

Mark D. Bjorklund and Michael D. Coburn*

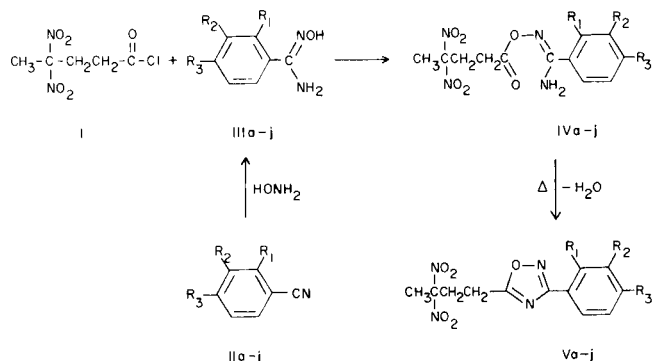
University of California, Los Alamos Scientific Laboratory, Los Alamos, New Mexico 87545

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The syntheses of 3,5-bis(3,3-dinitrobutyl)-1,2,4-oxadiazole and a series of 3-aryl-5-(3,3-dinitrobutyl)-1,2,4-oxadiazoles were accomplished by treating 4,4-dinitropentanoyl chloride with the appropriate amidoximes to yield the intermediate *O*-(4,4-dinitropentanoyl)amidoximes, which were dehydrated to the 1,2,4-oxadiazoles.

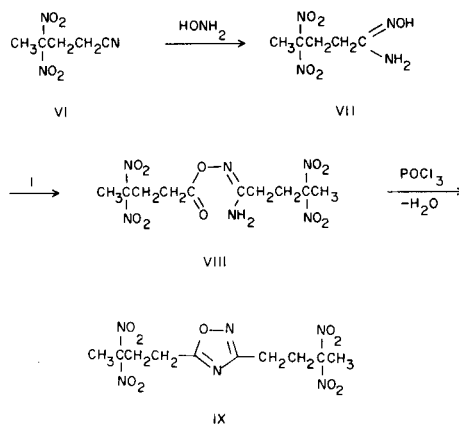
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Although the syntheses of various 1,2,4-oxadiazoles have been studied extensively (2), no nitroalkyl-1,2,4-oxadiazoles have been previously reported. We have found that various benzamidoximes (III), obtained by adding hydroxylamine to aryl nitriles (II), could be treated with 4,4-dinitropentanoyl chloride (I) to produce *O*-(4,4-dinitropentanoyl)benzamidoximes (IV). Thermal dehydration occurred when IV were heated to 130-135° to give 5-(3,3-dinitrobutyl)-3-aryl-1,2,4-oxadiazoles (V).



	R ₁	R ₂	R ₃
a	H	H	H
b	CH ₃	H	H
c	H	CH ₃	H
d	H	H	CH ₃
e	F	H	H
f	H	F	H
g	H	H	F
h	CH ₃ O	H	H
i	H	CH ₃ O	H
j	H	H	CH ₃ O

Different conditions were required for the thermal dehydration of *O*-(4,4-dinitropentanoyl)-4,4-dinitropentanamidoxime (VIII), which was obtained from the reaction of I with 4,4-dinitropentanamidoxime (VII). When VIII was heated above 120°, we found only a trace of the desired product, 3,5-bis(3,3-dinitrobutyl)-1,2,4-oxadiazole (IX). Instead of IX, numerous unidentified decomposition products were formed. Heating VII at a lower temperature (100°) gave no reaction; however, satisfactory yields of IX resulted from refluxing VIII in phosphorus oxychloride.



Also found to be effective was the periodic addition of aliquots of acetic anhydride over a period of 24 hours to a refluxing mixture of VIII in toluene. However, the addition of a single aliquot of acetic anhydride to the above solution was ineffective, as was refluxing VIII in pure acetic anhydride.

The nmr spectra of all the 1,2,4-oxadiazoles synthesized showed the four methylene hydrogens of the 5-(3,3-dinitrobutyl) groups to be a sharp singlet indicating very similar chemical shifts rather than multiplets observed with the adjacent methylene hydrogens in the other compounds. In addition, the methylene hydrogens of the 3-(3,3-dinitrobutyl) group of (IX) also occurred as a singlet.

