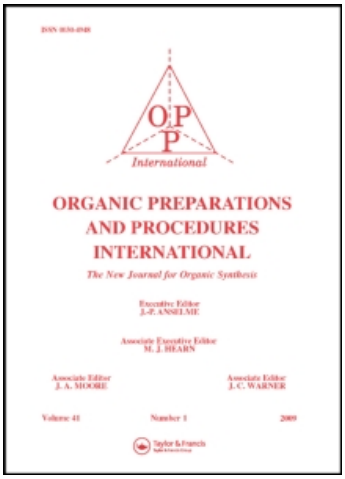

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THREE NEW PRODUCTS FROM METHYL 3,4-DIPHENYL-5-NITRO-2-FUROATE BY CATALYTIC REDDCTION

K. Yamamoto[a]; A. Tanaka[a]; M. Ichikawa[b]; S. Swaminathan[c]; G. T. Bryan[c]
[a] Faculty of Pharmaceutical Sciences, Josai University, Sakado, Saitama, JAPAN [b] Department of Pharmacy, School of Medicine, Nagasaki University, Nagasaki, JAPAN [c] Department of Human Oncology, University of Wisconsin Clinical Cancer Center, Madison, WI

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THREE NEW PRODUCTS FROM METHYL 3,4-DIPHENYL-5-NITRO-2-FUROATE BY CATALYTIC REDUCTION

Submitted by (08/29/86) K. Yamamoto*, A. Tanaka*, M. Ichikawa†, S. Swaminathan††, and G. T. Bryan††

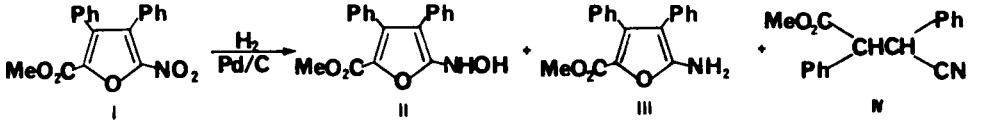
*Faculty of Pharmaceutical Sciences, Josai University, 1-1 Keyakidai, Sakado, Saitama 350-02, JAPAN

†Department of Pharmacy, School of Medicine, Nagasaki University, 7-1 Sakamoto Machi, Nagasaki 852, JAPAN

††Department of Human Oncology, University of Wisconsin Clinical Cancer Center, 600 Highland Avenue, Madison, WI 53792

All biological effects of 5-nitrofurans[1,2] seem to require the reduction of the 5-nitro group to a metabolically reactive intermediate.[3] In the case of the carcinogenic 5-nitrofurylthiazoles, the postulated reduction products 5-nitroso and 5-hydroxylamino derivatives have not been conclusively identified since authentic samples have not yet been synthesized, partly because of the extreme lability of these intermediates. Even the 2-aminofurans are generally unstable and undergo fission of the

furan ring to generate the ketonitrile derivatives.[3,4] Because phenyl groups at positions 3 and 4 could exert a stabilizing effect on the furan ring, we reduced methyl 3,4-diphenyl-5-nitro-2-furoate (I)[5] as a model com-



I II III IV

pound to generate these products. Three new stable products were identified as methyl 3,4-diphenyl-5-hydroxylamino-2-furoate (II), methyl 3,4-diphenyl-5-amino-2-furoate (III) and methyl 3,4-diphenyl-4-cyano-2-butanoate (IV).

EXPERIMENTAL SECTION

Mps are uncorrected. IR spectra were recorded on a Nippon Bunko DS-701G Infrared Spectrophotometer and ^{1}H-NMR spectra were taken with JNM-C-60H in ca. 4% (w/v) $CDCl_3$ with TMS as an internal standard. MS spectra were taken using JEOL-JMS-01SG Spectrometer. Elemental analyses were performed at Josai University.

Catalytic Hydrogenation of Methyl 3,4-Diphenyl-5-nitro-2-furoate (II).- A solution of I (10 g) in 400 ml of tetrahydrofuran (THF) was stirred with 5% Pd-C (3 g) over hydrogen at room temperature at atmospheric pressure, the absorption of hydrogen ceased after the calculated amount of hydrogen had been consumed. The catalyst was removed by filtration and the solvent removed *in vacuo*. The residue was dissolved in hot benzene (100 ml) and upon cooling, light yellow crystals deposited. Recrystallization from benzene yielded 6.2 g (65%) of II, mp. 178-180°. IR: 3300-3600 (NHOH), 1720 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 3.70 (3H, s, CH_3), 6.01 (1H, s, OH), 7.64 (10H, m, two phenyls), 8.25 (1H, br, NH); MS (m/Z): 309 (M^+, 13%); 250 (100%); 204 (26%).

Anal. Calcd. for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53

Found: C, 70.09; H, 4.71; N, 4.66

After separating II, the filtrate was concentrated and chromatographed on a silica gel column (100 g) and eluted with benzene. The first fraction (60 ml) was collected, concentrated, and recrystallized from benzene to yield 1.5 g (16%) of III as colorless plates, mp. 181-182°. IR: 3450 (NH_2), 1680 (C=O) cm^{-1}; ^1H-NMR ($CDCl_3$): δ 3.78 (3H, s, CH_3), 4.65 (2H, br, NH_2), 7.25 (10H, m, two phenyls); MS m/Z: 293 (M^+, 100%); 235 (54%); 206 (25%).

Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78

Found: C, 73.82; H, 4.98; N, 4.67

The second fraction (100 ml) was collected (0.5 g, 5%) and recrystallized from benzene to give IV, mp. 126-127°. IR: 2220 (CN), 1760, 1728 (C=O) cm^{-1}; ^1H-NMR ($CDCl_3$): δ 3.67 (3H, s, CH_3), 4.58 (1H, d, J=4.5 Hz, -CH-CH-), 5.00 (1H, d, J=4.5 Hz, -CH-CH-), 7.34 (10H, m, two phenyls); MS m/Z: 293 (M^+, 100%); 235 (40%); 234 (51%); 206 (93%); 179 (58%); 178 (57.0%).

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78

Found: C, 73.62; H, 4.99; N, 4.91

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