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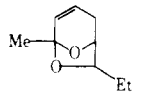


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# Syntheses of Some Furans and Naphtho[2,3-*c*] Derivatives of Furan, Pyrrole, and Thiophene


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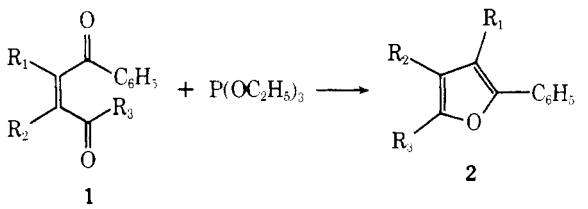
Treatment of aryl-substituted 2-butene-1,4-diones with triethyl phosphite caused ring closure reactions to furan derivatives. Simple routes to the preparation of 1,3-diphenylnaphtho[2,3-*c*]furan, 1,3-diphenyl-2-methylnaphtho[2,3-*c*]pyrrole, and 1,3-diphenylnaphtho[2,3-*c*]thiophene are described.

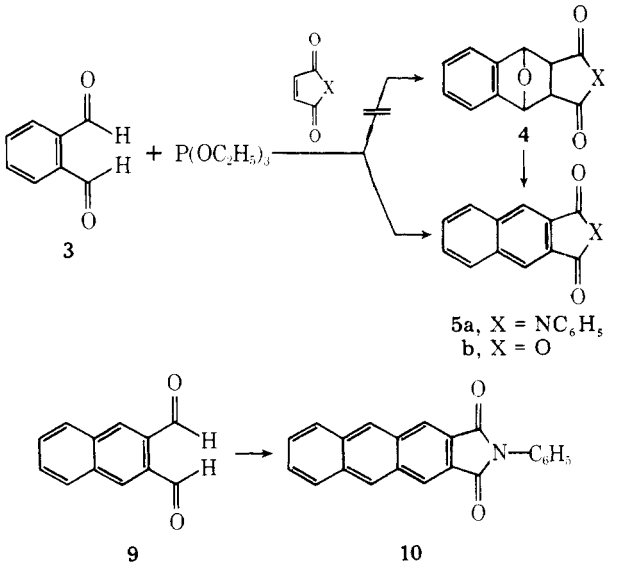

The reaction of aromatic aldehydes with hexaalkylphosphorus triamides to give aryl-substituted oxiranes has been reported by Mark.[1,2] Ramirez and co-workers[3] showed that the reaction of trimethyl phosphite with *trans*-1,2-dibenzoylethylene afforded 2,5-diphenylfuran. We planned to test the generality of the reaction of trialkyl phosphites with precursors that possess a 2-ene-1,4-dione functional group as a route to furans and isobenzofurans.[4]

It was found that the heating of a triglyme solution of 2-butene-1,4-diones **1a–e** with triethyl phosphite resulted in the formation of furans **2a–e**. These results encouraged us to examine the reaction of triethyl phosphite with aromatic *o*-diketones and *o*-dialdehydes. Treatment of o-dibenzoylbenzene, under various conditions, failed to produce any isolable quantity of 1,3-diphenylisobenzofuran although the latter was detected in traces by TLC. It was expected that the replacement of *o*-dibenzoylbenzene by *o*-phthalaldehyde (**3**) would improve the yield of the reaction and lead to the generation




**1** **2**

**a**, $R_1 = R_3 = C_6H_5$; $R_2 = H$
**b**, $R_1 = R_2 = R_3 = C_6H_5$
**c**, $R_1 = C_6H_5$; $R_2 = H$; $R_3 = p\text{-}CH_3C_6H_4$
**d**, $R_1 = C_6H_5$; $R_2 = H$; $R_3 = p\text{-}CH_3OC_6H_4$
**e**, $R_1 = C_6H_5$; $R_2 = H$; $R_3 = p\text{-}BrC_6H_4$