EXPERIMENTAL (3,4)

Benzamidoximes (IIIa-j).

Benzamidoxime (IIIa) (5), 2-methylbenzamidoxime (IIIb) (6), 4-methylbenzamidoxime (IIIc) (7), 2- and 4-methoxybenzamidoxime (IIIh and IIIi) (8), and 3-methoxybenzamidoxime (IIIj), were prepared by refluxing a solution of hydroxylamine (0.21 mole) and the corresponding nitrile (0.126 mole) in 300 ml. of ethanol for three hours. The solvent was removed under reduced pressure and the residue was recrystallized from water.

The fluorobenzamidoximes (IIIe-g) and 3-methylbenzamidoxime (IIIc) (9), were obtained by adding hydrogen sulfide to the corresponding nitriles to yield the thioamides, which were treated with hydroxylamine to give the amidoximes according to the procedure described for (IIIg) (10). The following compounds have not been previously reported.

2-Fluorothiobenzamide.

This compound had m.p. 83° and was obtained in 71% yield; ¹H-nmr (hexadeuterioacetone): δ 7.15 (m, 3H, aromatic), 7.80 (m, 1H, aromatic), 8.52 (bs, 1H, NH), 9.02 (bs, 1H, NH).

Anal. Calcd. for C_7H_6FNS : C, 54.18; H, 3.90; N, 9.03. Found: C, 54.34; H, 3.79; N, 8.97.

3-Fluorothiobenzamide.

This compound had m.p. 110° and was obtained in 60% yield; 1H -nmr (hexadeuterioacetone): δ 7.13 (m, 2H, aromatic), 7.58 (m, 2H, aromatic), 8.78 (bs, 2H, NH_2).

Anal. Calcd. for C_7H_6FNS : C, 54.18; H, 3.90; N, 9.03. Found: C, 54.31; H, 3.70; N, 8.91.

2-Fluorobenzamidoxime (IIIe).

This compound was obtained as an oil, n_D^{25} 1.5832, 80% yield; 1H -nmr (hexadeuterioacetone): δ 5.63 (bs, 2H, NH_2), 7.42 (m, 4H, aromatic), 9.20 (bs, 1H, OH).

Anal. Calcd. for $C_7H_7FN_2O$: C, 54.54; H, 4.58; N, 18.17. Found: C, 54.30; H, 4.25; N, 17.73.

3-Fluorobenzamidoxime (III f).

This compound had m.p. 76° and was obtained in 88% yield; 1H -nmr (hexadeuterioacetone): δ 5.68 (bs, 2H, NH_2), 7.35 (m, 4H, aromatic), 8.93 (bs, 1H, OH).

Anal. Calcd. for $C_7H_7FN_2O$: C, 54.54; H, 4.58; N, 18.17. Found: C, 54.34; H, 4.81; N, 18.21.

3-Methoxybenzamidoxime (III i).

This compound had m.p. 105° and was obtained in 75% yield; 1H -nmr (hexadeuterioacetone): δ 3.80 (s, 3H, CH_3), 5.50 (bs, 2H, NH_2), 6.95 (m, 1H, aromatic), 7.25 (m, 3H, aromatic), 9.17 (bs, 1H, OH).

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.63; H, 6.28; N, 16.89.

O-(4,4-Dinitropentanoyl)benzamidoximes (IVa-j).

A solution of the benzamidoxime (0.01 mole) in acetone (15 ml.) was treated with 4,4-dinitropentanoyl chloride (I) (11), (2.10 g., 0.01 mole) dropwise at 5-10°. The resulting solution was allowed to stir at 25° for 2 hours, during which the hydrochloride salt of the product precipitated. The salt was collected by filtration, dried, and stirred into a solution of sodium bicarbonate (0.84 g., 0.01 mole) in water (50 ml.) to liberate the O-(4,4-dinitropentanoyl)benzamidoxime, which was collected by filtration and dried. All compounds were recrystallized from aqueous ethanol, except IVh and IVi. These were recrystallized at room temperature from a mixture of acetone, methanol, and water. The following compounds were prepared.

O-(4,4-Dinitropentanoyl)benzamidoxime (IVa).

