p-nitrobenzoate (92%) that had formed was filtered. Dropwise addition of H_2O (~10 mL) to the filtrate precipitated **32**: 83.6 mg (61%); mp 224.0–225.0 °C. Recrystallization from *t*-BuOH/H_2O (1:5) formed **32**: 54.8 mg (40%); mp 225–225.5 °C; ^1H NMR ($CDCl_3$) δ 8.27 (AA'BB',4 H), 7.17 (s, 1 H), 2.52 (s, 3 H), 2.47 (s, 3 H), 2.28 (s, 3 H), 1.62 (s, 1 H); IR (Nujol) 3300, 2225, 1670, 1540, 1520, 1370, 1350, 1320, 1295, 1110, 1008, 914, 878, 864, 858, 826, 735, 708 cm^{-1}. Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.86; N, 13.39. Found: C, 66.08; H, 4.85; N, 13.39.

2,4,6-Trimethyl-3-chloroaniline Hydrochloride (40). To a solution of 810 mg (3.0 mmol) of **6b** in 15 mL of dry C_6H_6 was added a solution of 390 mg (2.89 mmol) of $SOCl_2$ in 3 mL of dry C_6H_6. The reaction mixture was stirred for 10 h and the **40** filtered. The filtrate was evaporated, and 20 mL of Et_2O was added to the residue. The resulting suspension was stirred 0.5 h and the additional **40** filtered. The two portions of **40** were combined and washed with ether to give 377 mg (63%) of crystals, mp 195–209 °C. Treatment of the free base of **40** with benzenesulfonyl chloride gave the known benzenesulfonanilide of **40**; mp 161–164 °C (lit.[9] 163–164 °C).

(9) R. Adams and M. J. Gortatowski, *J. Am. Chem. Soc.*, **79**, 5525 (1957).

2,6-Dimethyl-3-chloroaniline Hydrochloride (39). A solution of 1.42 g (5.24 mmol) of $SOCl_2$ in 11 mL of dry C_6H_6 was added slowly to a solution of 3.27 g (0.28 mmol) of **6a** in 75 mL of dry C_6H_6. The reaction mixture was stirred for 5 h and filtered. The crude **39** was slurried with ether for 10 min and filtered to give 1.71 g (74%) of **39**, mp 202–211 °C dec. Treatment of **39** with acetyl chloride gave the known acetanilide, mp 142–143 °C (lit.[10] 146–147°), and treatment of **39** with *p*-nitrobenzoyl chloride gave **33a**.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Camille and Henry Dreyfus Foundation for support of this research. We thank Dr. William VandenHeuvel of Merck Sharp & Dohme Research Laboratories for obtaining the mass spectra of many of the new compounds described here. We also thank Professor D. H. R. Barton for a sample of 2,6-dimethyl-6-(*p*-nitrobenzoyloxy)-cyclohexa-2,4-dienone.

(10) H. E. Dodswell and J. Kenner, *J. Chem. Soc.*, 1102 (1927).

Synthesis of 2*H*-Isoindole-4,7-diones by 1,3-Dipolar Addition of Oxazolium 5-Oxides to 1,4-Quinones

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A general, convenient synthesis of 2*H*-isoindole-4,7-diones from readily available starting materials is described. 3-Methyl-2,4-diphenyloxazolium 5-oxide, formed by dehydrative cyclization of *N*-methyl-*N*-benzoyl-*C*-phenylglycine, combines with 1,4-quinones to produce 2*H*-isoindole-4,7-diones in moderate yields. Conversion of other *N*-acyl amino acids to the corresponding less stable oxazolium 5-oxides in solution using 1 equiv of acetic anhydride or dicyclohexylcarbodiimide and subsequent reaction with 1,4-quinones also affords 2*H*-isoindole-4,7-diones.

Two reports on the synthesis of selected 2*H*-isoindole-4,7-diones (**1**) by photolysis of 2,3-diphenyl-2*H*-azirine in the presence of 1,4-quinones[1] and by zinc-induced intramolecular cyclization of 1,2,5-trimethyl-3,4-bis(bromoacetyl)pyrrole followed by dehydrogenation[2] have appeared. We are prompted to report the development of a general, convenient method for preparing this heterocyclic quinone system from readily available starting materials, i.e., *N*-acyl amino acids and 1,4-quinones.

