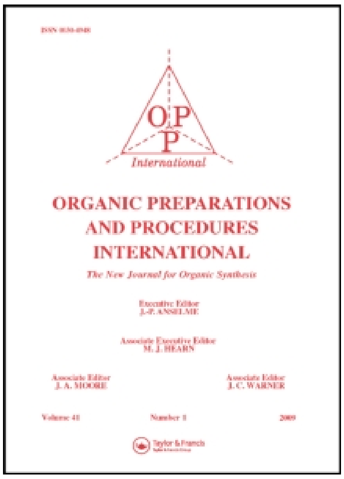

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2-NITROHOMOSYRINGIC ACID

R. M. Sotelo[a]; D. Giacopello[a]; M. J. Vernengo[b]
[a] Departamento de Quimica Organica, Facultad de Clencias Exactas y Naturales, Ciudad Universitaria, Buenos Aires, Argentina [b] Instituto Nacional de Formacologia y Bromatologia, Buenos Aires, Argentina

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OPPI BRIEFS

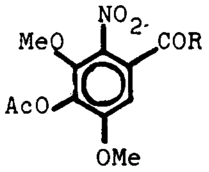
(by J.-P. Anselme, Editor)

2-NITROHOMOSYRINGIC ACID

Submitted by R. M. Sotelo and D. Giacopello*
(1/7/72)
Departamento de Quimica Organica
Facultad de Ciencias Exactas y Naturales
Ciudad Universitaria
Buenos Aires, Argentina

M. J. Vernengo
Instituto Nacional de Formacologia y Bromatologia
Caseros 2161, Buenos Aires, Argentina

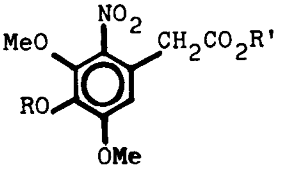
2-Nitrohomosyringic acid (IIb) has been synthesized in 26% yield from 4-acetoxy-3,5-dimethoxy-2-nitrobenzoic acid (Ia).[1]



I

$$\mathrm{Ia} \longrightarrow \mathrm{Ib} \longrightarrow \mathrm{Ic}$$

$$\mathrm{Ic} \longrightarrow \mathrm{IIa} \longrightarrow \mathrm{IIb}$$



II

a) R=OH; b) R=Cl; c) R=CHN_2 a) R=CH_3CO, R'=C_2H_5; b) R=R'=H

EXPERIMENTAL[2]

4-Acetoxy-3,5-dimethoxy-2-nitrobenzoic acid chloride (Ib).- To a stirred suspension of 20 g. (0.08 mole) of acetylnitrosyringic acid (Ia)[1] in 800 ml. of chloroform at room temperature was added slowly 70 g. (0.34 mole) of phosphorous pentachloride. The suspended material slowly dissolved (2 hr.) and when solution was complete, the solvent was removed in vacuo. The dried residue was crystallized from petroleum ether (bp. 61-69°) yielding 15 g. (80%), mp. 92-93°; UV, 245 (4.07) and 291 nm (3.56); IR, 1770 ($CH_3\underline{CO}.O$), 1730 (CO), 1575, 1540 and 860 cm^{-1} (NO_2); nmr, ($CDCl_3$) 2.42 (3H, s, $\underline{CH}_3CO.O$), 3.86 (3H, s, C_5-OCH_3) 4.02 (3H, s, C_3-OCH_3) and 7.53 (1H, s, ArH) ppm.

ω-Diazo-4-acetoxy-3,5-dimethoxy-2-nitroacetophenone (Ic).- A solution of 15 g. (0.05 mole) of Ib in 150 ml. of benzene was slowly added with stirring to a solution of diazomethane (from 88 g. of nitrosomethylurea) in 815 ml. of benzene. Stirring was continued for 10 min. and then occasionally over 4 hr. Excess of diazomethane was destroyed by addition of a few drops of acetic acid. The solvent was removed in vacuo and the oily residue chromatographed on a column of silica gel (100 g.), elution being performed with benzene-ethyl acetate (1:1).