This compound had m.p. $104-105^\circ$ and was obtained in 89% yield; 1H -nmr (hexadeuterioacetone): δ 2.27 (s, 3H, CH_3), 2.88 (m, 4H, CH_2), 6.30 (bs, 2H, NH_2), 7.44 (m, 3H, aromatic), 7.76 (m, 2H, aromatic).

Anal. Calcd. for $C_{12}H_{14}N_4O_6$: C, 46.45; H, 4.55; N, 18.06. Found: C, 46.13; H, 4.81; N, 18.01.

O-(4,4-Dinitropentanoyl)-2-methylbenzamidoxime (IVb).

This compound had m.p. 99° and was obtained in 80% yield; 1H -nmr (hexadeuterioacetone): δ 2.27 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.86 (m, 4H, CH_2), 6.20 (bs, 2H, NH_2), 7.27 (m, 4H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_6$: C, 48.15; H, 4.97; N, 17.28. Found: C, 48.23; H, 4.60; N, 17.21.

O-(4,4-Dinitropentanoyl)-3-methylbenzamidoxime (IVc).

This compound had m.p. 102° and was obtained in 88% yield; 1H -nmr (hexadeuterioacetone): δ 2.27 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.87 (m, 4H, CH_2), 6.27 (bs, 2H, NH_2), 7.29 (m, 2H, aromatic), 7.56 (m, 2H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_6$: C, 48.15; H, 4.97; N, 17.28. Found: C, 48.33; H, 5.04; N, 17.39.

O-(4,4-Dinitropentanoyl)-4-methylbenzamidoxime (IVd).

This compound had m.p. 116° and was obtained in 90% yield; 1H -nmr (hexadeuterioacetone): δ 2.24 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.83 (m, 4H,

CH_2), 6.13 (bs, 2H, NH_2), 7.10 (d, J = 8 Hz, 2H, aromatic), 7.54 (d, J = 8 Hz, 2H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_6$: C, 48.15; H, 4.97; N, 17.28. Found: C, 48.36; H, 4.79; N, 17.53.

O-(4,4-Dinitropentanoyl)-2-fluorobenzamidoxime (IVe).

This compound had m.p. 72° and was obtained in 89% yield; 1H -nmr (hexadeuterioacetone): δ 2.30 (s, 3H, CH_3), 2.87 (m, 4H, CH_2), 6.38 (bs, 2H, NH_2), 7.42 (m, 4H, aromatic).

Anal. Calcd. for $C_{12}H_{13}FN_4O_6$: C, 43.91; H, 3.99; N, 17.07. Found: C, 44.17; H, 3.95; N, 17.26.

O-(4,4-Dinitropentanoyl)-3-fluorobenzamidoxime (IVf).

This compound had m.p. 118° and was obtained in 79% yield; 1H -nmr (hexadeuterioacetone): δ 2.45 (s, 3H, CH_3), 2.90 (m, 4H, CH_2), 6.42 (bs, 2H, NH_2), 7.47 (m, 4H, aromatic).

Anal. Calcd. for $C_{12}H_{13}FN_4O_6$: C, 43.91; H, 3.99; N, 17.07. Found: C, 44.23; H, 3.91; N, 17.27.

O-(4,4-Dinitropentanoyl)-4-fluorobenzamidoxime (IVg).

This compound had m.p. 133° and was obtained in 72% yield; 1H -nmr (hexadeuterioacetone): δ 2.30 (s, 3H, CH_3), 2.88 (m, 4H, CH_2), 6.40 (bs, 2H, NH_2), 7.27 (d, $J_{H,H} = 8.5$ Hz, 2H, aromatic), 7.85 (dd, $J_{H,H} = 8.5$ Hz, $J_{F,H} = 5.5$ Hz, 2H, aromatic).

Anal. Calcd. for $C_{12}H_{13}FN_4O_6$: C, 43.91; H, 3.99; N, 17.07. Found: C, 44.45; H, 4.13; N, 17.20.

O-(4,4-Dinitropentanoyl)-2-methoxybenzamidoxime (IVh).

This compound had m.p. 65° and was obtained in 72% yield; 1H -nmr (hexadeuterioacetone): δ 2.19 (s, 3H, CH_3), 2.75 (m, 4H, CH_2), 3.73 (s, 3H, CH_3), 6.00 (bs, 2H, NH_2), 6.57-7.42 (m, 4H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.89; H, 4.74; N, 16.46. Found: C, 45.61; H, 5.03; N, 16.34.

