of K_2CO_3. The extract was dried and $CHCl_3$ was evaporated. The residue was again extracted with benzene several times. After the evaporation of benzene, 0.8 g. (61.5%) of a brown, viscous oil was obtained, fairly soluble in AcOEt. Chloroplatinate: Yellow crystals, m.p. 100~103. *Anal.* Calcd. for $C_{15}H_{17}O_3N \cdot \frac{1}{2}H_2PtCl_6 \cdot 2H_2O$: C, 41.70; H, 4.97. Found: C, 41.93; H, 4.65.

1-(3,4-Dimethoxyphenethyl)-2-chloropyridinium Iodide (IIIb)—A mixture of 0.5 g. of the pyridone (IVb) and 3 cc. of $POCl_3$ was refluxed in the presence of 5 cc. of toluene, gently in an oil bath for 2 hr. during which time the evolution of HCl was hardly observed and the color of the mixture turned dark brown. Excess of $POCl_3$ and toluene were mostly removed *in vacuo* and the residue was dissolved in 5 cc. of H_2O, its solution being decolorized with activated charcoal. From one part of its solution, a yellow crystalline chloroplatinate, m.p. 192~194° (decomp.), was formed. From an aqueous solution, the iodide was precipitated by the addition of 0.7 g. of KI and this was collected on a filter. This was purified from EtOH, forming yellow needles of m.p. 160~161°.[4] *Anal.* Calcd. for $C_{15}H_{17}O_2NCl$I: C, 44.42; H, 4.22. Found: C, 44.41, 44.08; H, 4.48, 3.99.

A solution of 108.2 mg. of the above iodide in 10 cc. of MeOH was converted to the corresponding chloride by heating for 1.5 hr. with 300 mg. of AgCl, and 73 mg. of the chloride was obtained as a white powder of m.p. 139~141°. The latter was converted as usual to the corresponding O-picrate. This was collected and purified from EtOH, forming brownish yellow crystals of m.p. 153~154°, which showed positive Beilstein test. *Anal.* Calcd. for $C_{15}H_{16}O_2NCl \cdot C_6H_2O_7N_3$: C, 49.76; H, 3.78. Found: C, 49.96; H, 3.74.

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Summary

1-Methyl- or 1-ethyl-2(1*H*)-pyridone was formed by alkaline treatment from their corresponding 1-alkyl-2-chloropyridinium salt of 2-iodo derivative.

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Hideaki Shirai and Noriichi Oda: New Synthesis of 2-Nitro-5-methoxybenzaldehyde.

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In connection with the synthesis of 2-methoxyphenanthrene, it was necessary to prepare 2-nitro-5-methoxybenzaldehyde (IV). The aldehyde has been previously prepared by two routes; one by the reaction of *m*-methoxybenzaldehyde with nitric acid[1] and the other by the nitration of bis-(*m*-formylphenyl) carbonate, followed by hydrolysis and subsequent methylation.[2] The former, however, involves rather troublesome separation of isomers and the latter consists of many steps.

A new convenient synthesis of the aldehyde was now achieved by means of the Reissert reaction. 2-Nitro-5-methoxybenzoic acid (I), needed in this synthesis as the starting material, was prepared by the method of Makino, *et al.*[3] from *m*-cresol. The chloride of (I) was converted into the Reissert compound (III), in the mixture of quinoline, hydro-

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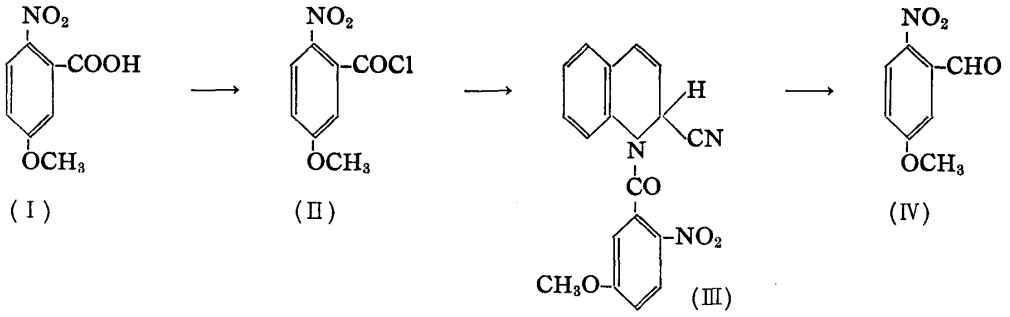
gen cyanide, and dehyd. benzene. The objective aldehyde was then obtained by hydrolysis of (III) with mineral acid. All the steps proceeded smoothly to give (IV) of satisfactory purity in good overall yield (approximately 62%, based on the starting acid).



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Experimental*2

2-Nitro-5-methoxybenzoyl Chloride (II)—A mixture of 4 g. of 2-nitro-5-methoxybenzoic acid (I)[3] and 20 cc. of $SOCl_2$ was warmed to 60° for 30 min. After removal of the excess $SOCl_2$ *in vacuo*, the residue was crystallized from petr. ether to yield 3.6 g. (82.2%) of colorless needles, m.p. 33~34°.

1-(2-Nitro-5-methoxybenzoyl)-1,2-dihydroquinaldonitrile (III)—To a solution of 1.5 cc. of anhyd. HCN in 7 g. of quinoline, protected from moisture and cooled to 0°, a solution of 5 g. of the chloride (II) in 5 cc. of dehyd. benzene was added. After 20 hr. at room temperature, the reaction mixture was diluted with benzene, washed successively with dil. H_2SO_4, $NaHCO_3$ solution, and water, and dried over Na_2SO_4. After evaporation of the solvent, the residue was crystallized from EtOH to give 7 g. (90.0%) of light yellow prisms, m.p. 153°. *Anal.* Calcd. for $C_{18}H_{13}O_4N_3$: C, 64.48; H, 3.91; N, 12.53. Found: C, 64.32; H, 4.19; N, 12.33.

2-Nitro-5-methoxybenzaldehyde (IV)—A mixture of 4 g. of the Reissert compound (III) and 100 cc. of 10*N* H_2SO_4 was boiled for 3 hr. After cool, the reaction mixture was extracted with Et_2O, the Et_2O layer was washed with $NaHCO_3$ solution and water, and dried over Na_2SO_4. Removal of the solvent left a yellow solid, which after recrystallization from dil. EtOH, afforded 1.8 g. (83.3%) of the aldehyde as colorless needles, m.p. 83°. A mixed m.p. determination with the authentic specimen obtained from the procedure of Smith, *et al.*,[2] showed no depression.

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*2 All m.p.s are uncorrected.

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Norio Sugimoto, Yoshio Kowa, and Ko Higaki*1; Shigeru Nakamura, and Shigeru Yasaka*2: Expectorant Effect and Clinical Efficacy of 1-Methyl-3-(di-2-thienylmethylene)piperidine Citrate (AT-327).

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It has already been reported[1] that 1-methyl-3-(di-2-thienylmethylene)piperidine citrate (hereinafter designated as AT-327) and its hydrochloride (hereinafter designated as AT-327-HCl) are powerful non-narcotic antitussive and numerous reports have been made on their clinical effect.[2,3] Majority of representative antitussives known to date did not

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