CONVENIENT SYNTHESIS OF A SIMPLE COUMARIN FROM SALICYLALDEHYDE AND WITTIG REAGENT (III)¹: SYNTHESIS OF NITROCOUMARINS

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Abstract---Reaction of nitrosalicylaldehydes (I) with carbethoxymethylenetriphenylphosphorane in Et₂NPh, in Ph₂O, and in the absence of solvent (neat) at 210-215°C was investigated. Reaction of 3-nitrosalicylaldehyde (1d) in Et₂NPh afforded the benzoxazole (6) and the aminocoumarin (3e) along with the expected coumarin (3d). It was clarified that the origin of carbon-unit introduced for the formation of the benzoxazole ring came from the alkyl group of solvent.

Recently, we reported a convenient method for synthesis of a simple 3,4-unsubstituted coumarin (3) by the Wittig reaction of salicylaldehydes (1) having a methoxy, hydroxy, bromo and carbomethoxy group with carbethoxymethylenetriphenylphosphorane (phosphorane) in N,N-diethylaniline (Et₂NPh) under reflux.¹,² Therein, we presented that i) an electron-donating group at C₄ on salicylaldehyde (1) accelerated the formation of

$$\text{CHO} \quad \overset{\text{Ph₃P=CHCO₂Et}}{\text{Et₂NPh, reflux}} \quad \overset{\text{CO₂Et}}{\text{OH}} \quad \overset{\text{R}}{\text{C₄}} \quad \text{CO₂Et} \quad \overset{\text{R}}{\text{C₄}} \quad \text{O}$$

Scheme 1
coumarin (3) from trans-cinnamate (2) and an electron-withdrawing group at C4 on 1 retarded the formation of 3; ii) a substituent group at C6 on 1 facilitated the formation of 3 irrespective of its electronic character. Then, we planned to investigate the Wittig reaction of 1 having a nitro group, which is a strong electron-withdrawing group, with phosphorane. Herein, we describe the results including an unusual behavior of 3-nitrosalicylaldehyde (1d) in Et2NPh.

Results and Discussion

Reaction of nitrosalicylaldehyde (1) with phosphorane in Et2NPh under reflux (at 210-215°C) was examined. The results are summarized in Table I. In order to improve yields of 3, reaction in the absence of solvent and in diphenyl ether (Ph2O) at 210-215°C was also examined. Yields were improved slightly in reaction in the absence of solvent and total-yields containing 2 and 3 were high in reaction in Ph2O, as indicated in Table I. Thus, 1a as well as other 6-substituted salicylaldehydes1,2 afforded the corresponding coumarin (3a)3 for a short reaction time and in a high yield, supporting the mechanism that a substituent group at C6 on 1 could facilitate generally the formation of 3 regardless of its electronic character, i.e. an electron-withdrawing group or an electron-donating group.2 However, other salicylaldehydes (1b-d) produced coumarins (3b-d), respectively, in low yields accompanied with by-product(s), which were formed by participation of Et2NPh.

Reaction of 5-nitrosalicylaldehyde (1b) and 4-nitrosalicylaldehyde (1c) with phosphorane in Et2NPh afforded the diethylaniline adducts (4 and 5) along with the coumarins (3b4 and 3c5), respectively. It should be noted that the cinnamate (2c) remains even after reflux for 6 h, indicating that an electron-withdrawing group such as a nitro group at C4 on cinnamate retards the formation of coumarin ring from cinnamate in comparison with an electron-donating group at C4 on cinnamate.1,2

