

## A New Synthesis of Anthraquinones

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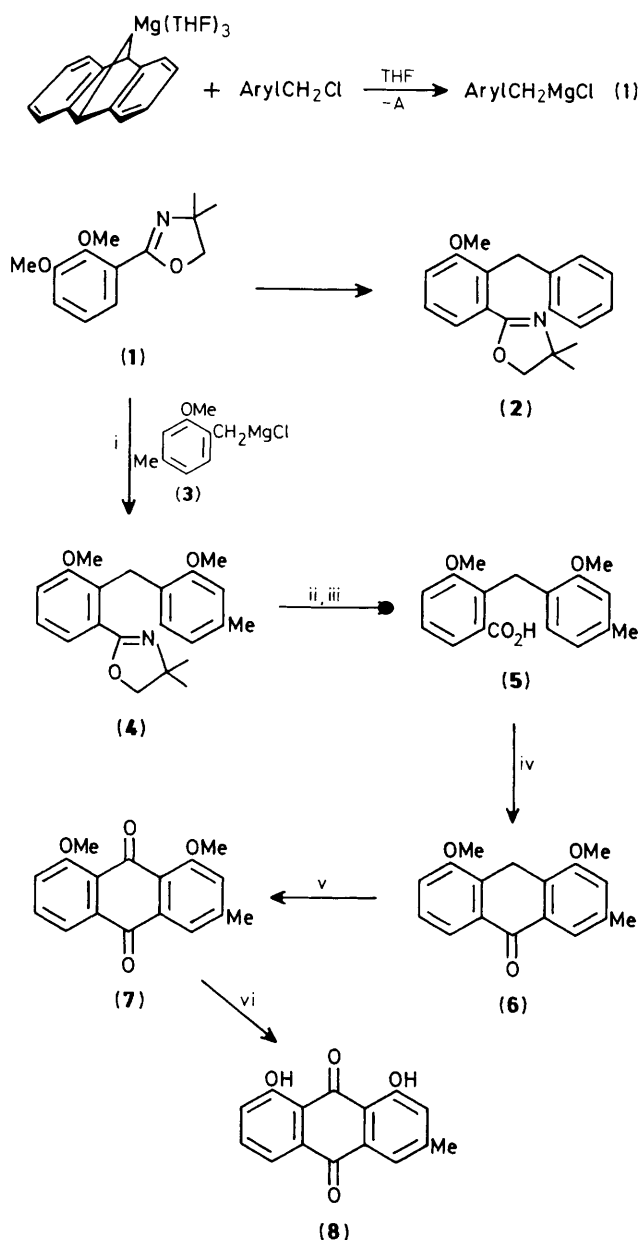
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Methoxy substituted benzyl magnesium chlorides formed by the use of a magnesium anthracene complex smoothly displace the *ortho*-methoxy group from (*o*-methoxyaryl) dihydro-oxazoles (oxazolines); the resultant masked *o*-benzylbenzoic acids are easily converted into anthraquinones.

There has recently been a resurgence of interest in methods for the synthesis of anthraquinones and we now describe a

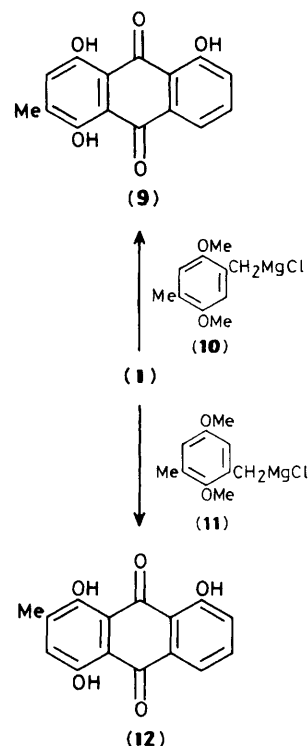
simple and convenient method based on the nucleophilic displacement of the *ortho*-methoxy group from an (*o*-methoxyaryl) dihydro-oxazole by a benzylic Grignard reagent and subsequent steps. Benzylic halides are prone to undergo Wurtz coupling with magnesium and consequently yields in reactions involving them are often reduced. We have found,