O-(4,4-Dinitropentanoyl)-3-methoxybenzamidoxime (IVi).

This compound had m.p. 133° and was obtained in 87% yield; 1H -nmr (hexadeuterioacetone): δ 2.29 (s, 3H, CH_3), 2.88 (m, 4H, CH_2), 3.83 (s, 3H, CH_3), 6.29 (bs, 2H, NH_2), 6.87-7.42 (m, 4H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.89; H, 4.74; N, 16.46. Found: C, 45.79; H, 4.88; N, 16.50.

O-(4,4-Dinitropentanoyl)-4-methoxybenzamidoxime (IVj).

This compound had m.p. 119° and was obtained in 77% yield; 1H -nmr (hexadeuterioacetone): δ 2.22 (s, 3H, CH_3), 2.80 (m, 4H, CH_2), 3.72 (s, 3H, CH_3), 5.98 (bs, 2H, NH_2), 6.72 (d, J = 8 Hz, 2H, aromatic), 7.45 (d, J = 8 Hz, 2H, aromatic).

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.89; H, 4.74; N, 16.46. Found: C, 45.77; H, 4.75; N, 16.60.

3-Aryl-5-(3,3-dinitrobutyl)-1,2,4-oxadiazoles (Va-j).

The O-(4,4-dinitropentanoyl)benzamidoximes (IVa-j) (0.01 mole) were heated in a test tube with an oil bath to $130-135^\circ$ for 1 hour or until the evolution of water vapor had ceased. The products that crystallized on standing were recrystallized from toluene-hexane. The oils were chromatographed over alumina with toluene to give analytically pure products. The following compounds were prepared according to this procedure.

5-(3,3-Dinitrobutyl)-3-phenyl-1,2,4-oxadiazole (Va).

This compound had m.p. $58-59^\circ$ and was obtained in 94% yield; 1H -nmr (hexadeuterioacetone): δ 2.37 (s, 3H, CH_3), 3.27 (s, 4H, CH_2), 7.53 (m, 3H, aromatic), 8.07 (m, 2H, aromatic).

Anal. Calcd. for $C_{12}H_{12}N_4O_5$: C, 49.32; H, 4.14; N, 19.17. Found: C, 49.42; H, 3.86; N, 19.53.

5-(3,3-Dinitrobutyl)-3-(2-methylphenyl)-1,2,4-oxadiazole (Vb).

This compound was obtained as an oil n_D^{25} 1.5451, 82% yield; 1H -nmr

(hexadeuterioacetone): δ 2.39 (s, 3H, CH₃), 2.59 (s, 3H, CH₃), 3.29 (s, 4H, CH₂), 7.37 (m, 3H, aromatic), 7.96 (m, 1H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₅: C, 50.98; H, 4.61; N, 18.29. Found: C, 51.19; H, 4.50; N, 18.53.

5-(3,3-Dinitrobutyl)-3-(3-methylphenyl)-1,2,4-oxadiazole (Vc).

This compound had m.p. 60° and was obtained in 96% yield; ¹H-nmr (hexadeuterioacetone): δ 2.40 (s, 6H, CH₃), 3.27 (s, 4H, CH₂), 7.35 (m, 2H, aromatic), 7.85 (m, 2H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₅: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.97; H, 4.45; N, 18.46.

5-(3,3-Dinitrobutyl)-3-(4-methylphenyl)-1,2,4-oxadiazole (Vd).

This compound had m.p. 56-57° and was obtained in 30% yield; ¹H-nmr (hexadeuterioacetone): δ 2.34 (s, 6H, CH₃), 3.20 (s, 4H, CH₂), 7.17 (d, J = 8 Hz, 2H, aromatic), 7.79 (d, J = 8 Hz, 2H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₅: C, 50.98; H, 4.61; N, 18.29. Found: C, 51.18; H, 4.59; N, 18.41.

5-(3,3-Dinitrobutyl)-3-(2-fluorophenyl)-1,2,4-oxadiazole (Ve).

This compound was obtained as an oil, $N_D^{25} = 1.5361$, 94% yield; ¹H-nmr (hexadeuterioacetone): δ 2.42 (s, 3H, CH₃), 3.33 (s, 4H, CH₂), 7.45 (m, 3H, aromatic), 8.07 (m, 1H, aromatic).