Reaction of 3-nitrosalicylaldehyde (1d) with phosphorane in Et2NPh provided two unexpected products, the benzoxazole (6) and the aminocoumarin (3e)6 besides the expected nitrocoumarin (3d).7 On the other hand, reaction of 1d with phosphorane in Ph2O provided 2d and 3d, and neither 6 nor 3e was produced, suggesting that Et2NPh would serve as a reducing agent for conversion of 3d to 3e and be responsible for the formation of benzoxazole ring. In fact, a solution of 3d in Et2NPh was heated for 3h under reflux to produce 3e in 17% yield along with recovery of the starting material (3d) in 69% yield. Moreover, heating of 2d in Et2NPh gave 3d, 3e, and 6 in 8%, 10%, and 45% yields, respectively, and heating of 2d in Me2NPh instead of Et2NPh gave the benzoxazole (9) and the benzoxazolone (10) in 30% and 34% yields, respectively, as shown in Scheme 3.
Table I. The Results of Reaction of Salicylaldehyde (I) with Carbethoxymethylene-triphenylphosphorane at 210-215°C

<table>
<thead>
<tr>
<th>Run</th>
<th>Salicylaldehyde (I)</th>
<th>Solvent</th>
<th>Reaction Time</th>
<th>Products (%) (^{a)})</th>
<th>2 / 3</th>
<th>Other(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6-NO₂ (Ia)</td>
<td>Et₂NPh</td>
<td>0.75 h</td>
<td>0 / 88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6-NO₂ (Ia)</td>
<td>None</td>
<td>1.5 h</td>
<td>0 / 55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6-NO₂ (Ia)</td>
<td>Ph₂O</td>
<td>1 h</td>
<td>0 / 86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5-NO₂ (Ib)</td>
<td>Et₂NPh</td>
<td>3 h</td>
<td>0 / 28 4 (14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5-NO₂ (Ib)</td>
<td>None</td>
<td>3 h</td>
<td>0 / 43 7 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5-NO₂ (Ib)</td>
<td>Ph₂O</td>
<td>6 h</td>
<td>12 / 77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>4-NO₂ (Ic)</td>
<td>Et₂NPh</td>
<td>6 h</td>
<td>17 / 13 5 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4-NO₂ (Ic)</td>
<td>None</td>
<td>6 h</td>
<td>14 / 32 8 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>4-NO₂ (Ic)</td>
<td>Ph₂O</td>
<td>6 h</td>
<td>20 / 44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3-NO₂ (Id)</td>
<td>Et₂NPh</td>
<td>2.5 h</td>
<td>0 / 10 6 (42), 3e (13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>3-NO₂ (Id)</td>
<td>None</td>
<td>6 h</td>
<td>2 / 35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>3-NO₂ (Id)</td>
<td>Ph₂O</td>
<td>6 h</td>
<td>52 / 24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a)}\) Isolated yield.

Scheme 2

Scheme 3
These results strongly indicate that the origin of carbon-unit introduced for the formation of the benzoxazole ring came from a used solvent, Et$_2$NPh or Me$_2$NPh. Structures of benzoxazole derivatives (6, 9, and 10) were elucidated on the basis of their elemental analyses and spectral data depicted in Experimental.

In this connection, heating of o-nitrophenol in Et$_2$NPh under reflux (at 210-215°C) gave 2-methylbenzoxazole (11) in about 45% yield, although a yield was variable, whereas neither heating of o-nitrophenol in Et$_2$NPh at 150°C nor heating in triethylamine under reflux (at 90°C) gave 11. Therefore, these facts seem to suggest that an o-nitrophenol moiety group is essential and a reaction temperature is crucial for the formation of oxazole ring. Recently, Oguchi et al. reported that photo-irradiation of o-nitrophenetole produced 11 through a radical mechanism. Then, heating of o-nitrophenetole in Et$_2$NPh under reflux was examined, and no 11 was produced and the starting material was recovered quantitatively, indicating at least that a present benzoxazole formation does not proceed through o-nitrophenetole from o-nitrophenol.

Studies on the mechanism and the generality of this new method for synthesis of the benzoxazole from o-nitrophenol derivative are now under investigation.

