

Anal. Calcd. for C₁₇H₁₇N₃O₂: C, 69.13; H, 5.80; N, 14.23. Found: C, 68.91; H 5.80; N, 14.34.

Bis-(4-chlorophenyl)hydrazone of 2-Hydroxyimino-1-phenylbutane-1,3-dione (**3g**).

This compound was obtained as a yellow solid mp 148-149°; ir (nujol): 3163, 1592, 1493, 1313, 992, 827, 761 cm^{-1} ; ms: m/z 315 (100), 297 (51), 214 (49), 193 (20), 111 (52), 105 (51), 77 (93).

Anal. Calcd. for $C_{22}H_{19}N_5OCl_2$: C, 60.00; H, 4.35; N, 15.91. Found: C, 60.20; H 4.45; N, 16.11.

Bis-(4-nitrophenyl)hydrazone of 2-Hydroxyimino-1-phenylbutane-1,3-dione (**3h**).

This compound was obtained as a yellow solid mp 192-193°; ir (nujol): 3300, 1595, 1400, 1293, 1036, 990, 874 cm^{-1} ; ms: m/z 308 (100), 261 (7), 241 (8), 179 (30), 105 (54), 76 (40).

Anal. Calcd. for $C_{22}H_{19}N_7O$: C, 66.48; H, 4.82; N, 24.67. Found: C, 66.31; H 4.95; N, 24.61.

Bisphenylhydrazone of 2-Hydroxyimino-1,2-diphenylpropane-1,3-dione (**3i**).

This compound was obtained as a yellow solid mp 124-125°; ir (nujol): 3204, 1593, 1494, 1049, 908, 748, 690 cm^{-1} ; ms: m/z 325 (48) [M^+ -PhNHNH₂], 103 (17), 91 (33), 77 (100), 51 (45).

Anal. Calcd. for $C_{27}H_{23}N_5O$: C, 74.80; H, 5.35; N, 16.16. Found: C, 74.96; H 5.45; N, 15.98.

Bisphenylhydrazone of 2-Hydroxyimino-5,5-dimethylcyclohexane-1,3-dione (**3j**).

This compound was obtained as a yellow solid mp 200-201°; ir (nujol): 3280, 1591, 1250, 1069, 970, 798, 692 cm^{-1} ; ms: m/z 349 (3) [M^+], 332 (9), 93 (22), 92 (53), 91 (14), 77 (100), 65 (49).

Anal. Calcd. for $C_{20}H_{23}N_5O$: C, 68.74; H, 6.63; N, 20.04. Found: C, 68.48; H 6.51; N, 19.81.

Lead Tetraacetate Oxidation of Bisphenylhydrazone of 3-Hydroxyiminopentane-2,4-diones **3**, to 5-Acetyl-4-methyl-2-phenyl-1,2,3-triazole 1-Oxides **5**. General Procedure.

To a stirred suspension of **3** (4 mmoles) in methylene chloride (20 ml), lead tetraacetate (9.5 mmoles) dissolved in the same solvent (20 ml) was added. The slight excess of the oxidant was checked throughout the experiment by the use of potassium iodide-starch paper and maintained, if necessary, by the addition of extra amounts of lead tetraacetate. When all the starting material was consumed the mixture was filtered and the filtrate was extracted successively with sodium thiosulfate and sodium carbonate. The dried solution was evaporated under reduced pressure and the residue was chromatographed on a medium pressure silica gel column using mixtures of petroleum ether-ethyl acetate of increasing polarity. Fair-to-excellent yields of 1,2,3-triazole 1-oxides **5** were isolated and recrystallized from ethyl acetate-petroleum ether in order to obtain samples for elemental analysis and spectroscopic measurements.

According to the general procedure described above all α -hydroxyimino mono- and bishydrazones **2** and **3** were oxidized. In some occasions the resulting from the oxidation *N*-oxides **5** were relatively insoluble and were isolated from the reaction mixture without resorting to column chromatography. In those cases mixtures of petroleum ether-ethyl acetate aided the crystallization. Product yields are reported in the Table. The crystals of all derivatives were colorless-to-straw colored.

5-Acetyl-4-methyl-2-phenyl-1,2,3-triazole 1-Oxide (**5a**).