Anal. Calcd. for C₁₂H₁₁FN₄O₅: C, 46.46; H, 3.57; N, 18.06. Found: C, 46.58; H, 3.54; N, 17.94.

5-(3,3-Dinitrobutyl)-3-(3-fluorophenyl)-1,2,4-oxadiazole (Vf).

This compound was obtained as an oil, $N_D^{25} = 1.5328$, 98% yield; ¹H-nmr (hexadeuterioacetone): δ 2.42 (s, 3H, CH₃), 3.33 (s, 4H, CH₂), 7.57 (m, 4H, aromatic).

Anal. Calcd. for C₁₂H₁₁FN₄O₅: C, 46.46; H, 3.57; N, 18.06. Found: C, 46.42; H, 3.14; N, 18.06.

5-(3,3-Dinitrobutyl)-3-(4-fluorophenyl)-1,2,4-oxadiazole (Vg).

This compound had m.p. 50° and was obtained in 82% yield; ¹H-nmr (hexadeuterioacetone): δ 2.42 (s, 3H, CH₃), 3.33 (s, 4H, CH₂), 7.39 (d, J_{H,H} = 8.5 Hz, 2H, aromatic), 8.12 (dd, J_{H,H} = 8.5 Hz, J_{F,H} = 5.5 Hz, 2H, aromatic).

Anal. Calcd. for C₁₂H₁₁FN₄O₅: C, 46.46; H, 3.57; N, 18.06. Found: C, 46.39; H, 3.60; N, 17.97.

5-(3,3-Dinitrobutyl)-3-(2-methoxyphenyl)-1,2,4-oxadiazole (Vh).

This compound had m.p. 66.5° and was obtained in 82% yield; ¹H-nmr (hexadeuterioacetone): δ 2.30 (s, 3H, CH₃), 3.17 (s, 4H, CH₂), 3.78 (s, 3H, CH₃), 6.6-7.7 (m, 4H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₆: C, 48.45; H, 4.38; N, 17.38. Found: C, 48.21; H, 4.42; N, 17.38.

5-(3,3-Dinitrobutyl)-3-(3-methoxyphenyl)-1,2,4-oxadiazole (Vi).

This compound had m.p. 92.5° and was obtained in 98% yield; ¹H-nmr (hexadeuterioacetone): δ 2.40 (s, 3H, CH₃), 3.31 (s, 4H, CH₂), 3.88 (s, 3H, CH₃), 6.9-7.7 (m, 4H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₆: C, 48.45; H, 4.38; N, 17.38. Found: C, 48.40; H, 4.42; N, 17.52.

5-(3,3-Dinitrobutyl)-3-(4-methoxyphenyl)-1,2,4-oxadiazole (Vj).

This compound had m.p. 69° and was obtained in 90% yield; ¹H-nmr (hexadeuterioacetone): δ 2.33 (s, 3H, CH₃), 3.18 (s, 4H, CH₂), 3.77 (s, 3H, CH₃), 6.83 (d, J = 8 Hz, 2H, aromatic), 7.71 (d, J = 8 Hz, 2H, aromatic).

Anal. Calcd. for C₁₃H₁₄N₄O₆: C, 48.45; H, 4.38; N, 17.38. Found: C, 48.55; H, 4.35; N, 17.53.

4,4-Dinitropentanamidoxime (VII).

4,4-Dinitropentanenitrile (VI) (12) (3.13 g., 0.018 mole) was added to a solution of hydroxylamine (0.054 mole) in methanol (25 ml.) and the

resulting solution was heated under reflux for 3 hours. The solvent was removed under reduced pressure and the residue was recrystallized from water to yield a first crop of 1.41 g. of VII, m.p. 94°.

Anal. Calcd. for C₅H₁₀N₄O₅: C, 29.13; H, 4.89; N, 27.18. Found: C, 29.23; H, 4.96; N, 26.79.

The filtrate was concentrated under reduced pressure to yield a second crop of 0.92 g., m.p. 88°. The combined yield was 2.33 g. (63%); ¹H-nmr (hexadeuterioacetone): δ 2.22 (s, 3H, CH₃), 2.25 (m, 2H, CH₂), 2.83 (m, 2H, CH₂), 5.27 (bs, 2H, NH₂), 8.33 (bs, 1H, OH).