**Preparation of Salicylaldehydes (1)**

The Duff reaction of m-nitrophenol with hexamethylenetetramine in 75% polyphosphoric acid gave 6-nitrosalicylaldehyde (1a) and 4-nitrosalicylaldehyde (1c) in 34% and 12% yields, respectively. 1c was also prepared alternatively according to the literature. On that occasion, alkaline hydrolysis of 1-acetoxy-2-dibromomethyl-5-nitrobenzene with 8% Na$_2$CO$_3$ aqueous solution produced 1c in much better yield (72% yield) than the reported acidic hydrolysis with conc. H$_2$SO$_4$. 3-Nitrosalicylaldehyde (1d) was prepared by ozonolysis of 2-methyl-7-nitrobenzo[b]furan (12). Thus, ozonolysis of 12 in methylene chloride at -78°C followed by alkaline hydrolysis gave 1d in 80% yield.

**EXPERIMENTAL**

Melting points were measured on a micro melting point hot-stage apparatus (Yanagimoto) and are uncorrected. Ir spectra were recorded in Nujol on a JASCO A-102 spectrophotometer and $^1$H- and $^{13}$C-nmr spectra in deuteriochloroform on a Hitachi R-1500 (60 MHz) or Varian VXR-500 (500 MHz) spectrometer unless otherwise stated. Nmr data are reported in parts per million down field from tetramethylsilane as an internal standard ($\delta$ 0.0) and coupling constants are given in hertz. Ms was taken on a VG-70SE spectrometer.
chromatography was carried out on silica gel (Merck, silica gel 60, No. 9385). All experiments were carried out in an argon atmosphere and the extract was washed with brine, dried over anhydrous MgSO₄, then filtered, and the filtrate was evaporated to dryness under reduced pressure, unless otherwise noted. The synthetic samples were identified by comparison of spectral (¹H-nmr and ir) data with those of commercial or synthetic authentic samples or by comparison with physical data in the cited references.

**General Procedure for Reaction of Salicylaldehyde (1) with Carbethoxymethylenetriphenylphosphorane in Diethylaniline under Reflux**

Reaction of salicylaldehyde (1) (1 mmol) with the Wittig reagent (1.2 mmol) in Et₂NPh (10 ml) was carried out for the reaction time indicated in Table I.

5-Nitrocoumarin (3a) The reaction mixture was diluted with 5% HCl solution and extracted with ether. The residue in CH₂Cl₂ was chromatographed on silica gel. Further elution with the same solvent gave 3a, mp 164-164.5°C (lit.,³ mp 160°C)(pale yellow needles from MeOH).

4-(4-N,N-Diethylaminophenyl)-6-nitro-3,4-dihydrocoumarin (4) and 6-Nitrocoumarin (3b)

The reaction mixture was concentrated under reduced pressure and the residue in hexane-AcOEt (4:1) was chromatographed on silica gel. Elution with the same solvent gave 4. Ir (neat) cm⁻¹ : 1785 (C=O), 1520 and 1345 (NO₂). ¹H-Nmr (60 MHz, CDCl₃) δ : 1.13 (6H, t, J=7.0 Hz, 2xNCH₂C₆H₃), 2.93 (2H, d, J=9.1 Hz, 2xC₃-H), 6.54 (2H, d, J=9.1 Hz, 2xC₃-H), 6.90 (2H, d, J=9.1 Hz, 2xC₂'-H), 7.10 (1H, d, J=8.8 Hz, C₈-H), 7.84 (1H, d, J=2.9 Hz, C₅-H), 8.07 (1H, dd, J=8.8, 2.9 Hz, C₇-H). Ms (FAB) m/z : 341 (M⁺+1). Successive elution with the same solvent gave 3b, mp 187-191°C (lit.,⁴ 181-182°C)(colorless prisms from hexane-AcOEt).

4-(4-N,N-Diethylaminophenyl)-7-nitrocoumarin (5), Ethyl trans-2-hydroxy-4-nitrocinnamate (2c), and 7-Nitrocoumarin (3e)

The reaction mixture was concentrated under reduced pressure and the residue in hexane-AcOEt (8:1) was chromatographed on silica gel. Elution with the same solvent afforded 5, mp 173-174°C (red needles from AcOEt).