**9** **10**

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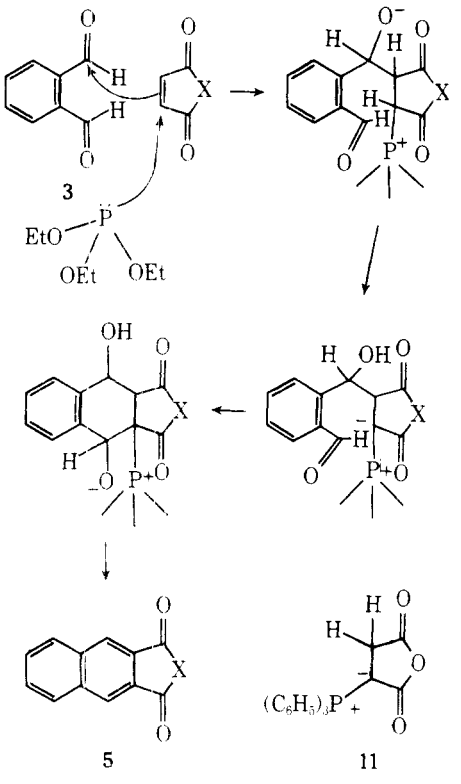
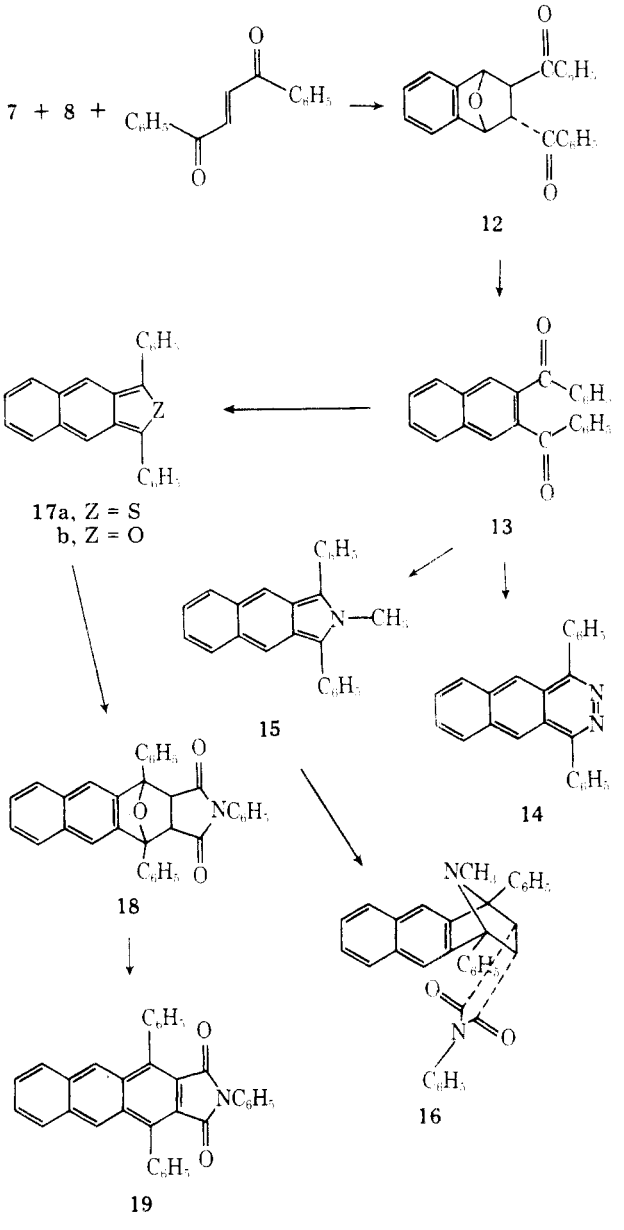
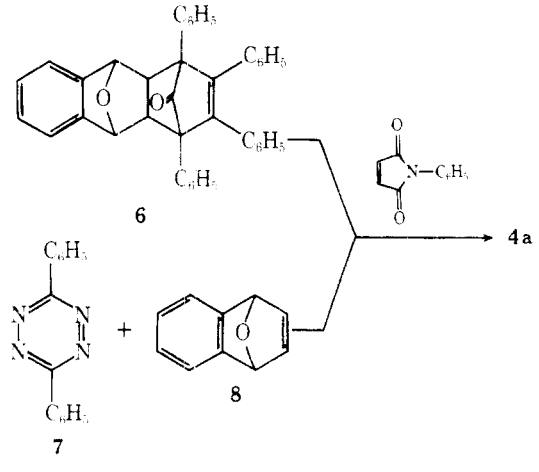
Scheme I



