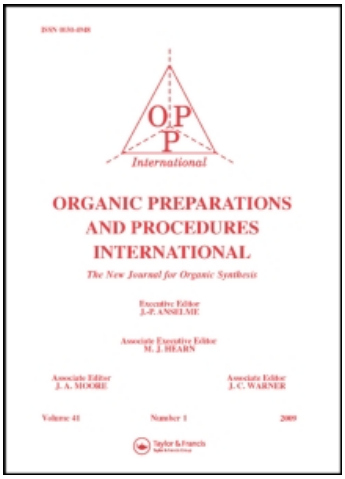

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A CONVENIENT SYNTHESIS OF (4-NITROPHENYL) (4-PIPERIDINYL) KETONE

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To cite this Article Monclus, Michel and Luxen, André(1992) 'A CONVENIENT SYNTHESIS OF (4-NITROPHENYL) (4-PIPERIDINYL) KETONE', Organic Preparations and Procedures International, 24: 6, 692 — 694
To link to this Article: DOI: 10.1080/00304949209356250
URL: http://dx.doi.org/10.1080/00304949209356250

under reflux for 1 hr. After the solution had been cooled, the silver salts were filtered off and the filtrate was evaporated. The solid residue was purified by preparative TLC (silica gel, chloroform) to afford 3.2 g (94%) of white crystals, mp. 134-136° (EtOH). ^{1}H NMR: ($CDCl_3$): δ 2.5 (s, 3H, CH_3), 3.90 (s, 6H, OCH_3), 6.35 (s, 1H, Ar-3), 8.20 (s, 1H, Ar-6).

Anal. Calcd. for $C_{10}H_{11}IO_3$: C, 39.23; H, 3.61. Found: C, 40.01, H, 3.70

2,5-*bis*-(2,4-Dimethoxyphenyl)thiophene.- This compound was obtained in 56% yield using the Schwenk[3a] and Vogel[3b] procedures. It was obtained as a brown oil which was purified by preparative TLC (silica gel, benzene). ^{1}H NMR ($CDCl_3$): δ 3.8-3.9 (s, 12H, OCH_3), 6.5 (m, 4H, Ar-3, Ar-5), 7.25 (d, 2H, Ar-6), 7.5 (d, 2H, H-3 and H-4).

Anal. Calcd. for $C_{20}H_{20}O_4S$: C, 67.40; H, 5.66. Found: C, 67.70, H, 5.70

Acknowledgement.- The authors express their gratitude to the SECYT, Universidad de Buenos Aires, and CONICET for support of this study.

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A CONVENIENT SYNTHESIS OF (4-NITROPHENYL) (4-PIPERIDINYL) KETONE

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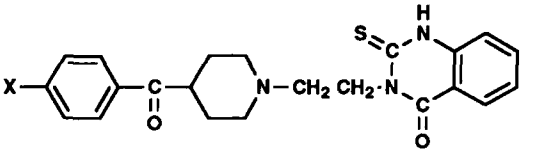
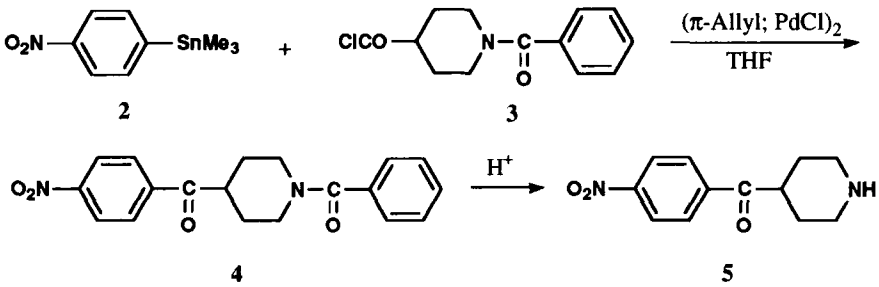
Recently altanserin (**1a**) labeled with ^{18}F has been described as a potential ligand for the mapping of 5-HT_2 receptors in humans using Positron Emission Tomography (PET).[1] [^{18}F]Altanserin

