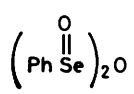
Oxidation of Phenols, Pyrocatechols, and Hydroquinones to *ortho*-Quinones using Benzeneseleninic Anhydride

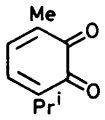
By **Derek H. R. Barton,* Andrew G. Brewster, Steven V. Ley, Christine M. Read,** and **Moshe N. Rosenfeld,** Department of Chemistry, Imperial College, London SW7 2AY

Benzeneseleninic anhydride has been used as a mild oxidising reagent to convert phenols into *o*-quinones including some examples where the *p*-position is unblocked. The method is limited to the production of *o*-quinones which are not susceptible to further reaction. Pyrocatechols and hydroquinones can also be oxidised to the corresponding quinones in excellent yield using benzeneseleninic anhydride.

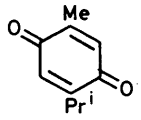
ALTHOUGH *o*-quinones can be prepared from 1,2-dihydroxybenzenes (pyrocatechols) by a variety of oxidation methods, formation from monohydroxybenzenes (phenols), particularly when the *p*-position is unsubstituted, is much less common.[1] Indeed, the



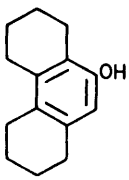
(1)



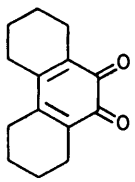
(2)



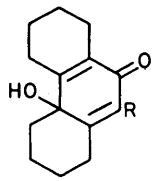
(3)



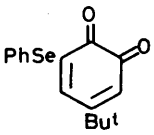
(4)



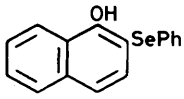
(5)



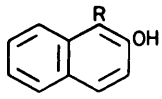
(6) R=H
(7) R=SePh



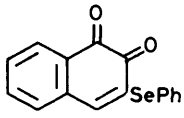
(8)



(9)



(10) R=SePh
(11) R=Se(O)Ph



(12)

majority of existing literature reactions can be regarded as special cases and, consequently, are not generally applicable.

As a result of the *ortho*-selectivity shown by benzeneseleninic anhydride[2] (1) towards hydroxylation of phenolate anions we were prompted to investigate the use of this reagent for quinone formation.

Optimum conditions[3] for the oxidation of a number of phenols to *o*-quinones were found to involve the addition of a THF (tetrahydrofuran) solution of the phenol to a stirred suspension of benzeneseleninic anhydride (1) in THF at 50 °C. The reactions were followed by t.l.c. until disappearance of starting material was indicated. The products were worked up by passage through a short column of silica gel. The diphenyl diselenide formed as a by-product in these reactions was recovered and reoxidised to the anhydride.[2]

Under these conditions both 1-naphthol and 2-naphthol gave 1,2-naphthoquinone in good yield. In some experiments 1-naphthol also gave up to 5% of the 1,4-quinone as an additional product.

Oxidation of 2,4-di-t-butylphenol with the anhydride produced the *ortho*-quinone in 68% yield. Similarly carvacrol and thymol gave the same quinone (2) as the major product. In more recent work with thymol and different batches of anhydride we have noticed that significant amounts (*ca.* 15%) of the *para*-quinone (3) were also formed.

Oxidation of the phenol † (4) under the usual conditions gave, in addition to the *o*-quinone (5) (37%), two other products. The first of these was the hydroxyketone (6) which was the major product, isolated in 44% yield. The structure of (6) is consistent with its spectral parameters and compares well with related compounds.[2] The remaining product, isolated in 19% yield, was red and from its spectral data clearly showed the presence of a carbonyl group, a hydroxy-group, and a phenylseleno-moiety. *X*-Ray crystallography ‡ confirmed that this product was the novel phenylselenohydroxyketone (7).

4-t-Butylphenol reacted with the anhydride to give two compounds. The major product, which was a deep purple substance, provided analytical results consistent with the molecular formula $C_{16}H_{16}O_2Se$ although the mass spectrum showed a molecular ion at 322. This molecular ion, however, could correspond to an $M + 2$ peak which are typically observed for *o*-quinones.[4] Together with the i.r. and ^1H n.m.r. spectra we therefore assign this product as the phenylselenated *o*-quinone (8). The other product, formed in low yield, was red, had a

† We thank Dr. J. Sepiol, Jagiellonian University, Krakow, Poland, for a generous sample of this compound.