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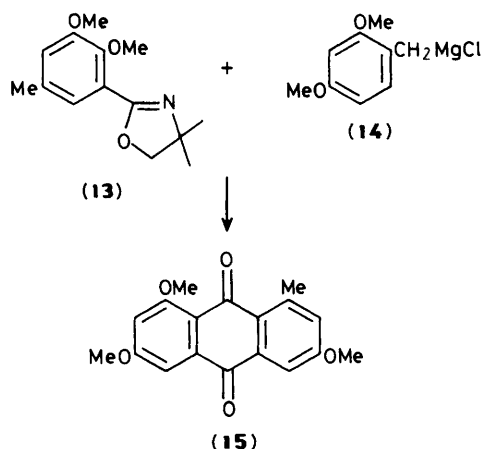


**Scheme 1.** Reagents and conditions: i, 1.13 mol. equiv. (3), THF, 25 °C, 18 h; ii, MeI, MeNO<sub>2</sub>, 70 °C, 18 h; iii, 20% aq. NaOH, MeOH, reflux, 44 h; iv, TFAA, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C, 30 min; v, CrO<sub>3</sub>, AcOH, 90 °C, 15 min; vi, HBr, AcOH, reflux, 0.5 h.

however, that when benzylic Grignard reagents are generated at 0 °C from 0.1 M solutions of benzyl chlorides in tetrahydrofuran (THF) using the magnesium anthracene (A) complex,  $\text{Mg}(\text{A})(\text{THF})_3$ ,<sup>1</sup> as a source of magnesium (equation 1), then no Wurtz coupling can be detected. Meyers and his co-workers<sup>2</sup> found that when the dihydro-oxazole (1) (Scheme 1) was treated with a slight excess of benzyl magnesium bromide at 25 °C only a 6% yield of the substitution product (2) was obtained. We have found that this yield can be considerably increased (80%) by using an excess of benzyl magnesium chloride generated by the above method. We have therefore used this method in the synthesis of a number of variously oxygenated naturally occurring anthraquinones or their derivatives. Thus the Grignard reagent (3) (Scheme 1) was



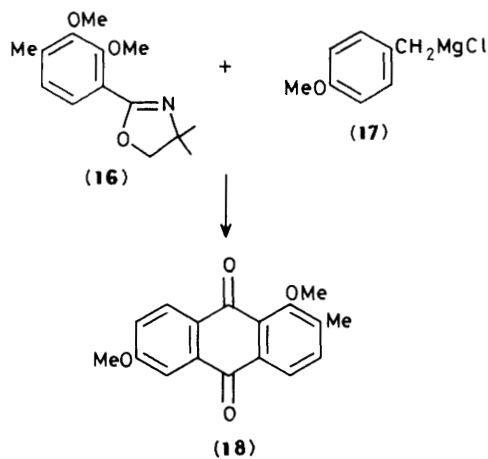
**Scheme 2**



**Scheme 3**

allowed to react with the dihydro-oxazole (1). The product (4) (86%), m.p. 155–156.5 °C, on deprotection provided the benzylbenzoic acid (5) (90%), m.p. 175–176.5 °C, which underwent ring-closure on treatment with trifluoroacetic anhydride (TFAA) thereby supplying the anthrone (6) (91%), m.p. 187.5–189 °C. Oxidation of the anthrone (6) yielded the anthraquinone (7) (85%), m.p. 191–191.5 °C (lit.<sup>3</sup> 190 °C), which on demethylation gave chrysophanol (8) (94%), m.p. 194–195 °C (lit.<sup>3</sup> 190 °C).

Islandicin (9)<sup>4</sup> and digitopurpone (12)<sup>5</sup> were prepared in a similar fashion using the dihydro-oxazole (1) and the benzylic Grignard reagents (10) and (11), respectively. Tri-O-methylemodin (15) (Scheme 3), identical with an authentic sample,<sup>6</sup> resulted from a sequence employing the dihydro-oxazole (13) and the benzyl magnesium chloride (14), whilst di-O-methylsoranjidiol (18)<sup>7</sup> (Scheme 4) resulted from the dihydro-oxazole (16)<sup>8</sup> and the benzyl magnesium chloride



Scheme 4

(17). These examples amply demonstrate the utility and versatility of this method of anthraquinone synthesis.

Received, 30th June 1988; Com. 8/02620C

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