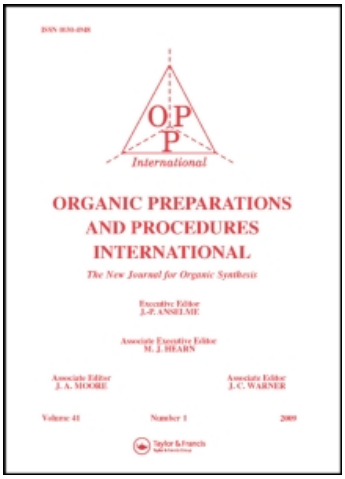


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

AN IMPROVED SYNTHESIS OF 5-(3,4-DIMETHOXYPHENYL)-3-HYDROXY-4-NITROCYCLOHEXENE

A. F. Ibañez[a]; A. R. Martinez[a]; G. Y. Moltrasio Iglesias[a]
[a] Departamento de Química Orgánica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Buenos Aires, ARGENTINA

To cite this Article Ibañez, A. F. , Martinez, A. R. and Iglesias, G. Y. Moltrasio(1993) 'AN IMPROVED SYNTHESIS OF 5-(3,4-DIMETHOXYPHENYL)-3-HYDROXY-4-NITROCYCLOHEXENE', Organic Preparations and Procedures International, 25: 5, 577 — 579
To link to this Article: DOI: 10.1080/00304949309458001
URL: http://dx.doi.org/10.1080/00304949309458001

ORGANIC PREPARATIONS AND PROCEDURES INT., 25 (5), 577-606 (1993)

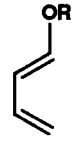
OPPI BRIEFS

AN IMPROVED SYNTHESIS OF 5-(3,4-DIMETHOXYPHENYL)-3-HYDROXY-4-NITROCYCLOHEXENE

Submitted by (12/14/92) A. F. Ibañez*, A. R. Martinez and G. Y. Moltrasio Iglesias

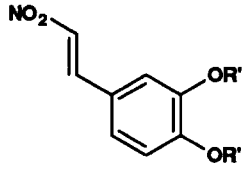
Departamento de Química Orgánica
Facultad de Farmacia y Bioquímica
Universidad de Buenos Aires
Junín 956 (1113) Buenos Aires, ARGENTINA

Substantial quantities of 5-(3,4-dimethoxyphenyl)-3-hydroxy-4-nitrocyclohexene (**3c**) were required for a multi-step synthesis. The preparation of precursor compound (**3a**) by the Diels-Alder reaction[1] of 3,4-methylenedioxy-β-nitrostyrene (**2a**) with 1-acetoxy-1,3-butadiene (**1a**) reported to proceed in 35% yield, afforded only a 15% yield of **3b** with 3,4-dimethoxy-β-nitrostyrene (**2b**).[3] We



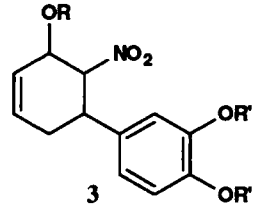
1

a) R = Ac
b) R = $SiMe_3$



2

a) R' = R' = CH_2
b) R' = CH_3



3

a) R = Ac; R' = R' = CH_2
b) R = Ac; R' = CH_3
c) R = H; R' = CH_3

decided to change the diene component for one containing a more potent electron-releasing group at the position 1. The reaction of 1-(trimethylsilyloxy)-1,3-butadiene (**1b**)[4,5] with 3,4-dimethoxy-β-nitrostyrene (**2b**) in toluene in a sealed tube at 130° for 72 hrs gave **3c** (after *in situ* hydrolysis) in 70% yield (see **Table** for conditions).

EXPERIMENTAL SECTION

The ^1H NMR spectra were recorded on a Bruker AW 80 spectrometer in $CDCl_3$ using TMS as internal reference. IR spectra were recorded on a Jasco A-200 as Nujol mulls. Elemental analyses were performed on a Coleman Analyzer. Melting points (uncorrected) were obtained on a Thomas Hoover apparatus.

TABLE 1. Diels-Alder Reaction of 3,4-Dimethoxy-β-nitrostyrene[a]

Diene	Temp. (°C)	Time (hrs.)	Recovered **2b** (%)	Adduct[b] (%)
1a	110	36	82	15
1a	140	36	48	–
1b	125	24	75	8
1b	120	60	25	45
1b	130	72	–	70
1b[c]	115	36	87	–
1b[d]	130	24	95	–

a) In toluene unless otherwise noted; b) Isolated as **3c** chloride after hydrolysis for reaction with **1b**; c) Anhydrous zinc chloride used as catalyst; d) In THF.