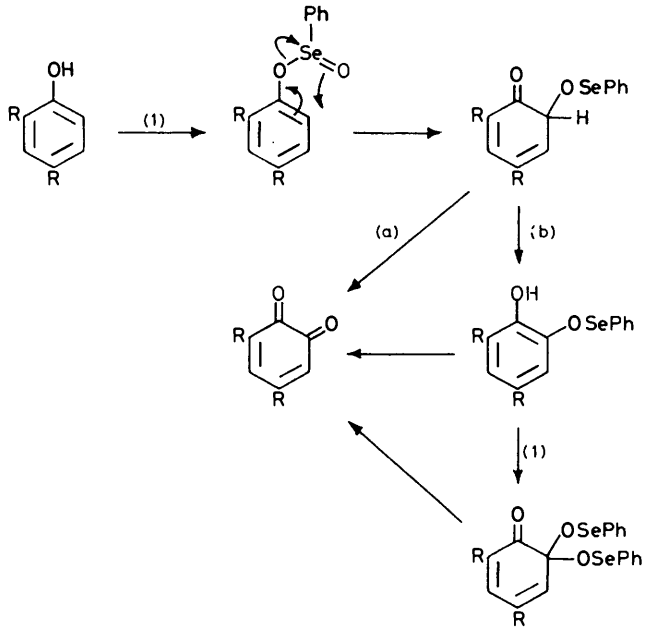
‡ We thank Dr. D. J. Williams, Imperial College, for this result.

molecular ion at 468, and gave analytical results consistent with the molecular formula $C_{26}H_{28}O_3Se$. It was not investigated further.

Attempted oxidation of other phenols such as 2,4-dimethyl-, 3,4-dimethyl-, or 2-nitro-phenol, and of resorcinol or phloroglucinol led to complex reaction mixtures presumably as a result of the instability of the derived products.

Recently Harvey [5] has successfully used the anhydride to prepare other *ortho*-quinones from phenols based on polycyclic aromatic hydrocarbons.

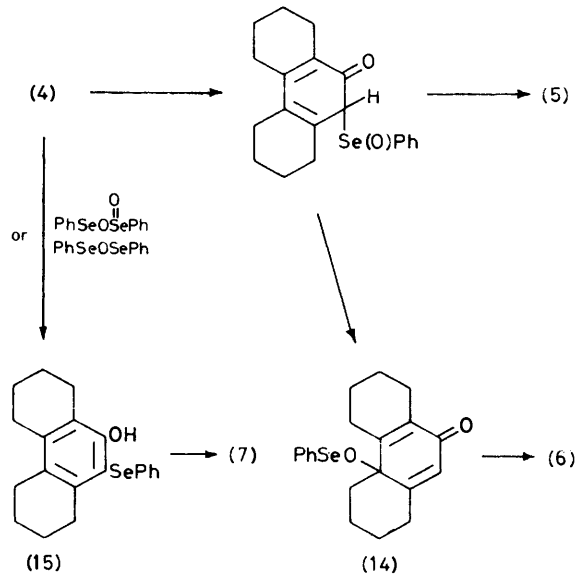
In an effort to characterise possible reaction intermediates in the oxidation pathway, 1- and 2-naphthols were separately treated with the anhydride at lower temperatures. For example, at room temperature 1-naphthol gives the *o*-quinone (55%) and 2-phenylseleno-1-naphthol (9) (23%), whereas 2-naphthol gave a 44% yield of the *o*-quinone and 43% of 1-phenylseleno-2-naphthol (10). The possibility exists therefore that (9) and (10) could be additional precursors of the *o*-quinone in the higher temperature reactions. In accord with this proposal (10) was treated with the anhydride at 50 °C to afford 1,2-naphthoquinone in 89% yield. In another experiment 1,2-naphthoquinone was formed in high yield when (9) was oxidised with hydrogen



SCHEME 1

peroxide.[6] This result implies that a possible intermediate selenoxide (11) would rearrange rapidly to the *o*-quinone.