O-(4,4-Dinitropentanoyl)-4,4-dinitropentanamidoxime (VIII).

A solution of 4,4-dinitropentanamidoxime (VII), (1.03 g., 0.005 mole) in acetone (15 ml.) was treated with 4,4-dinitropentanoyl chloride (I) (8) (1.05 g., 0.005 mole) at 5-10°. The solution was allowed to stir at 25° overnight and then evaporated to dryness under reduced pressure. The residue was treated with a solution of sodium bicarbonate (0.5 g., 0.006 mole) in water (25 ml.). The solid was collected and recrystallized from aqueous ethanol to yield 1.23 g. (65%) of VIII, m.p. 110°; ¹H-nmr (hexadeuterioacetone): δ 2.25 (s, 6H, CH₃), 2.70 (m, 8H, CH₂), 6.00 (bs, 2H, NH₂).

Anal. Calcd. for C₁₀H₁₆N₆O₁₀: C, 31.58; H, 4.24; N, 22.10. Found: C, 31.66; H, 3.89; N, 22.08.

3,5-Bis(3,3-dinitrobutyl)-1,2,4-oxadiazole (IX).

To 35 ml. of phosphorus oxychloride was added O-(4,4-dinitropentanoyl)-4,4-dinitropentanamidoxime (VIII) (3.5 g., 0.009 mole). The resulting mixture was heated under reflux for 6 hours, then poured over ice and stirred until all the excess phosphorus oxychloride had hydrolyzed. Compound IX was extracted with dichloromethane (3 × 50 ml.) and the extracts dried over anhydrous magnesium sulfate. The dichloromethane was removed under reduced pressure and the residual oil was chromatographed over alumina using toluene/ethanol (97.5/2.5) as the eluant to yield 1.37 g. (41%) of IX, $N_D^{25} = 1.4958$; ¹H-nmr (hexadeuterioacetone): δ 2.30 (s, 6H, CH₃), 2.93 (s, 4H, CH₂), 3.13 (s, 4H, CH₂); ¹³C-nmr (deuteriochloroform): δ 20.8, 21.3, 22.0, 22.2, 32.9, 33.3, 118.1, 118.7, 167.8, 176.8.

Anal. Calcd. for C₁₀H₁₄N₆O₅: C, 33.17; H, 3.89; N, 23.20. Found: C, 32.81; H, 3.67; N, 22.92.

REFERENCES AND NOTES

- (1) This work was performed under the auspices of the U.S. Department of Energy.
- (2) L. B. Clapp, in "Advances in Heterocyclic Chemistry," Vol. 20, A. R. Katritzky and A. J. Boulton, Eds., Academic Press, Inc., New York, N.Y., 1976, p. 65.
- (3) Microanalyses by M. J. Naranjo and T. L. McKinney.
- (4) Melting points were determined with a Mettler FP-1 apparatus and are corrected. The course and extent of dehydration reactions were followed by thin layer chromatography using a solvent mixture of 95:5 toluene and ethanol. ¹H-nmr spectra were obtained with a Varian A60A spectrometer and ¹³C-nmr spectra were obtained with a Varian S-XL FT-100 spectrometer.
- (5) T. Tieman, *Ber.*, **17**, 1685 (1884).
- (6) L. Schubart, *ibid.*, **22**, 2438 (1889).
- (7) L. Schubart, *ibid.*, **19**, 1488 (1886).
- (8) J. A. Miller, *ibid.*, **22**, 2790 (1889).
- (9) G. Prossel, E. Schinezel and G. Roesch, *German Patent* 2,724,368, 15 Dec. 1977; *Chem. Abstr.*, **88**, 192758q (1978).
- (10) L. Stephenson, W. K. Warburton and M. J. Wilson, *J. Chem. Soc. C*, 861 (1969).
- (11) M. H. Gold, M. B. Frankel, G. B. Linden and K. Klager, *J. Org. Chem.*, **27**, 334 (1962).
- (12) G. S. Shvekhegimer and G. A. Mikheichev, *Zh. Org. Khim.*, **7**, 29 (1971).