4-H-Nmr (60 MHz, CDCl₃) δ : 1.24 (6H, t, J=7.0 Hz, 2xNCH₂C₆H₃), 3.46 (4H, q, J=7.0 Hz, 2xNCH₂C₆H₃), 6.46 (1H, s, C₃-H), 6.78 (2H, d, J=9.0 Hz, 2xC₃'-H), 7.35 (2H, d, J=9.0 Hz, 2xC₂'-H), 7.95-8.05 (2H, m, C₇-H and C₆-H), 8.20 (1H, d, J=2.3 Hz, C₈-H). Ms (EI) m/z : 338 (M⁺). Elution with hexane-AcOEt (6:1) afforded 2c, mp 234-235°C (yellow prisms from AcOEt-benzene).

**Anal.** Calcd for C₁₁H₁₁NO₅ : C, 55.70; H, 4.67; N, 5.90. Found : C, 55.72; H, 4.70; N, 5.65. Ir cm⁻¹ : 3350(OH), 1690 (C=O), 1530 and 1350 (NO₂). ¹H-Nmr (60 MHz,
CDCl₃ δ : 1.28 (3H, t, J=7.0 Hz, CO₂CH₂CH₃), 4.22 (2H, q, J=7.0 Hz, CO₂CH₂CH₃), 6.78 (1H, d, J=16.4 Hz, CH=CHCO₂), 7.53-7.84 (3H, m, aromatic protons), 7.85 (1H, d, J=16.4 Hz, CH=CHCO₂), 11.25 (1H, s, OH). Ms (EI) m/z : 237 (M⁺). Elution with hexane-AcOEt (2 : 1) afforded 3c, mp 205-205.5°C (lit., 5 199-202°C)(yellow plates from benzene).

Ethyl trans-3-(2-methylbenzoxazole-7-yl)propenoate (6), 8-Aminocoumarin (3e), and 8-Nitrocoumarin (3d) The reaction mixture in hexane-AcOEt (5 : 1) was chromatographed on silica gel. Elution with the same solvent afforded 6, mp 101-102°C (pale yellow needles from ether). Anal. Calcd for C₁₃H₁₃N₀₃: C, 67.52; H, 5.66; N, 6.06. Found: C, 67.30; H, 5.57; N, 6.36.

IR cm⁻¹: 1700 (C=O). ¹H-Nmr (60 MHz, CDCl₃) δ: 1.38 (3H, t, J=7.0 Hz, CO₂CH₂CH₃), 2.70 (3H, s, CH₃), 4.32 (2H, q, J=7.0 Hz, CO₂CH₂CH₃), 6.86 (1H, d, J=15.8 Hz, CH=CHCO₂), 7.26-7.75 (3H, m, aromatic protons), 7.81 (1H, d, J=15.8 Hz, CH=CHCO₂). ¹³C-Nmr (125 MHz) δ: 14.4 (CH₃), 14.6 (CH₃), 60.7 (CH₂), 119.0 (C), 121.2 (CH), 122.0 (CH), 124.5 (CH), 126.2 (CH), 138.8 (CH), 142.2 (C), 149.1 (C), 164.2 (C), 167.0 (C). Ms (FAB) m/z : 231 (M⁺+1). Elution with hexane-AcOEt (2 : 1) afforded 3e, mp 144-145°C (lit., 6 145-146°C)(pale yellow needles from benzene). Elution with hexane-AcOEt (1 : 1) afforded 3d, mp 190-192°C (lit., 7 187°C)(pale yellow plates from benzene).

General Procedure for Reaction of 1 with Phosphorane in the Absence of Solvent at 210-215°C Reaction of 1 (1 mmol) with phosphorane (1.2 mmol) was carried out for the reaction time indicated in Table I. After cooling, the reaction mixture was dissolved in CHCl₃ and the solution was chromatographed on silica gel.