The formation of the initial phenylseleno-derivatives undoubtedly arises by attack of the naphthol by an electrophilic phenylselenenating species, a number of which could be present in the reaction mixtures. One such compound could be a partially reduced form of the anhydride such as PhSeO·Se(O)Ph. For this reason an attempt was made to prepare this species by allowing benzeneselenenyl chloride to react with the lithium benzeneseleninate. Although a colour change took place from deep orange to pale yellow only benzeneseleninic acid and diphenyl diselenide could be isolated on work-up. However by adding 2-naphthol directly to the pale yellow solution a 62% yield of (10) could be isolated. On prolonged treatment with the above reagent 2-naphthol gave (10) (43%) together with 1-chloro-2-naphthol (20%), and a third component to which we assign the structure (12) (23%) on the basis of



SCHEME 2

its spectral properties and by comparison with other similar compounds discussed above.

In view of the *ortho*-selectivity shown in many of the oxidation reactions, we propose that phenols react initially on oxygen to form seleninyl esters. Rapid 2,3-sigmatropic rearrangement produces intermediate selenenyl esters which could decompose by loss of benzeneselenol to give the quinone (pathway *a*) or *via* aromatization to a pyrocatechol intermediate (pathway *b*). The latter could either afford the quinone directly by reaction with a nucleophilic species or *via* a less likely second oxidation to an acetal derivative and hence the quinone (Scheme 1). Various attempts to trap possible pyrocatechol intermediates, however, failed.

However, the formation of the *p*-hydroxylated dienone (6), as major product from the oxidation of phenol (4), shows that another mechanism must also be operative. We propose (Scheme 2) that electrophilic attack of the reagent could also occur *ortho* to the phenolic group to give the intermediate (13). Elimination, as for intermediate (11), by a Pummerer-type rearrangement,[7a] would give the *o*-quinone (5). The latter could, of course, also be formed by the processes summarised in Scheme 1.

The major product of the reaction would then arise

from 2,3-sigmatropic rearrangement to give (14) which by nucleophilic cleavage by $PhSeO_2^-$ or $PhSeO^-$ would give (6). The compound (7) would then arise from a comparable process on the seleno-derivative (15) generated as already discussed above.

In general, the behaviour of enolic systems towards benzeneseleninic anhydride is comparable to that of enols. The mechanistic possibilities involved for the latter have recently been discussed.[7b]

Finally, it was of interest to compare the use of benzeneseleninic anhydride as an oxidising reagent for pyrocatechols and hydroquinones as these are the usual precursors of *o*- and *p*-quinones. Accordingly, a number of pyrocatechols and hydroquinones (see Experimental section) were converted into the corresponding quinones in excellent yield (84—92%) by reaction with (1) at room temperature. This new method is mild and compares favourably with other literature procedures.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. ^1H n.m.r. spectra were obtained for solutions in $CDCl_3$ (Me_4Si as internal standard) at 60 MHz. Thin-layer and preparative layer chromatography were carried out on silica gel (Merck GF_{254} Type 60); isolated products are listed in order of decreasing R_F value. Light petroleum refers to the fraction b.p. 40—60 °C. Solutions were dried over magnesium sulphate and solvents by standard techniques.

General Method for the Oxidation of Phenols to Quinones.—A solution of the phenol (0.5 mmol) in dry tetrahydrofuran (5 ml) was added dropwise during 15 min to a stirred suspension of benzeneseleninic anhydride (180 mg, 0.5 mmol) in tetrahydrofuran (10 ml) at 50 °C. The reaction was monitored by t.l.c. and further oxidant (*ca.* 0.1 equiv.) was added until no phenol remained. The cooled reaction mixture was diluted with chloroform (25 ml), washed with aqueous sodium hydrogencarbonate solution (10% 2 × 20 ml) and water (20 ml) and then dried. Evaporation under reduced pressure followed by column chromatography [silica gel, using ether–light petroleum (1 : 4) followed by ether as eluants] gave the quinone as a crystalline solid.

Oxidation of 1-*Naphthol.*—1-Naphthol (72 mg, 0.5 mmol) on oxidation gave 1,2-naphthoquinone (50 mg, 62%), m.p. 146—147 °C (lit.,[8] 145—146 °C).

Oxidation of 2-*Naphthol.*—2-Naphthol (72 mg, 0.5 mmol) on oxidation afforded 1,2-naphthoquinone (51 mg, 63%), m.p. 144—146 °C.

Oxidation of 2,4-*Di-t-butylphenol.*—2,4-Di-t-butylphenol (103 mg, 0.5 mmol) was converted into 3,5-di-t-butyl-1,2-benzoquinone (74 mg, 68%), m.p. 108—112 °C (lit.,[9] 114 °C).