The product was crystallized from ethanol to give 10.3 g. (67%), mp. 118-120°; tlc, Rf 0.59; UV, 253 (4.00) and 295 nm (4.08); IR, 2100 (CHN_2), 1760 ($CH_3CO.O$), 1625 ($COCHN_2$), 1580, 1530 and 860 cm^{-1} (NO_2); nmr, $CDCl_3$) 2.38 (3H, s, $\underline{CH}_3CO.O$), 3.94 (6H, s, 2 x OCH_3), 5.88 (1H, s, $COHN_2$) and 6.95 (1H, s, ArH) ppm.

Ethyl-4-acetoxy-3,5-dimethoxy-2-nitrophenylacetate (IIa).- To a warm (60°) solution of 2.07 g. (7 mmole) of Ic in 150 ml. of ethanol, was added 400 mg. of silver oxide with vigorous stirring while the same temperature was maintained. The initial evolution of nitrogen subsided very slowly (8 hr.). The end of the reaction was ascertained by the addition of conc. hydrochloric acid to an aliquot of the reaction mixture and no gas was evolved. The solid material was filtered through Celite and the filtrate was evaporated to dryness. A small portion of silver oxide in the residue was removed by passing a benzene solution of the product in benzene down a short column of neutral alumina (20 g.). Elution was completed with benzene-methanol (3:2). The collected eluents were evaporated to dryness affording 1.9 g. (76%) of IIa, mp. 82-84°. Further purification by recrystallization from ethanol raised the mp. to 85-86°; tlc, Rf 0.86; UV, 241 sh (4.59), 274 (4.46) and 331 sh nm (4.09); IR, 1760 ($CH_3\underline{CO}.O$), 1740 ($\underline{CO}.OEt$), 1600, 1525 and 870 cm^{-1} (NO_2); nmr, (acetone-d_6) 1.2. (3H, t, $\underline{J}$ 7.5 Hz, $CH_2\underline{CH_3}$), 2.35 (3H, s, $\underline{CH_3}CO.O$), 3.82 (2H, s, CH_2), 3.94 (6H, s, 2 x OCH_3), 4.18 (2H, q, $\underline{J}$ 7.5 Hz, $\underline{CH_2}CH_3$), 7.07 (1H, s, ArH) ppm.

3,5-Dimethoxy-4-hydroxy-2-nitrophenylacetic acid (IIb).- A suspension of 2.47 g. (8 mmole) of IIa in 50 ml. of 5% hydrochloric acid was refluxed for 3 hrs. After addition of activated carbon, the mixture was refluxed for an additional 10 min. and the insoluble material was filtered warm through Celite. On cooling, the acid IIb precipitated, mp. 152-154°, 1.24 g. (64%). Recrystallization from ethyl acetate gave pure IIb, mp. 152-154°; tlc, Rf 0.29; UV, 228 sh (4.02), 255 (3.67) and 292 sh nm (3.43); IR, 3400 (OH), 1700 (CO), 1600, 1520 and 860 cm^{-1} (NO_2); nmr, (acetone-d_6) 3.73 (2H, s, CH_2), 3.95 (3H, s, C_5-OCH_3), 3.97 (3H, s, C_3OCH_3) and 6.92 (1H, s, ArH) ppm.

Elemental Analyses

	Calculated				Found			
	C	H	N	Cl	C	H	N	Cl
Ib	43.50	3.53	4.62	11.67	43.50	3.51	4.74	11.59
Ic	46.61	3.59	13.59	---	46.43	3.58	13.60	---
IIa	51.37	5.24	4.28	---	51.07	5.30	3.99	---
IIb	46.69	4.31	5.45	---	46.98	4.55	5.59	---

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1. a) W. Bradley and R. Robinson, J. Chem. Soc., 1541 (1928).
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2. Melting points are uncorrected. Except where stated otherwise, UV spectra were determined with a Beckman DK-2 instrument for solutions in ethanol; log ε follows λ_{max}. IR were recorded on a Perkin-Elmer 137-B Infracord spectrophotometer as suspensions in Nujol. Nmr spectra were obtained in a Varian A60 spectrometer with TMS as internal reference. Tlc were performed in silica gel plates; solvent; benzene-dioxane-acetic acid, 95:25:4 using acetic acid : oleum, 80:20 and heat as reagent.