This compound was obtained as a yellow solid mp 49-50°(ethyl acetate-petroleum ether); ir (nujol): 1670, 1305, 1062, 952, 770, 734, 690 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.52 (s, 3H, 4-CH₃), 2.71 (s, 3H, COCH₃), 7.20-8.08 (m, 5H, aromatic); ms: m/z 217 (68) [M^+], 175 (12), 158 (19), 132 (17), 91 (100), 77 (85), 43 (51).

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.35. Found: C, 60.70; H 5.24; N, 19.48.

5-Acetyl-4-methyl-2-(4-methylphenyl)-1,2,3-triazole 1-Oxide (**5b**).

This compound was obtained as a yellow solid mp 118-119°(ethyl acetate-petroleum ether); ir (nujol): 1670, 1315, 11170, 1015, 956, 814, 730 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.38 (s, 3H, 4-CH₃C₆H₄), 2.56 (s, 3H, 4-CH₃), 2.70 (s, 3H, COCH₃), 7.28 (d, J = 8.0 Hz, 2H, H-3', H-5'), 7.72 (d, J = 8.0 Hz, 2H, H-2', H-6'); ms: m/z 231 (M^+ , 48), 189 (14), 172 (19), 105 (100), 91 (83), 65 (44), 43 (41).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.50; H 5.76; N, 17.93.

5-Acetyl-4-methyl-2-(4-chlorophenyl)-1,2,3-triazole 1-Oxide (**5c**).

This compound was obtained as a yellow solid mp 138-139°(ethyl acetate-petroleum ether); ir (nujol): 1668, 1315, 1023, 1059, 1009, 950, 828 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.55 (s, 3H, 4-CH₃), 2.71 (s, 3H, COCH₃), 7.12-8.02 (m, 4H, aromatic); ms: m/z 251 (M^+ , 49), 209 (21), 192 (16), 125 (100), 111 (68), 75 (31), 43 (90).

Anal. Calcd. for $C_{11}H_{10}N_3O_2Cl$: C, 52.49; H, 4.00; N, 16.70. Found: C, 52.61; H 4.11; N, 16.72.

5-Acetyl-4-methyl-2-(4-nitrophenyl)-1,2,3-triazole 1-Oxide (**5d**).

This compound was obtained as a yellow solid mp 158-159°(ethanol); ir (nujol): 1670, 1304, 1075, 950, 858, 830, 744 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.53 (s, 3H, 4-CH₃), 2.71 (s, 3H, COCH₃), 8.32 (bs, 4H, aromatic); ms: m/z 262 (8) [M^+], 136 (6), 122 (14), 91 (7), 75 (8), 43 (100).

Anal. Calcd. for $C_{11}H_{10}N_4O_4$: C, 50.38; H, 3.84; N, 21.37. Found: C, 50.41; H 3.91; N, 21.41.

5-Benzoyl-4-methyl-2-phenyl-1,2,3-triazole 1-Oxide (**5e**).

This compound was obtained as a yellow solid mp 139-140°(ethyl acetate-petroleum ether); ir (nujol): 1638, 1594, 1507, 1093, 916, 718, 686 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.43 (s, 3H, 4-CH₃C₆H₄), 7.15-8.18 (m, 10H, aromatic); ms: m/z 279 (28) [M^+], 263 (3), 132 (8), 105 (100), 91 (48), 77 (81), 51 (11).

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.80; H, 4.69; N, 15.05. Found: C, 68.93; H 4.73; N, 15.16.

5-Benzoyl-4-methyl-2-(4-methylphenyl)-1,2,3-triazole 1-Oxide (**5f**).

This compound was obtained as a yellow solid mp 165-166°(ethyl acetate-petroleum ether); ir (nujol): 1638, 1335, 1091, 912, 812, 720, 682 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.38 (s, 3H, 4'-CH₃C₆H₄), 2.45 (s, 3H, 4-CH₃), 7.18-8.04 (m, 9H, aromatic); ms: m/z 293 (10) [M^+], 105 (100), 91 (21), 77 (32), 65 (12), 51 (8).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 65.39; H 5.10; N, 14.11.

5-Benzoyl-4-methyl-2-(4-chlorophenyl)-1,2,3-triazole 1-Oxide (**5g**).