Scheme II



of isobenzofuran. The reaction of a benzene solution of **3** with triethyl phosphite, in the presence of *N*-phenylmaleimide as a trapping dienophile, proceeded smoothly to give naphthalene-2,3-phenylimide (**5a**) and not the expected adduct **4a**. The isolation of **5a** does not seem to support the assumption that the reaction of **3** and triethyl phosphite leads to the formation of isobenzofuran, which, in turn, would give adduct **4a**. However, the possibility that adduct **4a** was formed and subsequently dehydrated to imide **5a** cannot be excluded. In order to test this possibility, adduct **4a** was synthesized by two different methods.[5,6] The heating of a diglyme solution of **6**, a precursor to isobenzofuran,[5] with *N*-phenylmaleimide gave adduct **4a** in low yield, whereas the reaction of 3,6-diphenyl-1,2,4,5-tetrazine (**7**), 1,4-dihydronaphthalene 1,4-oxide (**8**),



and *N*-phenylmaleimide in warm $Me_2SO$ lead to the isolation of **4a** (80%) as a mixture of exo and endo adducts which were separated by preparative TLC. Adducts *exo*-**4a** and/or *endo*-**4a** were recovered unchanged after treatment with triethyl phosphite. Therefore, the postulate that isobenzofuran was an intermediate in the above reaction was dismissed, and a likely mechanism that explains the formation of **5a** is shown in Scheme I. It is known[7] that triphenyl phosphine reacts with maleic anhydride to give ylide **11**. Whether an ylide analogous to **11** is involved in the formation of **5a,b** is yet to be established. The conversion of **4a** to **5a** was eventually achieved, in quantitative yield, by the brief warming of an acetic acid–concentrated sulfuric acid solution of **4a**. Furthermore, triethyl phosphite effected the condensation of **3** and maleic anhydride into naphthalene-2,3-dicarboxylic anhydride (**5b**)[8] and naphthalene-2,3-dialdehyde (**9**) and *N*-phenylmaleimide into **10**.[9]

Of the three *o*-dicarbonyl aromatic compounds used in this study, *o*-dibenzoylbenzene, *o*-phthalaldehyde (**3**), and 2,3-dibenzoylnaphthalene (**13**), the latter is not commercially available. The literature method[10] for its preparation is rather lengthy. A simple synthesis of **13** and its conversion to some naphtho[2,3-*c*] heterocycles is described. We found that the trapping of isobenzofuran, generated according to Scheme II, with *trans*-1,2-dibenzoylethylene gave *trans*-2,3-dibenzoyl-1,4-dihydronaphthalene 1,4-oxide (**12**) in high yield. The structure of **12** was confirmed by infrared and NMR. All attempts to convert **12** into **13** under various acid conditions were unsatisfactory and the reaction was often accompanied by a succession of colors and the formation of gummy products. However, the treatment of **12** with alcoholic base resulted

in the formation of **13** in quantitative yield. Since the melting point of **13** (125–7 °C) differed from that reported in the literature[10] (143–5 °C), further characterization of **13** was carried out. Diketone **13** showed carbonyl bands at 1670 and 1645 $cm^{-1}$ and lacked the ether band of **12** at 1200 $cm^{-1}$. The NMR of **13** displayed a singlet at $\delta$ 8.1 (2 H) and a multiplet centered at $\delta$ 7.65 (14 H). Furthermore, treatment of **13** with hydrazine gave a quantitative yield of 3,6-diphenylnaphtho[2,3-*d*]pyridazine (**14**).

The reaction of **13** with methylamine followed by reduction with sodium borohydride resulted in the immediate precipitation of 1,3-diphenyl-2-methylnaphtho[2,3-*c*]pyrrole (**15**) as a bright orange solid the structure of which was assigned on the basis of its infrared and NMR spectra. Pyrrole **15** lost its color instantaneously on the addition of *N*-phenylmaleimide, at room temperature, and adduct **16** was isolated in high yield. Pyrrole **15** is more reactive as a diene than 1,3-diphenyl-2-methylpyrrolo[3,4-*b*]quinoline and 1,3-diphenyl-2-methylpyrrolo[3,4-*b*]quinoxaline.[11] The heating of a pyridine solution of **13** with phosphorus pentasulfide, under nitrogen, gave 1,3-diphenylnaphtho[2,3-*c*]thiophene (**17a**). An attempt to prepare 1,3-diphenylnaphtho[2,3-*c*]furan (**17b**) by the reaction of triethyl phosphite with **13** failed. Nevertheless, the reduction of **13** with sodium borohydride in methanol, at room temperature, gave a mixture of unreacted **13** and a hydroxy-containing compound(s). Treatment of this mixture with hot acetic acid resulted in the immediate precipitation of 1,3-diphenylnaphtho[2,3-*c*]furan (**17b**) as deep reddish-brown glistening plates. As expected, furan **17b** reacted with *N*-phenylmaleimide immediately at room temperature to give adduct **18** which was converted to imide **19** on treatment with acid. Both thiophene **17a** and furan **17b** were prepared by Cava and VanMeter[10] through an elegant multistep synthesis. We believe that the present syntheses are simpler.

## Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 or 621 spectrophotometer using potassium bromide disks. $H^1$ NMR spectra were taken on a Varian T60 instrument in $CDCl_3$ with $Me_4Si$ as internal reference. TLC was carried out on freshly prepared Merck $GF_{254}$ type (60) silica gel plates. Elemental analysis was run by E. Pascher, Bonn, Germany.

**Starting Materials.** 1,2,4-Triphenyl-2-butene-1,4-dione (**1a**),[12] 1,2,3,4-tetraphenyl-2-butene-1,4-dione (**1b**),[13] 1,2-diphenyl-4(*p*-methylphenyl)-2-butene-1,4-dione (**1c**),[12] 1,2-diphenyl-4(*p*-methoxyphenyl)-2-butene-1,4-dione (**1d**),[12] 1,2-diphenyl-4(*p*-bromophenyl)-2-butene-1,4-dione (**1e**),[12] naphthalene-2,3-dialdehyde (**9**),[14] 3,6-diphenyl-1,2,4,5-tetrazine (**7**),[15] and 1,4-dihydronaphthalene 1,4-oxide (**8**)[5] were prepared according to known procedures.

**General Procedure for the Preparation of Furans 2a–e.** A solution of the specific 2-butene-1,4-dione (0.01 mol) and triethylphosphite (2 mL, 0.011 mol) in triethylene glycol dimethyl ether (triglyme, 25 mL) was heated for 2–3 h at reflux temperature. Water was added to the cold solution and thereafter decanted to leave an oily residue which solidified on rubbing with methanol–water. The solid was collected and recrystallized from the proper solvent.

**2,3,5-Triphenylfuran (2a):** mp 91–93 °C (methanol) (lit.[16] mp 93–94 °C); 66% yield; IR 3020, 1590, 1480, 1450, 1435, 1140, 1070, 1050, 1020, 950, 930, 800, 760, 740, 720, 690 $cm^{-1}$.

**2,3,4,5-Tetraphenylfuran (2b):** mp 169–171 °C (acetic acid) (lit.[17] mp 172–4 °C); 42% yield; IR 3040, 1595, 1485, 1440, 1150, 1107, 1070, 1055, 1028, 950, 920, 800, 764, 750, 700, 688 $cm^{-1}$.

**2,3-Diphenyl-5-(*p*-methylphenyl)furan (2c):** mp 103–5 °C (methanol); 80% yield; IR 3020, 1590, 1490, 1435, 1140, 1070, 1020, 945, 925, 900, 820, 800, 750, 680 $cm^{-1}$.

**2,3-Diphenyl-5-(*p*-methoxyphenyl)furan (2d):** mp 94–96 °C (methanol) (lit.[18] mp 94–95 °C); 70% yield; IR 3030, 1600, 1570, 1500, 1440, 1300, 1250, 1180, 1140, 1110, 1050, 1020, 950, 930, 910, 830, 800, 760, 690 $cm^{-1}$.

**2,3-Diphenyl-5-(*p*-bromophenyl)furan (2e):** mp 107–8 °C (methanol); 85% yield; IR 1475, 1170, 1150, 1070, 1045, 1020, 1000, 945, 925, 910, 800, 750, 690 $cm^{-1}$.

**Naphthalene-2,3-phenylimide (5a).** A mixture of *N*-phenylmaleimide (8.65 g, 0.05 mol), acid-free *o*-phthaldehyde (6.7 g, 0.5 mol), and triethyl phosphite (10 mL, 0.05 mL) was dissolved in benzene (90 mL) and heated at reflux temperature for 15 min during which **5a** precipitated. Recrystallization of **5a** from $CHCl_3$–methanol gave plates that melted at 279–280 °C (lit.[8] mp 277–8 °C); 8.5 g (62% yield); IR 1775, 1720, 1710 $cm^{-1}$.

