

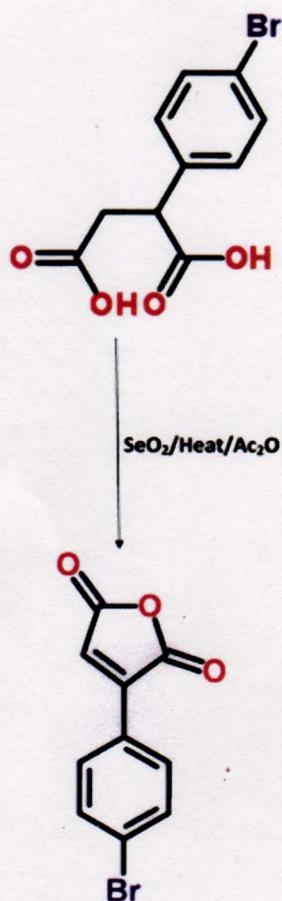
# A Facile General Synthesis of Arylmaleic Anhydrides; p-Bromophenylmaleic Anhydride and other Aryl Substituted Maleic Anhydrides

SyntheticPage 525

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## Chemicals Used

Aryl succinic acids  
Selenium Dioxide  
Acetic Anhydride

## Procedure

### Phenyl Maleic Anhydride (3a)

A 250 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 14.7 g (0.076 mol) phenyl succinic acid (2a), 8.3 g (0.075 mol) selenium dioxide, and 60 ml acetic anhydride. The solution was heated at reflux for 6 hours and filtered hot through a sintered glass Buchner funnel. Concentration of the filtrate on a rotovap gave an orange solid. The solid was boiled with 150 ml diethyl ether for one hour, then again suction filtered, yielding 9.8 g (73.7%) phenylmaleic anhydride, 3a, mp 118-22°, (Lit mp 119-199.5°C).

### p-Fluorophenyl Maleic Anhydride (3b)

A 100 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 3.3 g (0.0156 mol) p-fluoro phenyl succinic acid (2b), 1.9 g (0.0171 mol) selenium dioxide and 40 ml acetic anhydride. The mixture was refluxed for 24 hrs and worked up as in 3a above, yielding 1.8 g (60%) of 3b, tan crystals, mp 111-114°C).

IR (CDCl<sub>3</sub>) 3140(w), 1860(m), 1840(m), 1810(m), 1770(vs), 1620(m), 1600(s), 1505(s), 1415(w), 1310(m), 1300(m), 1290(w), 1225(vs), 1160(s), 1090(m), 1050(m), 1005(w), 830(s), 800(m) cm<sup>-1</sup>.

Nmr (60 Mhz, DMSO-D<sub>6</sub>) δ 8.1 (d of d, 2H, meta to F, J<sub>om</sub> = 10Hz, J<sub>oF</sub> = 5Hz), 7.55 (s, 1H, olefinic), 7.26(t, 2H, ortho to F, J<sub>om</sub> = J<sub>oF</sub> = 10Hz).

### p-Methoxyphenyl (Anisyl) Maleic Anhydride (3c)

A 250 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 33.5 g (0.150 mol) p-Methoxyphenyl succinic acid, (2c), 19.4 g, (0.150 mol) selenium dioxide, and 125 ml acetic anhydride. The solution was heated for 21 hours and filtered hot through a sintered glass funnel. The filtrate was concentrated on the rotovap yielding brown semisolids, which were titrated with hexane then ether, then hot CCl<sub>4</sub>, yielding 9.3 g (43.2%) 3c, mp 140-143°C, (Lit mp 142.5-143.5°C).

Nmr (60 Mhz, DMSO-D<sub>6</sub>) δ 3.9 (s, 3H, OCH<sub>3</sub>), 7.1 (d, J = 9Hz, 2H, Aromatics), 8.1 (d, J = 9Hz, 2H, Aromatics), 7.5 (s, 1H, olefinic).

