



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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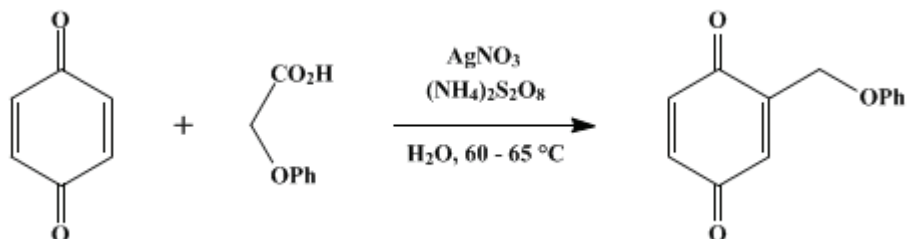
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

*Organic Syntheses, Coll. Vol. 6, p.890 (1988); Vol. 56, p.68 (1977).*

## FREE-RADICAL ALKYLATION OF QUINONES: 2-PHENOXYMETHYL-1,4-BENZOQUINONE

[2,5-Cyclohexadiene-1,4-dione, 2-(phenoxyethyl)-]



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Checked by R. J. DeFranco and R. E. Benson.

### 1. Procedure

A 250-ml., three-necked flask fitted with a mechanical stirrer, a thermometer, and a 25-ml., graduated, pressure-equalizing dropping funnel is charged with 7.60 g. (0.0500 mole) of [phenoxyacetic acid](#) (Note 1), 5.40 g. (0.0500 mole) of [1,4-benzoquinone](#) (Note 2), 1 g. (0.006 mole) of [silver nitrate](#) (Note 3), and 125 ml. of water (Note 4). The mixture is stirred and heated to 60–65° with a heating mantle until dissolution is complete. The resulting solution is stirred vigorously while a solution of 13.7 g. (0.0601 mole) of [ammonium peroxydisulfate](#) (Note 5) in 25 ml. of water is added at a rate of 0.5 ml. per minute for the first 40 minutes, then at a rate of 0.25 ml. per minute for the last 20 minutes. Throughout the addition, the reaction mixture is maintained at 60–65° (Note 6) and (Note 7).

After the addition is complete the mixture is stirred for 5 minutes at 65° then cooled to 5–10° in an ice bath. The precipitated solid is collected by suction filtration (Note 8), washed with 50 ml. of cold water, and pressed, removing most of the liquid. Inorganic contaminants, usually present in small amounts, are removed by dissolving the solid in 350 ml. of boiling [acetone](#) and filtering the hot solution through fluted filter paper. Concentration of the filtrate on a rotary evaporator gives a dark red crude product (10.5–11.4 g.), which is dissolved in 220–240 ml. of boiling 95% [ethanol](#). On cooling the solution to 5°, the alkylated quinone crystallizes in brownish-yellow needles, which are collected by filtration and air-dried, yielding 6.7–8.0 g., m.p. 135–137°. Recrystallization from 30 ml. of [ethanol](#) per gram of product gives 6.6–7.4 g. (61–69%) of [2-phenoxyethyl-1,4-benzoquinone](#), m.p. 137–138° (Note 9).

### 2. Notes

1. The submitter used Fluka *puriss* grade [phenoxyacetic acid](#). The checkers used material available from Eastman Organic Chemicals.
2. The submitter used Fluka *purum* grade [benzoquinone](#), recrystallized once from petroleum ether (b.p. 60°), m.p. 111–113°. The checkers used Fisher purified grade material without recrystallization.
3. The submitter used reagent grade [silver nitrate](#) available from Merck & Company, Inc.
4. In the case of a water-insoluble quinone or carboxylic acid, [acetonitrile](#) can be used as a co-solvent.<sup>2</sup>
5. Fluka *purum* grade [ammonium peroxydisulfate](#) was used by the submitter. The checkers used ACS reagent grade material available from Fisher Scientific Company.
6. The reaction is slightly exothermic, but it is necessary to heat the mixture occasionally in order to maintain it at 60–65°.
7. The checkers found that increasing the addition rate of persulfate solution to 1.5 ml. per minute, while giving a somewhat lower initial yield (62% after one recrystallization), resulted in a product of sufficient purity (m.p. 137–138°) as to require no further recrystallization.
8. This work-up procedure applies only when the crude product can be crystallized from the reaction

mixture. If the product is partly soluble in the reaction medium or if it separates as a gum, an extraction procedure is employed.