Oxidation of Carvacrol.—Carvacrol (75 mg, 0.5 mmol) was converted into 6-*isopropyl*-3-*methyl*-1,2-*benzoquinone* (2) (50 mg, 60%), m.p. 60—61 °C, $\nu_{max.}$ 1 680 cm^{-1}, τ 3.0—3.6 (2 H, m), 6.6—7.2 (1 H, m), 7.8 (3 H, s), and 8.8 (6 H, d, J = 6 Hz); $\lambda_{max.}$ 273 (ε 2 375) and 415 nm (1 770); *m/e* 166 (M^+) (Found: C, 73.25; H, 7.5. $C_{10}H_{12}O_2$ requires C, 73.2; H, 7.3%).

Oxidation of Thymol.—Thymol (75 mg, 0.5 mmol) on oxidation gave the quinone (2) (49 mg, 59%), m.p. 60—61 °C.

Oxidation of 9-*Hydroxy*-1,2,3,4,5,6,7,8-*octahydrophenanthrene* (4).—Compound (4) (180 mg) on oxidation gave (i) the *quinone* (5) (40 mg, 37%), m.p. 120—122 °C (from ethyl acetate), $\nu_{max.}$ 1 650 and 1 580 cm^{-1}; $\nu_{max.}$ 269infl. (ε 4 580), 444 nm (1 900); δ 2.53—2.20 (8 H, m) and 1.88—1.48 (8 H, m); *m/e* 218 (base peak), 216, 201, 199, 190, 188, 160, 128, 115, and 91 (Found: C, 77.7; H, 7.4. $C_{14}H_{16}O_2$ requires C, 77.6; H, 7.5%); (ii) the *hydroxyketone* (6) (48 mg, 44%), m.p. 148—149 °C (from ether); $\nu_{max.}$ 3 350, 1 665, and 1 620 cm^{-1}; $\lambda_{max.}$ 241 nm (ε 10 980), 274infl (2 580); δ 6.76 (1 H, d, J 1.5 Hz) and 2.93 (1 H, m); *m/e* 218 (base peak), 200, 190, 177, 161, and 147 (Found: C, 77.3; H, 8.4. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%), and (iii) the *phenylselenohydroxycyclohexadienone* (7) (35 mg, 19%), m.p. 162.5—163.5 °C (from ethyl acetate), $\nu_{max.}$ 3 410, 1 625, and 1 590 cm^{-1}; $\lambda_{max.}$ 249 (ε 13 870), 273infl. (9 850), and 336 nm (820); δ 7.49—6.96 (5 H, m) (Found: C, 64.4; H, 6.0. $C_{20}H_{22}O_2Se$ requires C, 64.3; H, 6.0%).

Oxidation of p-4-*t-Butylphenol.*—*p*-4-t-Butylphenol (150 mg, 1 mmol) in tetrahydrofuran (2 ml) was added to a stirred suspension of benzeneseleninic anhydride (360 mg, 1 mmol) in tetrahydrofuran (2 ml). The mixture was warmed to 45 °C for 30 min followed by reaction at room temperature for 24 h. Chromatography afforded (i) an unknown compound as red needles from ethanol (49 mg), m.p. 210—215 °C, $\nu_{max.}$ 1 660 cm^{-1}; $\lambda_{max.}$ 227 (ε 21 320), 254 (24 340), 288s (13 450), and 378 nm (1 120); τ 8.85 (8 H, m), 4.32 (1 H, d, J 1.1 Hz), 4.28 (1 H, d, J 1.1 Hz), and 3.85—3.35 (7 H, m) (Found: C, 66.65; H, 6.0. $C_{26}H_{28}O_2Se$ requires C, 66.8; H, 6.05%); and (ii) 6-*phenylseleno*-4-*t-butyl*-1,2-*benzoquinone* (8) (96 mg, 30%), m.p. 120 °C (purple crystals from ether), $\nu_{max.}$ 1 665 cm^{-1}; $\lambda_{max.}$ 246 (ε 26 150) and 372 nm (1 420); τ 9.08 (9 H, s), 3.96 (1 H, d, J 2 Hz), 3.63 (1 H, d, J 2 Hz), and 2.3—2.7 (5 H, m); *m/e* 322 (Found: C, 60.0; H, 5.0. $C_{16}H_{16}O_2Se$ requires C, 60.2; H, 5.05%).