**Naphthalene-2,3-dicarboxylic Anhydride (5b).** Anhydride **5b** was prepared by the same procedure used for **5a** with the reaction heating time of 1.5 h. **5b** was recrystallized from acetic acid: mp 240–2 °C (lit.[8] mp 246 °C); 10% yield; IR 1830, 1772 $cm^{-1}$.

Imide **5a** and hydride **5b** were separately hydrolyzed into naphthalene 2,3-dicarboxylic acid by heating either compound in aqueous hydrochloric acid at reflux temperature for 2 days. The diacid melted at 237–40 °C (lit.[8] mp 237–40 °C); however, upon recrystallization from acetic acid the melting point rose to 260–2 °C dec (IR 3300–2500, 1710–1600 $cm^{-1}$).

***N*-Phenyl-2,3-anthracenedicarboximide (10).** A mixture of freshly prepared naphthalene-2,3-dialdehyde (100 mg, 5.4 mmol), *N*-phenylmaleimide (93 mg, 5.4 mmol), and triethyl phosphite (0.5 mL) in benzene (10 mL) was heated for 15 min. Upon cooling the reaction mixture, the product precipitated as a yellow solid which was recrystallized from $CHCl_3$–ethanol and obtained as yellow plates a benzene solution of which exhibited an intense blue fluorescence: 52 mg (35%); mp 368–70 °C (lit.[9] mp 355–8 °C); IR 1770 (sh), 1700, 1580, 1440, 1420, 1370, 1130, 1110, 910, 740, 730, 690 $cm^{-1}$.

**1,2,3,4-Tetrahydronaphthalene-1,4-oxido-2,3-phenylimide (4a).** A mixture of 3,6-diphenyl-1,2,4,5-tetrazine (2.34 g, 0.01 mol), *N*-phenylmaleimide (1.73 g, 0.01 mol), and 1,4-dihydronaphthalene 1,4-oxide (1.44 g, 0.01 mol) in $Me_2SO$ (30 mL) was heated gently on a steam bath until the tetrazine red color disappeared. The reaction mixture was allowed to cool to room temperature during which 3,6-diphenylpyridazine crystallized out and was collected. Water was added to the mother liquor and a creamy solid precipitated (1.15 g, 80%). The mixture was separated into *exo*- and *endo*-**4a** by preparative TLC.

*exo*-**4a:** mp 203–5 °C; IR 3480 (w), 3040–2850, 1770 (sh), 1700, 1600, 1500, 1390, 1300, 1190, 980, 940, 880, 850, 790, 760, 730, 710, 690 $cm^{-1}$.

*endo*-**4a:** mp 223–5 °C; IR 3470 (w), 3050–2850, 1770 (sh), 1700, 1600, 1500, 1460, 1390, 1285, 1190, 1050, 980, 940, 910, 870, 860, 790, 760, 750, 705, 690 $cm^{-1}$; $H^1$ NMR $\delta$ 7.3 (m, 7 H), 6.5 (m, 2 H), 5.9 (m, 2 H), 3.98 (m, 2 H). Anal. Calcd for $C_{18}H_{13}NO_3$: C, 74.31; H, 4.5; N, 4.81. Found: C, 74.03; H, 4.52; N, 4.78.

**4a** (100 mg, 0.34 mmol) was dissolved in warm acetic acid (3 mL). Concentrated sulfuric acid (1 mL) was added and the solution was heated on the steam bath for a few minutes during which **5a** precipitated in quantitative yield (93 mg).

***trans*-2,3-Dibenzoyl-1,2,3,4-tetrahydronaphthalene 1,4-Oxide (12).** A mixture of 3,6-diphenyl-1,2,4,5-tetrazine (**7**, 2.34 g, 0.01 mol), *trans*-dibenzoylethylene (2.36 g, 0.01 mol), and 1,4-dihydronaphthalene 1,4-oxide (**8**, 1.44 g, 0.01 mol) in $Me_2SO$ (30 mL) was gently heated on a steam bath until the tetrazine red color disappeared. 3,6-Diphenylpyridazine precipitated out of the cold solution and was collected. Water was added to the mother liquor and the resulting white solid was recrystallized from $CHCl_3$–methanol to afford white needles of **12:** 3.36 g (94%); mp 165–6 °C; IR 3050, 3000, 1670, 1590, 1575, 1445, 1330, 1295, 1280, 1265, 1215, 1200, 1020, 980, 950, 908, 850, 780, 760, 710, 690 $cm^{-1}$; $H^1$ NMR $\delta$ 4.3 (d, 1 H), 4.9 (t, 1 H), 5.6 (d, 2 H), 5.7 (m, 10 H), 8.14 (m, 4 H). Anal. Calcd for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12. Found: C, 81.20; H, 5.05.