9. IR (CHCl<sub>3</sub>) cm<sup>-1</sup>: 1660 strong, 1600 medium, 1590 medium; UV (95% C<sub>2</sub>H<sub>5</sub>OH) nm. max (ε): 220 (12,700), 248 (18,600), 269 shoulder, 276 shoulder; <sup>1</sup>H NMR (CDCl<sub>3</sub>), δ (multiplicity, coupling constant *J* in Hz., number of protons): 4.9 (d, *J* = 2, 2H, CH<sub>2</sub>O), 6.7–7.5 (m, 8H).

### 3. Discussion

The procedure described above has been used to prepare various, alkylated 1,4-benzoquinones and 1,4-naphthoquinones,<sup>2,3</sup> including some naturally occurring quinones.<sup>4</sup> A few examples are listed in Table I, showing the scope of the method.

TABLE I  
SUBSTITUTED QUINONES DERIVED BY ALKYLATION

| Parent Quinone               | Acid                   | Derived Substituted Quinone     | Yield (%) <sup>a</sup> | Reference |
|------------------------------|------------------------|---------------------------------|------------------------|-----------|
| 1,4-Benzoquinone             | Pivalic                | 2- <i>tert</i> -Butyl           | 67 <sup>b</sup>        | 2         |
| 1,4-Benzoquinone             | Phenylacetic           | 2-Benzyl                        | 87                     | 2         |
| 1,4-Benzoquinone             | α-Chloropropionic      | 2-(α-Chloroethyl)               | 45 <sup>b</sup>        | 2         |
| 1,4-Naphthoquinone           | Methoxyacetic          | 2-Methoxymethyl                 | 50                     | 2         |
| 1,4-Naphthoquinone           | Adipic                 | 2-(ω-Carboxybutyl)              | 51                     | 2         |
| 2-Methyl-1,4-naphthoquinone  | Cyclopropanecarboxylic | 2-Cyclopropyl-3-methyl          | 37                     | 3         |
| 2-Acetoxy-1,4-naphthoquinone | 4-Methyl-3-pentenoic   | 2-Acetoxy-3-(γ,γ-dimethylallyl) | 73                     | 4         |

<sup>a</sup>Yields are based on the parent quinone.

<sup>b</sup>Modified procedure (see Discussion).

The reaction is a free-radical alkylation in which radicals are derived from a carboxylic acid by decarboxylation with silver peroxydisulfate. It has the advantage that the reaction medium can be adjusted so that the monoalkylated product precipitates as it is formed, thereby suppressing di- or polyalkylation.<sup>5</sup>

The reaction fails if the decarboxylation produces a radical that is easily oxidized, such as an α-hydroxyalkyl radical.<sup>2</sup> In intermediate cases, such as *tert*-alkyl or α-alkoxyalkyl radicals,<sup>2</sup> the yield based on the parent quinone is usually improved by using an excess of the peroxydisulfate and carboxylic acid to compensate for the loss of radicals due to oxidation (footnote *b*, Table I).

This preparation is referenced from:

- Org. Syn. Coll. Vol. 9, 741

### References and Notes

1. Department of Organic Chemistry, University of Aarhus, 8000 Aarhus C, Denmark. [Present address: A/S Cheminova, P. O. Box 9, DK-7620 Lemvig, Denmark.]
2. N. Jacobsen and K. Torssell, *Justus Liebigs Ann. Chem.*, **763**, 135 (1972).
3. J. Goldman, N. Jacobsen, and K. Torssell, *Acta Chem. Scand.*, **28**, 492 (1974).
4. N. Jacobsen and K. Torssell, *Acta Chem. Scand.*, **27**, 3211 (1973).
5. B. M. Bertilsson, B. Gustafsson, I. Kühn, and K. Torssell, *Acta Chem. Scand.*, **24**, 3590 (1970); N. Jacobsen, *J. Chem. Soc., Perkin Trans. II*, 569 (1979).

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**Appendix**  
**Chemical Abstracts Nomenclature (Collective Index Number);**  
**(Registry Number)**

petroleum ether

ethanol (64-17-5)

acetonitrile (75-05-8)

silver nitrate (7761-88-8)

acetone (67-64-1)

Quinone,  
1,4-benzoquinone,  
benzoquinone (106-51-4)

1,4-Naphthoquinone (130-15-4)

ammonium peroxydisulfate (7727-54-0)

2-methyl-1,4-naphthoquinone

2-Phenoxyethyl-1,4-benzoquinone,  
2,5-Cyclohexadiene-1,4-dione, 2-(phenoxyethyl)- (7714-50-3)

phenoxyacetic acid (122-59-8)

silver peroxydisulfate

2-Acetoxy-1,4-naphthoquinone