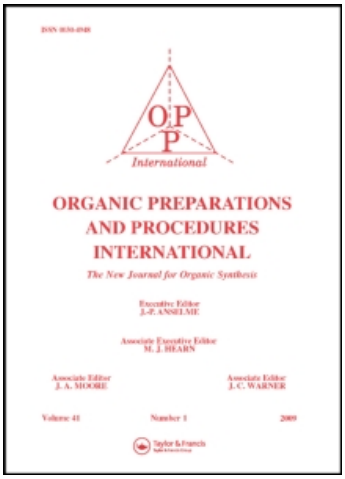

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NITRATION OF 2-CARBONYL-3,4-DICHLOROFURAN DERIVATIVES

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NITRATION OF 2-CARBONYL-3,4-DICHLOROFURAN DERIVATIVES

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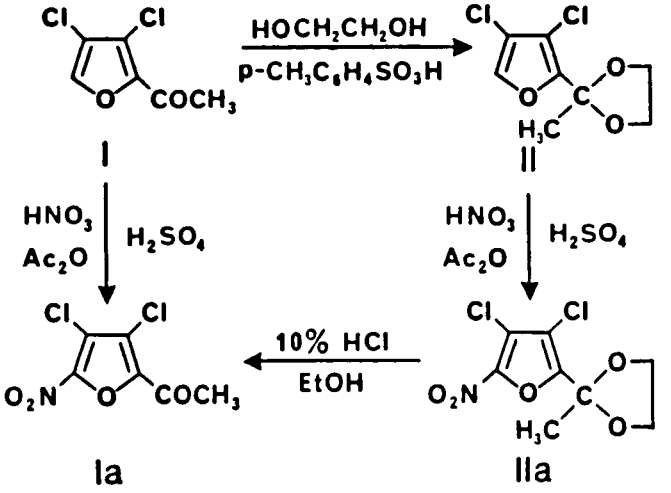
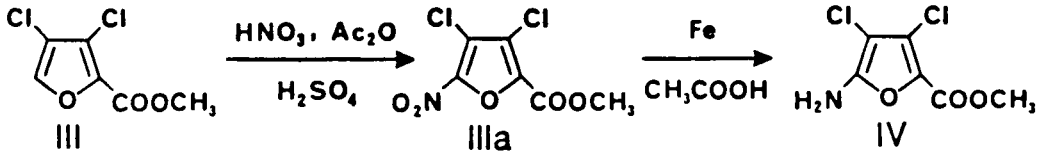
2-Acetyl-3,4-dichlorofuran (I), 3,4-dichloro-2-(2-methyl-1,3-dioxolan-2-yl) furan (II) and methyl 3,4-dichloro-2-furoate (III) were nitrated to give the corresponding new nitro derivatives (Ia-IIIa) which may serve as possible model compounds for the carcinogenic 5-nitrofurylthiazole derivatives.[1]



Nitration of II was more efficient compared to I. Ia could be obtained by hydrolysis of IIa in yields about six-fold greater than that obtained by direct nitration of I. Methyl 3,4- dichloro-5-nitro-2-furoate was reduced using iron/acetic acid to methyl 3,4- dichloro-5-amino-2-furoate (IV). In contrast to the amino derivatives obtained from carcinogenic 5-nitro-2-furylthiazoles which undergo furan ring fission to yield the ketonitrile derivatives,[2,3] methyl 3,4-dichloro-5-



amino-2-furoate was relatively more stable.

EXPERIMENTAL SECTION

Mps are uncorrected. IR spectra were recorded on a JASCO-IR 810 Infrared Spectrophotometer and ^{1}H-NMR spectra were taken with JNM-PMX 60SI in $CDCl_3$ with TMS as an internal standard. MS spectra were taken using JASCO DX-300 Mass Spectrometer. Elemental analyses were performed at Josai University.

Synthesis of 3,4-Dichloro-2-(2-methyl-1,3-dioxolan-2-yl)furan (II).- A mixture of I (10 g), ethylene glycol (4 g) and p-toluenesulfonic acid (0.4 g) in absolute benzene (150 ml) was refluxed to generate a calculated amount of water (1 ml). The reaction mixture was neutralized with sodium bicarbonate and then filtered. The filtrate was evaporated and the residue distilled under reduced pressure to give 10.8 g (87%) of a colorless liquid (II), bp. 129-130°/19 torr. ^{1}H-NMR ($CDCl_3$), δ: 7.35 (1H, s, furan C_5-H), 4.00 (4H, s, -CH_2- CH_2-), 1.82 (3H, s, CH_3). MS m/Z: 222 (M^+); 224 (M^++2), 226 (M^++4).