Oxidation of 1-*Naphthol at Room Temperature.*—To a stirred suspension of benzeneseleninic anhydride (360 mg, 1 mmol) in tetrahydrofuran (3 ml) was added a solution of 1-naphthol (144 mg, 1 mmol) in tetrahydrofuran (1 ml) during 15 min. The yellow reaction mixture was worked up as above and gave (i) 2-*phenylseleno*-1-*naphthol* (9) (69 mg, 23%), m.p. 61—62 °C (yellow crystals after sublimation at 70 °C/2 mmHg), $\nu_{max.}$ 3 450 cm^{-1}; $\lambda_{max.}$ 224 (ε 28 000), 245 (32 150), 259s (18 050), 307 (7 000), 317s (5 200), and 322 nm (4 150) (Found: C, 64.2; H, 4.2. $C_{16}H_{12}OSe$ requires C, 64.2; H, 4.45%); and (ii) 1,2-*naphthoquinone* (87 mg, 55%), m.p. 145—146 °C.

Oxidation of 2-*Naphthol at Room Temperature.*—Benzeneseleninic anhydride (360 mg, 1 mmol) was added to a stirred solution of 2-naphthol (144 mg, 1 mmol) in tetrahydrofuran (4 ml) and after 4 h, gave: (i) *diphenyl diselenide* (280 mg), (ii) 1-*phenylseleno*-2-*naphthol* (10) (132 mg, 44%), m.p. 77—78 °C (from methanol), $\nu_{max.}$ 3 450 cm^{-1}; $\lambda_{max.}$ 225 (ε 25 500), 245 (27 000), 276 (18 350), 288 (s) (16 200), 322 (8 150), and 335 nm (11 900); τ 1.7—3.2 (m) (Found: C, 64.15; H, 4.35. $C_{16}H_{12}OSe$ requires C, 64.2; H, 4.45%); and (iii) 1,2-*naphthoquinone* (68 mg, 43%), m.p. 146 °C (from ether), $\lambda_{max.}$ 250 (ε 20 200), 340 (2 350), and 405 nm (2 400).

Oxidation of 1-*Phenylseleno*-2-*naphthol* (10).—A solution of (10) (150 mg, 0.5 mmol) in dry tetrahydrofuran (5 ml) was added to a stirred suspension of benzeneseleninic anhydride (180 mg, 0.5 mmol) in tetrahydrofuran (5 ml) maintained at 50 °C. After 30 min, the cooled orange reaction mixture

was worked up to give 1,2-naphthoquinone as orange crystals (72 mg, 90%), m.p. 143—145 °C.

Preparation of Benzeneseleninyl Selenenate.—A solution of benzeneselenenyl chloride (85 mg, 0.5 mmol) in dry tetrahydrofuran (5 ml) was added to a stirred suspension of lithium benzeneseleninate (107 mg, 0.5 mmol) in tetrahydrofuran (3 ml) with careful exclusion of moisture. The initial orange colour disappeared rapidly to give a pale yellow solution. Attempts to crystallize the benzeneseleninyl selenenate directly from the reaction mixture failed. Attempted isolation by chromatography gave diphenyl diselenide (94 mg, 60%) and benzeneseleninic acid (19 mg, 20%) as the only characterisable products.

Subsequent experiments with the reagent were therefore carried out using the yellow solution without further purification.

Reaction of 2-Naphthol with Benzeneseleninyl Seleninate.—A solution of 2-naphthol (72 mg, 0.5 mmol) in tetrahydrofuran (5 ml) was added to a solution of the reagent (0.5 mmol prepared as above) in tetrahydrofuran (8 ml). After 2 h at room temperature work-up gave 1-phenylseleno-2-naphthol (10) (93 mg, 62%), m.p. 75—77 °C.

Reaction of 2-Naphthol with Benzeneseleninyl Seleninate for Longer Reaction Times.—2-Naphthol (155 mg, 1 mmol) in tetrahydrofuran was added to a solution of benzeneseleninyl selenenate [from sodium benzeneseleninate (213 mg, 1 mmol) and benzeneselenyl chloride (191 mg, 1 mmol) in tetrahydrofuran (5 ml)]. The mixture was stirred at room temperature for 48 h and after chromatography gave (i) *1-phenylseleno-2-naphthol* (10) (130 mg, 43%), m.p. 77 °C, (ii) *1-chloro-2-hydroxynaphthalene* (36 mg, 20%), m.p. 70 °C (from aqueous MeOH), (lit.,[8] 70 °C) and (iii) *3-phenylseleno-1,2-naphthoquinone* (12) as black platelets from ether (102 mg, 23%), m.p. 172 °C (decomp.), $\nu_{max.}$ 1 660—1 680 cm^{-1}; $\lambda_{max.}$ 272 (ε 23 500), 325 (15 200), and 344 nm (16 300); τ 3.25 (1 H, s) and 3.05—1.95 (9 H, m); M^+ 314 (Found: C, 61.35; H, 3.4. $C_{16}H_{10}O_2Se$ requires C, 61.35; H, 3.2%).