5-Nitrocoumarin (3a) Elution with hexane-AcOEt (6 : 1) gave 3a, mp 163-164°C.

Ethyl trans-2-ethoxy-5-nitrocinnamate (7) and 6-Nitrocoumarin (3b) Elution with hexane-AcOEt (7 : 1) afforded 7, mp 81-82°C (colorless needles from ether-hexane). Anal. Calcd for C₁₃H₁₅NO₅: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.40; H, 5.77; N, 5.29. IR cm⁻¹: 1705 (C=O), 1507 and 1340 (NO₂). ¹H-Nmr (60 MHz, CDCl₃) δ: 1.35 (3H, t, J=7.0 Hz, OCH₂CH₃), 1.53 (3H, t, J=7.0 Hz, CO₂CH₂CH₃), 4.24 (2H, q, J=7.0 Hz, OCH₂CH₃), 4.28 (2H, q, J=7.0 Hz, CO₂CH₂CH₃), 6.60 (1H, d, J=16.4 Hz, CH=CHCO₂), 6.97 (1H, d, J=9.4 Hz, C₃-H), 7.96 (1H, d, J=16.4 Hz, CH=CHCO₂), 8.22 (1H, dd, J=9.4, 2.9 Hz, C₄-H), 8.20 (1H, d, J=2.9 Hz, C₆-H). Ms (EI) m/z : 265 (M⁺). Elution with hexane-AcOEt (5 : 1) gave 3b, mp 188-190°C.
Ethyl trans-2-ethoxy-4-nitrocinnamate (8), Ethyl trans-2-hydroxy-4-nitrocinnamate (2c) and 7-Nitrocoumarin (3c) Elution with hexane-AcOEt (7:1) afforded 8, mp 92-93°C (pale yellow needles from ether-hexane). Anal. Calcd for C_{13}H_{15}N_{05}: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.52; H, 5.68; N, 5.17. \textit{IR} \textit{cm}^{-1}: 1715 (C=O), 1520 and 1350 (NO_2).

\textit{1H-NMR} (60 MHz, CDCl_3) \delta: 1.35 (3H, t, J=7.0 Hz, OCH_2C&), 1.53 (3H, t, J=7.0 Hz, CO_2CH_2C&), 4.22 (2H, q, J=7.0 Hz, OCF_2CH_3), 4.30 (2H, q, J=7.0 Hz, CO_2C&CH_3), 6.62 (1H, d, J=16.4 Hz, CH=CHC&), 7.53-7.94 (3H, m, aromatic protons), 7.97 (1H, d, J=16.4 Hz, CH=CHC&). \textit{MS} (EI) \textit{m/z}: 265 (M^+).

Elution with hexane-AcOEt (6:1) gave 2c, mp 233-235°C and elution with hexane-AcOEt (2:1) gave 3c, mp 204-205°C.

Ethyl trans-2-hydroxy-3-nitrocinnamate (2d) and 8-Nitrocoumarin (3d) Elution with hexane-AcOEt (5:1) gave 2d, mp 83-85°C (yellow pillars from benzene). Anal. Calcd for C_{11}H_{11}N_{05}: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.74; H, 4.77; N, 5.63. \textit{IR} \textit{cm}^{-1}: 1715 (C=O), 1540 and 1330 (NO_2).

\textit{1H-NMR} (60 MHz, CDCl_3) \delta: 1.36 (3H, t, J=7.0 Hz, CO_2CH_2C&), 4.30 (2H, q, J=7.0 Hz, CO_2C&CH_3), 6.62 (1H, d, J=16.4 Hz, CH=CHC&), 7.02 (1H, t, J=7.9 Hz, C_5-H), 7.83 (1H, dd, J=7.9, 1.7 Hz, C_6-H), 7.96 (1H, d, J=16.4 Hz, CH=CHC&), 8.15 (1H, dd, J=7.9, 1.7 Hz, C_4-H), 11.27 (1H, s, OH, exchangeable with D_2O). \textit{MS} (FAB) \textit{m/z}: 238 (M^++1). Elution with hexane-AcOEt (1:1) gave 3d, mp 190-191°C.