### p-Bromo Phenyl Maleic Anhydride (3d)

A 250 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 8.0 g (0.0293 mol) 3-bromophenyl succinic acid (2d), 3.5 g (0.0310 mol) selenium dioxide and 70 ml acetic anhydride. The mixture was refluxed for 22 hrs and worked up by concentrating to 40 ml on a rotovap, cooling, and washing with 50/50 ether/hexane. Vacuum drying gave 4.75 g (64.2%) 3d, mp 152-154°C, tan crystals.

IR (CDCl<sub>3</sub>), 1860(m), 1820(m), 1800(m), 1775(vs), 1620(m), 1405(m), 1320(w), 1300(w), 1250(w), 1230(w), 1185(w), 1160(w), 1090(m), 1070(m), 1050(m), 1005(m), 820(s) cm<sup>-1</sup>.

### 3-Chloro-4-Methyl Phenyl Maleic Anhydride (3e)

A 250 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 7.5 g (0.031 mol) 3-chloro-4-methyl succinic acid, 2e, and 100 ml acetic anhydride. The mixture was refluxed for 22 hrs and worked up as in 3a above, yielding 4.3 g (62.3%) 3e, mp 98-102°C.

IR (CDCl<sub>3</sub>) 3070(w), 2990(w), 1840(m), 1770(s), 1610(m), 1550(w), 1490(m), 1310(m), 1290(m), 1270(m), 1220(s), 1150(w), 1080(m), 1060(m), 1040(m), 980(m), 810(m) cm<sup>-1</sup>.

Nmr (60 Mhz, DMSO-D<sub>6</sub>) δ 7.95(d, 1H, aromatic, J<sub>o-o</sub><sup>1</sup> = 2Hz), 7.75 (d of d, 1H, H ortho, J<sub>om</sub> = 8Hz, J<sub>o-o</sub><sup>1</sup> = 2Hz), 7.40 (d, 1H, Hm, J<sub>om</sub> = 8Hz), 7.05(s, 1H, olefinic), 2.50 (s, 3H, methyl).

### Chlorophenyl Maleic Anhydride (3f)

A 300 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 15.6 g (0.069 mol) o-chlorophenyl succinic acid (**2f**), 8.3 g (0.075 mol) selenium dioxide and 60 ml acetic anhydride. The mixture was refluxed for 8 hours. The acetic anhydride was removed on a rotovap, yielding a dark brown oil, which was taken up in 15 ml benzene and cooled to room temperature. 5 ml cyclohexane was added and the solution cooled in an ice chest, yielding 9.9 g (70.2 %) **3f**, mp 64-5°C, (Lit mp 68-9°C).

### 3,4-Dichlorophenyl Maleic Anhydride (3g)

A 250 ml round bottom flask with heating mantel, magnetic stirrer and water condenser was charged with 32.2 g (0.122 mol) 3,4-dichloro phenyl succinic acid (**2g**), 14.7 g (0.1325 mol) selenium dioxide and 130 ml acetic anhydride. The mixture was refluxed for 20 hrs and worked up as in **3a** above, yielding 22.8 g (77%) **3g**, mp 110 -115°C, (lit mp 115-116°C).

IR (CDCl<sub>3</sub>) 3120(w), 1840(m), 1770(vs). 1620(m), 1590(w), 1300(w)1250(w), 1220(s), 1130(m), 1080(m), 1050 (m), 1020 (m). 980(m), 810(m) cm<sup>-1</sup>

NMR (60 Mhz, CDCl<sub>3</sub>) δ 7.71 (m, 3H, aromatics), 7.0(s, 1H, olefinic).

### Author's Comments

#### A FACILE GENERAL SYNTHESIS OF ARYLMALEIC ANHYDRIDES

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By a sequence involving Knoevenagel condensation, Michael addition of cyanide, hydrolysis, and selenium dioxide oxidation, a series of seven aryl maleic anhydrides were prepared in excellent overall yields. The regiospecificity of reaction of these anhydrides with various nucleophilic species, e.g. Me<sub>3</sub>SiN<sub>3</sub>, NH<sub>3</sub>, and PhNH<sub>2</sub> was investigated. Except for a few cases, the nucleophile attacks the more hindered carbonyl, in a reaction controlled by electronic rather than steric factors. These anhydrides are of particular utility in the synthesis of 4-and 5-Aryl Substituted 1,3(3H) Oxazine-2,6-Diones (Oxauracils).