**2,3-Dibenzoylnaphthalene (13).** A solution of **12** (0.2 g, 0.6 mmol) in 10% methanolic potassium hydroxide (25 mL) was heated at reflux temperature for 0.5 h. The product precipitated out upon cooling of the reaction mixture. Recrystallization from methanol gave white needles of **13**: 0.9 g (100%); mp 125–7 °C (lit.[10] mp 143–5 °C); IR 3060, 1670, 1645, 1590, 1450, 1440, 1300, 1280, 1260, 950, 890, 860, 795, 750, 720, 690 $cm^{-1}$; $H^1$ NMR $\delta$ 7.68 (m, 14 H), 8.09 (s, 2 H). Anal. Calcd for $C_{24}H_{16}O_2$: C, 85.69; H, 4.79. Found: C, 85.78; H, 4.94.

**1,4-Diphenylnaphtho[2,3-*d*]pyridazine (14).** A hot methanolic solution of **13** (0.2 g, 0.6 mmol) was treated with excess hydrazine hydrate and the solution was heated on a steam bath for a few minutes. Upon cooling, a bright yellow solid, which precipitated out, was recrystallized from methanol: 0.18 g (90%) of yellow needles; mp 232–3 °C; IR 3050, 1460, 1440, 1420, 1370, 1340, 1270, 1175, 1020, 890, 760, 745, 695 $cm^{-1}$. Anal. Calcd for $C_{24}H_{16}N_2$: C, 86.72; H, 4.85; N, 8.43. Found: C, 85.65; H, 4.83; N, 8.39.

**1,3-Diphenyl-2-methylnaphtho[2,3-*c*]pyrrole (15) and Adduct 16.** To a hot methanolic solution of 2,3-dibenzoylnaphthalene (**13**, 0.2 g, 0.6 mmol) excess methylamine (40%) was added and the solution was heated on a steam bath for 5 min. Upon the addition of sodium borohydride (0.1 g) to the cold solution, a bright orange solid immediately crystallized out of solution. The product was collected and

washed with water. Recrystallization from methanol was accompanied with considerable loss of product and no improvement of the melting point: 0.18 g (90%); mp 167–70 °C; IR 3020, 2920, 1585, 1500, 1470, 1438, 1420, 1270, 1230, 1160, 1120, 1070, 850, 750, 740, 730, 690 $cm^{-1}$; $H^1$ NMR $\delta$ 4.17 (s, 3 H), 7.62 (m, 14 H), 8.35 (s, 2 H). Anal. Calcd for $C_{25}H_{19}N$: C, 90.05; H, 5.74; N, 4.20. Found: C, 89.21, H, 5.79; N, 4.20.

Pyrrole **15** (100 mg, 0.3 mmol) in benzene reacted immediately with *N*-phenylmaleimide (52 mg, 0.3 mmol) at room temperature. Evaporation of benzene and recrystallization of the product from methanol gave white needles of adduct **16**: 100 mg (76%); mp 203–5 °C; IR 3050, 3020, 2960, 1760 (sh), 1700, 1490, 1440, 1380, 1325, 1190, 1160, 1150, 985, 860, 750, 710, 690, 680 $cm^{-1}$.

**1,3-Diphenylnaphtho[2,3-*c*]thiophene (17a).** A mixture of **13** (0.2 g, 0.6 mmol) and phosphorus pentasulfide (0.26 g, 1.2 mmol) in pyridine (7 mL) was heated under nitrogen for 15 min. The cold reaction mixture furnished thiophene **17a** as deep red needles: 0.19 g (95%); mp 194–5 °C (lit.[10] mp 198–202 °C); IR 3040, 1590, 1500, 1445, 1120, 1030, 870, 765, 750, 740, 690 $cm^{-1}$. As reported,[10] thiophene **17a** did not add *N*-phenylmaleimide easily even on heating.