Nitration of 3,4-Dichloro-2-(2-methyl-1,3-dioxolan-2-yl)furan (a).- Fuming nitric acid (d = 1.49, 30.4 ml) was added dropwise to acetic anhydride (70 ml) below 0° with stirring following which eight drops of sulfuric acid were added. To the above was added a solution of II (7.4 g) in acetic anhydride (20 ml) at about -10° and the mixture was stirred for 5 hrs (should be handled cautiously because the mixture may contain explosive acetyl nitrate). At the end of the reaction the contents were poured into ice water and neutralized with sodium bicarbonate. The sample was extracted with ether and the organic phase was evaporated. The residue was dissolved in methanol (100 ml) and refluxed with sodium acetate for 1 hr to yield IIa which was recrystallized from petroleum-benzin to afford 4.7 g (53%) of colorless prisms, mp. 99-101°. IR: 1315-1335 and 1535-1560 (NO_2).

Anal. Calcd for $C_8H_7Cl_2NO_5$: C, 35.85; H, 2.63; N, 5.23 Found: C, 35.92; H, 2.72; N, 5.33

Synthesis of 2-Acetyl-3,4-dichloro-5-nitrofuran (Ia) and methyl 3,4-dichloro-5-nitro-2- furoate (IIIa) .- To a suspension of IIa (1.0 g) in 50% aqueous ethanol solution (100 ml) was added dropwise 10% HCl (11.4 ml) and the reaction mixture was heated at 90° for 1 hr. After cooling, the separated crystalline mass was collected by suction and recrystallized from petroleum benzin to give 0.7 g (84%) of Ia as colorless plates, mp. 100-102°. The product exhibited physical and chemical characteristics identical to those of 2-acetyl-3,4-dichloro-5-nitrofuran obtained by direct nitration of I. However, the yield of Ia was about six-fold higher using the ketal intermediate than obtained by direct nitration procedure.

Anal. Calcd for $C_6H_3Cl_2NO_4$: C, 32.17; H, 1.35; N, 6.25 Found: C, 32.14; H, 1.33; N, 6.44

Nitration of methyl 3,4-dichloro-2-furoate was conducted at about -5° for 2 hrs using the same procedure described above. The final product (IIIa) was obtained as light yellow plates (0.5 g, 43%, mp 112-114°).

Anal. Calcd for $C_6H_3Cl_2NO_5$: C, 30.03; H, 1.26; N, 5.84 Found: C, 30.18; H, 1.36; N, 6.01

Synthesis of Methyl 5-Amino-3,4-dichloro-2-furoate (IV).- To a solution of IIIa (2.8 g) in acetic acid (50 ml) was added 2.0 g of iron powder. The reaction mixture was stirred at 70° for

30 min, and then filtered. The filtrate was poured into ice water (100 ml), and neutralized with sodium bicarbonate. The precipitate was collected by suction, washed with water and dried. The product was recrystallized from benzene as light beige crystals (1.6 g, 67%, mp 120-124°). IR (KBr): 3430 and 3320 (NH_2), 1690 (C = O) cm^{-1}; ^{1}H-NMR ($CDCl_3$), δ: 3.95 (3H, s, CH_3) 4.6 (2H, broad s, NH_2); MS m/z: 209 (M^+), 211 (M^++2), 213 (M^++4).

Anal. Calcd for $C_6H_5Cl_2NO_3$: C, 34.45; H, 2.34; N, 6.7. Found: C, 34.51; H, 2.28; N, 6.81

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FACILE PREPARATION OF

L-2-OXOTHIAZOLIDINE-4-CARBOXYLIC ACID (OTC)

Submitted by (04/18/88) T. Kömives†

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The title compound (OTC) has recently been identified as a non-toxic precursor for the introduction of L-cysteine into living cells and as a stimulant of the biosynthesis of glutathione (g-L-glutamyl-L-cysteinyl-glycine).[1] The preparation of OTC normally involves the use of dangerous phosgene;[2,3] in addition, we encountered inordinate difficulties in purifing OTC prepared this way. Attempted recrystallizations from hot water[2] resulted in a gum, while the laborious modification of Shah et al.[3] (repeated extractions of OTC with ethyl acetate from acidified water) gave pure OTC albeit in only 5% yield.