General Procedure for Reaction of 1 with Phosphorane in Diphenyl Ether at 210-215°C Reaction of 1 (1 mmol) with phosphorane (1.2 mmol) in Ph_2O (10 ml) was carried out for the reaction time indicated in Table I. The reaction mixture in hexane was chromatographed on silica gel.

5-Nitrocoumarin (3a) Elution with hexane-AcOEt (2:1) gave 3a, mp 162.5-163.5°C.

6-Nitrocoumarin (3b) and Ethyl trans-2-hydroxy-5-nitrocinnamate (2b) Elution with hexane-AcOEt (3:1) gave 3b, mp 181.5-182.5°C and elution with hexane-AcOEt (2:1) gave 2b, mp 175-176°C (lit.,\textsuperscript{18} mp 170-172°C)(yellow prisms from benzene).

Ethyl trans-2-hydroxy-4-nitrocinnamate (2c) and 7-Nitrocoumarin (3c) Elution with hexane-AcOEt (3:1) gave 2c, mp 235-237°C and elution with hexane-AcOEt (2:1) gave 3c, mp 203-204.5°C.

Ethyl trans-2-hydroxy-3-nitrocinnamate (2d) and 8-Nitrocoumarin (3d) Elution with hexane-AcOEt (4:1) gave 2d, mp 82-83°C and elution with hexane-AcOEt (1:1) gave 3d, mp 190-192°C.

Heating of 3d in Et_2NPh at 210-215°C A solution of 3d (100 mg, 0.52 mmol) in Et_2NPh (5 ml) was refluxed for 3 h. After cooling, the reaction mixture was diluted with hexane and the solution was subjected to
column chromatography on silica gel. Elution with hexane-AcOEt (2 : 1) gave 3e (14 mg, 17% yield), mp 142-143°C. Elution with hexane-AcOEt (1 : 1) gave the starting material (3d) (69 mg, 69% yield).

**Heating of 2d in Et2NPh at 210-215°C** A solution of 2d (500 mg, 2.11 mmol) in Et2NPh (30 ml) was heated for 15 min under reflux. After cooling, the reaction mixture was diluted with hexane and a solution was subjected to column chromatography on silica gel. Elution with hexane-AcOEt (5 : 1) provided 6 (218 mg, 45% yield), mp 101-102°C and elution with hexane-AcOEt (2 : 1) provided 3e (35 mg, 10% yield), mp 143-145°C. Elution with hexane-AcOEt (1 : 1) provided 3d (33 mg, 8% yield), mp 185-187°C.

**Heating of 2d in Me2NPh under Reflux** A solution of 2d (500 mg, 2.11 mmol) in Me2NPh (30 ml) was heated for 15 min under reflux. After cooling, the reaction mixture was diluted with a large quantity of ether and the ethereal solution was washed with 5% HCl solution. The residue in CH2Cl2 was subjected to column chromatography on silica gel. Elution with hexane-AcOEt (5 : 1) gave ethyl trans-3-(benzoxawle-7-y1)propenoate (9) (138 mg, 30% yield), mp 91-92°C (pale yellow needles from ether-hexane). Anal. Calcd for C12H11N03: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.54; H, 5.04; N, 6.30. 1H-Nmr (60 MHz, CDCl3) δ : 1.37 (3H, t, J=7.0 Hz, CO2CHZCH), 4.31 (2H, q, J=7.0 Hz, CO2C&CH3), 6.90 (IH, d, J=16.4 Hz, CH=CHCO2), 7.20-7.92 (3H, m, aromatic protons), 7.83 (IH, d, J=16.4 Hz, CH=CHCO2), 8.18 (IH, s, OCH=N). Elution with hexane-AcOEt (2 : 1) gave ethyl trans-3-(2-benzoxazolon-7-yl)propenoate (10) (166 mg, 34% yield), mp 182-184°C (colorless needles from benzene). Anal. Calcd for C12H11N04: C, 61.80; H, 4.75; N, 6.01. Found : C, 61.91; H, 4.63; N, 5.91. 1H-Nmr (60 MHz, DMSO-d6) δ : 1.29 (3H, t, J=7.0 Hz, CO2CH2CH3), 4.22 (2H, q, J=7.0 Hz, CO2CH2CH3), 6.70 (IH, d, J=16.4 Hz, CH=CHCO2), 7.05-7.53 (3H, m, aromatic protons), 7.67 (IH, d, J=16.4 Hz, CH=CHCO2), 11.84 (IH, s, NH).