**1,3-Diphenylnaphtho[2,3-*c*]furan (17b) and Adduct 18.** A methanolic solution of **13** (1 g, 3 mmol in 15 mL) was heated to boiling on a steam bath. Sodium borohydride (0.1 g, 30 mmol) was added to the hot solution, and the reaction mixture was allowed to stand at room temperature for 20 min. Water was added and the resulting solid was collected and dried. TLC showed the presence of unreacted **13** in the mixture; nevertheless, the mixture (0.3 g) was treated with hot acetic acid and furan **17b** crystallized out as deep reddish-brown glistening plates. The product was collected and washed with acetic acid: 0.15 g (50% based on complete reduction of one carbonyl group); mp 140–3 °C (lit.[10] mp 148–51 °C); IR 1595, 1470, 1190, 910, 855, 770, 740, 690 $cm^{-1}$.

As reported by Cava and VanMeter,[10] furan **17b** is unstable in organic solvents and added *N*-phenylmaleimide instantaneously at room temperature to give adduct **18** (85%): mp 284–6 °C (lit.[10] mp 287–90 °C); IR 3060, 3000, 1775 (sh), 1700, 1600, 1500, 1450, 1380, 1345, 1315, 1285, 1200, 1055, 1000, 960, 920, 890, 790, 770, 750, 730, 713, 650 $cm^{-1}$. Adduct **18** (100 mg, 0.2 mmol) was dissolved in acetic acid–concentrated sulfuric acid (3:1 mL) and heated on a steam bath. The yellow imide **19** precipitated out in quantitative yield (95 mg): mp 378–80 °C; IR 1750, 1700, 1430, 1360, 1160, 1120, 885, 750, 685 $cm^{-1}$.

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**Registry No.**—**1a,** 5435-97-2; **1b,** 7510-34-1; **1c,** 33315-71-8; **1d,** 53476-29-2; **1e,** 53476-31-6; **2a,** 6307-20-6; **2b,** 1056-77-5; **2c,** 68630-10-4; **2d,** 68630-11-5; **2e,** 68630-12-6; **3,** 643-79-8; *exo*-**4a,** 68681-89-0; *endo*-**4a,** 68681-90-3; **5a,** 21815-18-9; **5b,** 716-39-2; **8,** 573-57-9; **9,** 7149-49-7; **10,** 68630-13-7; **12,** 68630-14-8; **13,** 18929-62-9; **14,** 36724-38-6; **15,** 68682-85-9; **16,** 68630-15-9; **17a,** 18929-58-3; **17b,** 18929-57-2; **18,** 18944-83-7; **19,** 68630-16-0; *N*-phenylmaleimide, 941-69-5; maleic anhydride, 108-31-6; *trans*-dibenzoylethylene, 959-28-4; hydrazine, 302-01-2; methylamine, 74-89-5.

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# Nickel Peroxide Dehydrogenation of Oxygen-, Sulfur-, and Nitrogen-Containing Heterocycles

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Twenty-seven partially reduced O-, S-, and N-containing heterocycles have been oxidized by the use of nickel peroxide. Of particular interest were the conversions of several oxazolines to the corresponding oxazoles, a conversion apparently without precedent in the chemical literature, and the efficient oxidation of thiazolines to thiazoles. Since $NiO_2$ can effect thiazoline dehydrogenations in the presence of other functionalities, as may be judged by the successful oxidation of phleomycin $A_2$ to bleomycin $A_2$, the oxidant should be of utility for the preparation of natural products containing thiazoles.

Although the potential of nickel peroxide as an oxidant in organic synthesis has been recognized for a number of years,[5] and a remarkable variety of transformations have been recorded,[6] there have been few reported examples of the use of this reagent for heterocyclic dehydrogenations.[7] We have recently utilized nickel peroxide for the oxidation of several $\Delta^2$-thiazolines to the corresponding thiazoles;[8] in most cases, especially those involving thiazoline moieties that were part of relatively complex molecules, this oxidant was clearly the reagent of choice. Since the oxidation of partially reduced heterocycles is a topic of continuing interest and investigation,[9] we have studied the potential utility of $NiO_2$ for other types of heterocyclic dehydrogenations. Of special concern in these studies was the oxidation of oxazolines to the corresponding 1,3-oxazoles, a conversion apparently without precedent in the chemical literature.

## Results and Discussion

A series of eight substituted 4,5-dihydro-1,3-oxazoles were prepared as described[10] and utilized in efforts to effect oxidation to the corresponding oxazoles. Although Barco et al.[9a] have recently described the dehydrogenation of several isox-

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