This compound was obtained as a yellow solid mp 172-173°(ethyl acetate-petroleum ether); ir (nujol): 1642, 1511, 1340, 1192, 918, 830, 722 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 2.48

(s, 3H, 4-CH₃), 7.18-8.14 (m, 9H, aromatic); ms: m/z 313 (88) [M⁺], 297 (16), 141 (6), 125 (25), 105 (100), 77 (45), 51 (12).

Anal. Calcd. for C₁₆H₁₂N₃O₂Cl: C, 61.25; H, 3.85; N, 13.39. Found: C, 61.31; H 3.98; N, 13.37.

5-Benzoyl-4-methyl-2-(4-nitrophenyl)-1,2,3-triazole 1-Oxide (5h).

This compound was obtained as a yellow solid mp 191-192° (ethyl acetate-petroleum ether); ir (nujol): 1638, 1593, 1527, 1089, 913, 852, 722 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.51 (s, 3H, 4-CH₃), 8.33 (s, 4H, H-2', 3', 5', 6'), 7.23-8.74 (m, 5H, aromatic); ms: m/z 324 (37) [M⁺], 177 (98), 136 (49), 105 (43), 90 (42), 74 (93), 41 (100).

Anal. Calcd. for C₁₆H₁₂N₄O₄: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.08; H 3.80; N, 17.11.

5-Benzoyl-2,4-diphenyl-1,2,3-triazole 1-Oxide (5l).

This compound was obtained as a yellow solid mp 167-168° (ethyl acetate-petroleum ether); ir (nujol): 1636, 1585, 1484, 1328, 892, 739, 690 cm⁻¹; ¹H nmr (deuteriochloroform): δ 7.19-8.21 (m, aromatic); ms: m/z 341 (7) [M⁺], 105 (55), 91 (19), 77 (100), 51 (9).

Anal. Calcd. for C₂₁H₁₅N₃O₂: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.70; H 4.28; N, 12.28.

2-Phenyl-5,5-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzo-1,2,3-triazole 1-Oxide (5j).

This compound was obtained as a yellow solid mp 107-108° (methylene chloride-petroleum ether); ir (nujol): 1737, 1516, 1232, 1013, 768, 722, 690 cm⁻¹; ¹H nmr (deuterio-

chloroform): δ 1.04 (s, 3H, 5-CH₃), 1.20 (s, 3H, 5-CH₃), 2.33-3.08 (m, 4H, 4-H, 6-H), 7.20-8.12 (m, 5H, aromatics); ms: m/z 258 (57) [M⁺+1], 242 (8), 105 (13), 92 (16.3), 91 (14), 77 (100), 43 (44).

Anal. Calcd. for C₁₄H₁₅N₃O₂: C, 65.35; H, 5.88; N, 16.33. Found: C, 65.34; H 6.00; N, 16.45.

REFERENCES AND NOTES

- [1] A. Albini and S. Pietra, *Heterocyclic N-Oxides*, CRC Press, Boca Raton, Florida, 1991, Chapter 3.
- [2] M. Begtrup and J. Holm, *J. Chem. Soc., Perkin Trans. 1*, 503 (1981)
- [3a] G. Ponzio, *Gazz. Chim. Ital.*, **28**, 173 (1898); [b] *Gazz. Chim. Ital.*, **29**, 277 (1899); [c] *Gazz. Chim. Ital.*, **29**, 283 (1899); [d] *Gazz. Chim. Ital.*, **29**, 349 (1899); [e] *Gazz. Chim. Ital.*, **30**, 459 (1900); [f] *Gazz. Chim. Ital.*, **31**, 413 (1901).
- [4] A. M. Talati and B. V. Shah, *Indian J. Chem.*, **11**, 1077 (1973).
- [5] H. Lind and H. Kristinsson, *Synthesis*, 198 (1974).
- [6] S. K. Talapatra, P. Chaudhuri and B. Talaparta, *Heterocycles*, **14**, 1279 (1980).
- [7] N. Henning, T. Dassler and W. Jugelt, *Z. Chem.*, **22**, 25 (1982).
- [8] M. A. Shafeev, A. A. Almukhamedov, V. V. Shcherbakov, G. A. Gareev and L. I. Vereshchagin, *Zh. Org. Khim.*, **30**, 918 (1994).
- [9] G. L. McNew and N. K. Sundholm, *Phytopathology*, **39**, 721 (1949).
- [10] D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 1966.