3-Acetoxy-5-(3,4-dimethoxyphenyl)-4-nitrocyclohexene (3b).- A mixture of 10 g (0.09 mole) of 1-acetoxy-1,3-butadiene,[2] 4 g (0.02 mole) of 3,4-dimethoxy-β-nitrostyrene[3] and 50 mg of hydroquinone in toluene (30 mL) was heated in a sealed tube (**CAUTION**). The mixture was allowed to come to room temperature and the unreacted 3,4-dimethoxy-β-nitrostyrene was filtered off. In order to recover some adduct, 3,4-dimethoxy-β-nitrostyrene was recrystallized from ethanol. The ethanolic mother liquors and the filtrate (from above) were combined and then evaporated *in vacuo*. The adduct-rich residue was chromatographed (silica gel 30-70 mesh, toluene) to give **3b**, which was crystallized from ethanol to yield 0.96 g (15%) of **3b** as yellow crystals, mp. 141-142°. ^{1}H NMR ($CDCl_3$): δ 2.0 (s, 3H), 2.5 (m, 2H), 3.6 (m, 1H), 3.8 (s, 6H), 5.1 (m, 1H), 5.9 (m, 3H), 6.8 (s, 3H); IR: 1710 (C=O); 1610 (HC=CH); 1530 and 1350 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.81; H, 5.93; N, 4.36

5-(3,4-Dimethoxyphenyl)-3-hydroxy-4-nitrocyclohexene (3c).- A mixture of 10 mL (0.055 mole) of **1b**,[4b] 2.5 g (0.012 mole) of **2b** and toluene (10 mL) was heated in a sealed tube at 130° for 72 hrs. The cooled reaction mixture was diluted with 25 mL of tetrahydrofuran, acidified with 5% HCl (25 mL) and then stirred for 2 hrs at room temperature. The mixture was extracted with diethyl ether (3 x 40 mL), the organic layer was dried with sodium sulfate and the solvent evaporated *in vacuo*. The resulting residue was purified by chromatography (silica gel 30-70 mesh, benzene-ethyl acetate, 95:5), to yield 2.3 g (70%) of pure **3a**, mp. 119-120°. ^{1}H NMR ($CDCl_3$): δ 2.5 (m, 3H), 3.6 (m, 1H), 3.8 (s, 6H), 5.0 (m, 1H), 5.9 (m, 3H), 6.8 (s, 3H); IR: 3500 (OH); 1540 and 1335 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{14}H_{17}NO_5$: C, 60.20; H, 6.13; N, 5.02. Found: C, 60.25; H, 6.12; N, 5.01

Acknowledgement.- This work was supported by SECYT and CONICET grants.

REFERENCES

1. R. K. Hill, J. A. Joule and L. J. Loeffler, *J. Am. Chem. Soc.*, **84**, 4951 (1962).

2. P. Y. Blanc, *Helv. Chim. Acta*, **44**, 1 (1961).

3. R. M. Letcher and M. P. Samroes, *J. Chem. Ed.*, **62**, 262 (1985).

4. a) J. Bélanger, N. L. Landry, J. R. Paré and K. Jankowski, *J. Org. Chem.*, **47**, 3649 (1982); b) H.O. House, L. J. Czuba, M. Gall and H. D. Olmstead, *ibid.*, **34**, 2324 (1969).

5. Rhône-Poulenc S. A., Belg. 670, 769 April 12, 1966; Ft. Appl. Oct. 12, 1964 and June 29, 1965; *C.A.*: **65**, 5487d (1966).

****

AN IMPROVED PROCEDURE FOR THE PREPARATION OF 1,6-DICARBOXYHEX-3-ENE

Submitted by (10/14/92)

Pradeep T. Deota* and Sugra Abid

Department of Chemistry, Faculty of Science
M. S. University of Baroda, Baroda-390 002, INDIA

Generation of *cisoid* C=C bonds has been one of the crucial steps in the synthesis of many natural products.[1] The Z-olefinic diester **4c** has been employed as a suitable starting material in a few instances.[2] For the preparation of this diester, we previously reported a method using H_2WO_4-H_2O_2 for the vicinal hydroxylation of *cis,cis*-1,5-cyclooctadiene (**1**) to obtain the *trans*-diol **2** in 65% yield.[3] The *trans*-diol **2** was readily cleaved with sodium metaperiodate in moist ether to give the dialdehyde **4a** which, on oxidation with Jones' reagent,[4] furnished the diacid **4b** in 65% overall yield from the *trans*-diol **2**. The diacid **4b** was esterified with methanol in the presence of conc. H_2SO_4 to afford the diester **4c** in 64% yield. This method, though favorably comparable with others,[5] required large quantities of the expensive reagent, sodium metaperiodate. We now report a shorter and inexpensive method for the preparation of the Z-olefinic acid **4b** from the *trans*-diol **2**. Jones' reagent itself[6] can be used for the cleavage of the *trans*-diol **2** as well as for the oxidation of the dialdehyde **4a** formed *in situ*. The treatment of the *trans*-diol **2** with Jones' reagent at 5° furnished the diacid **4b** in one step directly in 70% yield.[7] This new method not only avoids the use of expensive oxidant but also gives better yields of the diacid **4b** by a shorter route. The Jones' reagent is also equally effective in cleaving *cis*-diol **3** to diacid **4b**.