Oxidation of 3,5-Di-t-butylpyrocatechol.—A solution of 3,5-di-t-butylpyrocatechol (111 mg, 0.5 mmol) in tetrahydrofuran (5 ml) with benzeneseleninic anhydride (180 mg, 0.5 mmol) at room temperature for 15 min, gave 3,5-di-t-butylbenzoquinone (96 mg. 88%), m.p. 109—112 °C (lit.,[9] 114 °C).

Oxidation of 2,6-Dimethylhydroquinone.—Benzeneseleninic anhydride (180 mg, 0.5 mmol) was added to a solution of 2,6-dimethylhydroquinone (69 mg, 0.5 mmol) in tetrahydrofuran at room temperature. Further oxidant (*ca.* 0.2 mmol) was added until t.l.c. showed no starting material present. The reaction mixture was filtered and after p.l.c. gave 2,6-dimethylbenzoquinone (60 mg, 88%), m.p. 71—73 °C (lit.,[10] 72—73 °C).

Oxidation of 1,4-Dihydroxynaphthalene.—Benzeneseleninic anhydride (180 mg, 0.5 mmol) was added to a solution of 1,4-dihydroxynaphthalene (80 mg, 0.5 mmol) in tetrahydrofuran (5 ml) at room temperature. Work-up in the usual way gave 1,4-naphthoquinone (73 mg, 92%), m.p. 123—124 °C (lit.,[11] 125 °C).

Oxidation of Hydroquinone.—Benzeneseleninic anhydride (180 mg, 0.5 mmol) was added to hydroquinone (55 mg, 0.5 mmol) in tetrahydrofuran (5 ml) at room temperature. Filtration and p.l.c. then gave benzoquinone (45 mg, 84%), m.p. 114—116 °C (lit.,[12] 115—117 °C).

We thank the S.R.C. for a Research Studentship (to A. G. B.) and the Wellcome Foundation for a Fellowship (to M.N.R.).

[0/1572 *Received*, 14*th October*, 1980]

REFERENCES

[1] (*a*) 'The Chemistry of the Quinoid Compounds,' ed. S. Patai, J. Wiley and Sons, London, 1974; (*b*) 'Houben-Weyl Methoden der Organischen Chemie; Chinone II,' Verlag, Berlin, 1979.

[2] D. H. R. Barton, S. V. Ley, P. D. Magnus, and M. N. Rosenfeld, *J. Chem. Soc., Perkin Trans. 1*, 1977, 567.

[3] For a preliminary account of this work see D. H. R. Barton, A. G. Brewster, S. V. Ley, and M. N. Rosenfeld, *J. Chem. Soc., Chem. Commun.*, 1976, 985.

[4] J. Heiss, K.-P. Zeller, and A. Rieker, *Org. Mass. Spectrom.*, 1969, **2**, 1325.

[5] K. B. Sukumaran and R. G. Harvey, *J. Am. Chem. Soc.*, 1979, **101**, 1353; *J. Org. Chem.*, 1980, **45**, 4407.

[6] D. H. R. Barton, S. V. Ley, and R. A. H. F. Hui, unpublished observations.

[7] (*a*) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434; (*b*) D. H. R. Barton, D. J. Lester, and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2209.

[8] L. F. Fieser, *Org. Synth.*, 1937, **XVII**, 68.

[9] A. Rieker, W. Rundel, and H. Kessler, *Z. Naturforsch.*, 1969, **24b**, 547.

[10] W. T. Sumerford and D. N. Dalton, *J. Am. Chem. Soc.*, 1944, **66**, 1330.

[11] E. A. Braude and J. S. Fawcett, *Org. Synth.*, 1953, **33**, 50.

[12] H. W. Underwood, jun., and W. L. Walsh, *Org. Synth.*, 1936, **XVI**, 73.