was prepared *via* a radiofluorodenitration of **1b** using potassium [^{18}F] fluoride in DMSO.[1] We report a new and shorter route for the preparation of (4-nitrophenyl) (4-piperidinyl) ketone (**5**), a key intermediate in the synthesis of **1b**. According to the literature, **5** has been obtained in low yield through a Friedel-Craft reaction followed by an oxidation of the amino function.[2] A second route including the nitration of 4-benzylpiperidine and an oxidation of the benzylic methylene has been reported,[3] but the oxidation step described is not reproducible. Therefore, we developed a synthesis of a intermediate ketone **4** using the coupling of tin derivative (**2**) and an acid chloride (**3**) in THF catalyzed by π-allyl palladium chloride[4] dimer to afford **4** which after acid hydrolysis, gave **5** (37%); the nitro derivative **1b** was then easily obtained as described.[1]



1

a) X = F b) X = NO_2



2 **3** **4** **5**

EXPERIMENTAL SECTION

Melting points were determined on a Mettler FP5 capillary apparatus and are uncorrected. ^{1}H NMR were recorded on a Bruker WM instrument operating at 250 MHz. Fast atom bombardment (FAB) mass spectra were obtained on a AEI MS-902 mass spectrometer. All commercial compounds were purchased from Aldrich and were used without further purification.

N-(Benzoyl)isonipecotyl Chloride (3).- N-(Benzoyl)isonipecotic acid[2] (2.3 g, 10 mmol) was dissolved in dry ether (30 mL) at 0° under argon. Et_3N (1.53 g, 11 mmol) was added, followed by $SOCl_2$ (0.81 mL, 11 mmol). The reaction mixture was stirred for 10 min at 0° and then at room temperature for 12 hrs. The reaction mixture was filtered through Celite, which was then washed with Et_2O (2 x 10 mL). The combined ethereal solution was evaporated under reduced pressure to give the crude material **3** as an oil. The oil was then kept under high vacuum for at least 1 hr and then used immediately.

(4-Nitrophenyl (1-Benzoyl-4-piperidinyl)ketone (4).- N-(Benzoyl)isonipecotyl chloride (**3**) (1.78 g,

5.5 mmol) was dissolved in dry THF (30 mL) under argon. Molecular sieves (10 g, 4 Å, 8-12 mesh) were added, and then the reaction mixture was stirred for 5 min at room temperature. 4-Nitrophenyltrimethyltin[5] (**2**) (1.4 g, 4.9 mmol) and bis(π-allyl palladium chloride) (0.018 g, 0.049 mmol) were added. The reaction mixture became dark. The reaction was stirred at room temperature and was monitored by TLC on silica gel [petroleum ether/ether, (9:1); R_f 2 = 0.45] until its completion (5 hrs). The reaction mixture was filtered and the filtrate was treated with water (100 mL) and extracted with methylene chloride (3 x 20 mL). The extracts were dried over sodium sulfate and filtered, and the solvent was evaporated to give a crude material as an oil. The oil was chromatographed on silica gel [methylene chloride/acetonitrile (80:20)] to give **4** (0.71 g, 43%), mp 149°, lit.[2] mp 134°. ^{1}H NMR (250 MHz, $CDCl_3$/TMS): δ 1.78-1.88 (m, 4 H), 3.0-3.26 (m, 3 H), 3.4-3.65 (m, 2 H), 7.42 (s, 5 H), 8.09 (d, 2 H, J = 9 Hz), 8.34 (d, 2 H, J = 9 Hz). FAB mass spectrum: (m/e (rel int)) 340 (1.1), 339 (4.3, $[MH]^+$), 262 (9.8), 132 (13.9), 131 (12.3),129 (15.0), 106 (13.9) and 105 (100).

(4-Nitrophenyl) (4-Piperidinyl) Ketone (5).- (4-Nitrophenyl) (1-benzoyl-4-piperidinyl) ketone (**4**, 1.18 g, 3.5 mmol) dissolved in ethanol (12.5 mL) and 6 N HCl (25 mL) was boiled for 15 hrs. The solvent was evaporated under reduced pressure, and the residue was triturated with acetone. The solid obtained was collected to yield **5** as its hydrochloride (0.81 g, 81% yield), mp. 251°, lit.[2] mp 252°; TLC silica gel ($MeOH/H_2O/HOAc$, (9:1:0.1), R_f 5 = 0.24).

Acknowledgement.- This research was supported by the National Fund for Scientific Research (FNRS 2.4555.88).

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