**2-Methylbenzoxazole (11)** A solution of o-nitrophenol (500 mg, 3.59 mmol) in Et2NPh (15 ml) was reflux for 3 h. After cooling, the reaction mixture in hexane was subjected to column chromatography on silica gel. Elution with hexane-AcOEt (2 : 1) afforded 11 (216 mg, 45% yield).

**The Duff reaction of m-Nitrophenol** Hexamethylenetetramine (7.10 g, 50.7 mmol) was added to a stirred solution of m-nitrophenol (7.0 g, 50.3 mmol) in 75% polyphosphoric acid (40 ml) at 100°C and the mixture was stirred for 45 min. After cooling, the reaction mixture was diluted with cold water and extracted with AcOEt. The residue in CHCl3 was chromatographed on silica gel. Elution with hexane-AcOEt (8 : 1) provided 1a (2.82 g, 34% yield), mp 52-53°C (lit.,11 mp 54-55°C)(yellow prisms from ether-hexane). Elution
with hexane-AcOEt (6 : 1) provided 1c (1.01 g, 12% yield), mp 137-138°C (lit.,\textsuperscript{12} mp 133-134°C)(pale yellow plates from benzene).

4-Nitrosalicylaldehyde (1c) A solution of 1-acetoxy-2-dibromomethyl-5-nitrobenzene\textsuperscript{12} (6.44 g, 18.2 mmol) in 8% Na\textsubscript{2}CO\textsubscript{3} aqueous solution (70 ml) was boiled under reflux for 4 h. After cooling, the reaction mixture was acidified with 10% HCl solution and the solution was extracted with AcOEt. The residue in AcOEt was subjected to column chromatography on silica gel. Elution with hexane-AcOEt (6 : 1) gave 1c (2.20 g, 72% yield), mp 137-138°C.

3-Nitrosalicylaldehyde (1d) Benzofuran (12)\textsuperscript{14} (500 mg, 2.82 mmol) was dissolved in dry CH\textsubscript{2}Cl\textsubscript{2} (92 ml) and cooled to -78°C. Ozone was bubbled through the solution for 15 min with stirring. The reaction mixture was stirred at -78°C for a further 15 min. Excess ozone was removed by bubbling argon through the solution for about 10 min at -78°C. Me\textsubscript{2}S (1 ml, 13.6 mmol) was added with stirring and the whole was stirred at room temperature for 1 h. The reaction mixture was concentrated under reduced pressure. The residue in EtOH (35 ml) and 1% NaHCO\textsubscript{3} aqueous solution (36 ml) was warmed at 40-45°C for 5 min. The reaction mixture was poured into water, acidified in 1% HCl solution and then extracted with ether. The residue in AcOEt was subjected to column chromatography on silica gel. Elution with the same solvent gave 1d, (380 mg, 80% yield), mp 110-111°C (lit.,\textsuperscript{13} 109-110°C)(yellow prisms from benzene)

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REFERENCES AND NOTES
8. *N*-Ethylaniline and *N*-methylaniline were isolated, respectively, from the corresponding reaction mixture. Interestingly, neither 3d nor 3e was produced in the reaction using Me2NPh.
16. Preparation of 1d from 9 using osmium tetroxide method was examined. However, the yield was 35% and much less than that of ozonolysis method.

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