### Data

#### p-fluorophenyl Maleic Anhydride

IR (CDCl<sub>3</sub>) 3140(w), 1860(m), 1840(m), 1810(m), 1770(vs). 1620(m), 1600(s), 1505(s), 1415(w), 1310(m), 1300(m), 1290(w), 1225(vs), 1160(s), 1090(m), 1050(m), 1005(w), 830(s), 800(m) cm<sup>-1</sup>.

Nmr (60 Mhz, DMSO-D<sub>6</sub>) δ 8.1 (d of d, 2H, meta to F, J<sub>om</sub> = 10Hz, J<sub>oF</sub> = 5Hz), 7.55 (s, 1H, olefinic), 7.26(t, 2H, ortho to F, J<sub>om</sub> = J<sub>oF</sub> = 10Hz).

### p-Methoxyphenyl (Anisyl) Maleic Anhydride

Nmr (60 Mhz, DMSO-D<sub>6</sub>),  $\delta$  3.9 (s, 3H, OCH<sub>3</sub>), 7.1 (d, J= 9Hz, 2H, Aromatics), 8.1 (d, J= 9Hz, 2H, Aromatics), 7.5 (s, 1H, olefinic).

### p-Bromo Phenyl Maleic Anhydride

IR (CDCl<sub>3</sub>), 1860(m), 1820(m), 1800(m), 1775(vs), 1620(m), 1405(m), 1320(w), 1300(w), 1250(w), 1230(w), 1185(w), 1160(w), 1090(m), 1070(m), 1050(m), 1005(m), 820(s) cm<sup>-1</sup>.

### 3-Chloro-4-Methyl Phenyl Maleic Anhydride

IR (CDCl<sub>3</sub>) 3070(w), 2990(w), 1840(m), 1770(s), 1610(m), 1550(w), 1490(m), 1310(m), 1290(m), 1270(m), 1220(s), 1150(w), 1080(m), 1060(m), 1040(m), 980(m), 810(m) cm<sup>-1</sup>.

Nmr (60 Mhz, DMSO-D<sub>6</sub>)  $\delta$  7.95(d, 1H, aromatic, J<sub>o-o</sub><sup>1</sup> = 2Hz), , 7.75 (d of d, 1H, H ortho, J<sub>om</sub> = 8Hz, J<sub>o-o</sub><sup>1</sup> = 2Hz), 7.40 (d, 1H, Hm, J<sub>om</sub> = 8Hz), 7.05(s, 1H, olefinic), 2.50 (s, 3H, methyl).

### 3,4-Dichlorophenyl Maleic Anhydride

IR (CDCl<sub>3</sub>) 3120(w), 1840(m), 1770(vs). 1620(m), 1590(w), 1300(w)1250(w), 1220(s), 1130(m), 1080(m), 1050 (m), 1020 (m). 980(m), 810(m) cm<sup>-1</sup>

NMR (60 Mhz, CDCl<sub>3</sub>),  $\delta$  7.71 (m, 3H, aromatics), 7.0(s, 1H, olefinic).

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### Lead Reference

J.H. MacMillan and S.S. Washburne "Further Investigation of the Interaction of Trimethylsilyl Azide with Substituted Maleic Anhydrides, Synthesis of 4-and 5-Aryl Substituted 1,3(3H) Oxazine-2,6-Diones" J.Heterocyclic Chemistry Vol. 12, p1215 (1975).

### Other References

J.D. Warren, J.H. MacMillan and S.S. Washburne "Synthesis of Substituted 2H-1,3-Oxazine-2,6-Diones by Reaction of Trimethylsilyl Azide with Maleic Anhydrides" J.Org.Chem., Vol. 40, p743 (1975).

### Supplementary Information

*e.g. Actual NMR spectra (as images or jdx files for interactive spectra), photographs of apparatus, TLC's or crystals or videos. Please contact the ChemSpider team (ChemSpider-at-rsc.org) for help with*

*this.*

[ArylMaleic-Anhydrides-Spectra.doc](#)

**Keywords:** aromatics/arenes, esters, heterocyclic compounds, oxidation