We have previously reported[3] the 1,3-dipolar addition of 3-methyl-2,4-diphenyloxazolium 5-oxide (**2a**) to cyclopentadienequinone and to anthracenequinone. Initially, 1:1 adducts were isolated. Decomposition of the adducts in refluxing benzene yielded 2-pyrroline derivatives **9** and **10**, respectively. Aqueous sodium hydroxide converted the primary adducts to pyrroles **7** and **8**.[3] We now describe facile cycloaddition reactions of **2a** and other less stable oxazolium 5-oxides (**2b** and **2c**), generated in solution by dehydrative cyclization from the *N*-acyl amino acid precursors **3**, with a variety of 1,4-quinones **4** to produce the desired 2*H*-isoindole-4,7-diones (**1**) in moderate yields.[4]

(1) P. Gilgen, B. Jackson, H.-J. Hansen, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **57**, 2634 (1974).
(2) E. Ghera, Y. Gaoni, and D. H. Perry, *J. Chem. Soc., Chem. Commun.*, 1034 (1974).
(3) J. A. Myers, W. W. Wilkerson, and S. L. Council, *J. Org. Chem.*, **40**, 2875 (1975).

Results and Discussion

1,3-Dipolar cycloaddition reactions of oxazolium 5-oxides have been intensely studied,[5-13] notably by Huisgen and colleagues.[5-7] The mesoionic compounds were prepared by cyclodehydration of *N*-acyl amino acids with reagents such as acetic anhydride or dicyclohexylcarbodiimide. Since the N-substituted 2,4-diaryloxazolium 5-oxides are the only examples stable enough for isolation, less stable

(4) Portions of this work were presented at the 2nd Xavier-MBS Biomedical Symposium in New Orleans, LA, Apr 1974, and at the 6th Annual Minority Biomedical Support Symposium in Atlanta, GA, Mar 1978.
(5) (a) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Schaefer, *Chem. Ber.*, **103**, 2611 (1970); (b) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Shaefer, *Agnew. Chem., Int. Ed. Engl.*, **3**, 136 (1964).
(6) (a) H. Gotthardt and R. Huisgen, *Chem. Ber.*, **103**, 2625 (1970); (b) H. Gotthardt, R. Huisgen, and F. C. Schaefer, *Tetrahedron Lett.*, 487 (1964).
(7) E. Brunn, E. Funke, H. Gotthardt, and R. Huisgen, *Chem. Ber.*, **104**, 1562 (1971).
(8) (a) K. T. Potts and U. P. Singh, *Chem. Commun.*, 66 (1969); (b) K. T. Potts and J. Baum, *J. Chem. Soc., Chem. Commun.*, 833 (1973).
(9) G. V. Boyd and P. H. Wright, *J. Chem. Soc., Perkin Trans. 1*, 909, 914 (1972).
(10) G. Manecke and J. Klawitter, *Makromol. Chem.*, **175**, 3383 (1974).
(11) L. M. Hershenson, *J. Org. Chem.*, **40**, 1260 (1975).
(12) (a) I. A. Benages and S. M. Albonico, *J. Org. Chem.*, **43**, 4273 (1978); (b) M. T. Pizzorno and S. M. Albonico, *ibid.*, **42**, 909 (1977).
(13) J. W. ApSimmon, D. G. Durham, and A. H. Rees, *Chem. Ind. (London)*, 275 (1973).

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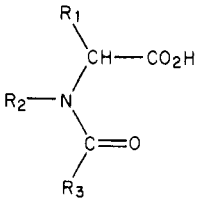

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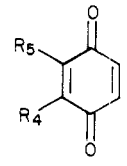

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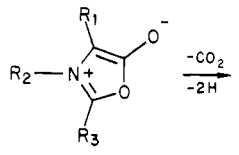
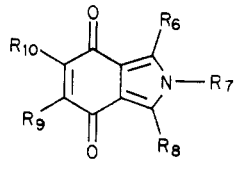


2

	R_4	R_5
4a	H	H
4b	-CH=CHCH=CH-	
4c	H	CH_3
4d	OCH_3	CH_3

	R_1	R_2	R_3
2a	Ph	CH_3	Ph
2b	Ph	CH_3	CH_3
2c	$-CH_2CH_2CH_2-$		Ph



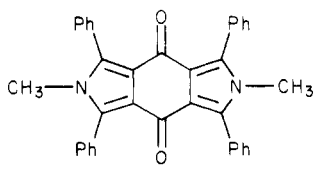
1

	R_6	R_7	R_8	R_9	R_{10}
1a	Ph	CH_3	Ph	H	CH_3
1b	Ph	CH_3	Ph	OCH_3	CH_3
1c	CH_3	CH_3	Ph	CH_3	H
1d	CH_3	CH_3	Ph	H	CH_3
1e	CH_3	CH_3	Ph	CH_3	OCH_3
1f	CH_3	CH_3	Ph	OCH_3	CH_3
1g	Ph	$-(CH_2)_3-$		CH_3	H
1h	Ph	$-(CH_2)_3-$		H	CH_3
1i	Ph	$-(CH_2)_3-$		CH_3	OCH_3
1j	Ph	$-(CH_2)_3-$		OCH_3	CH_3

oxazolium 5-oxides were generated in solution in the presence of suitable dipolarophiles.

Initial attempts to generate 3-methyl-2,4-diphenyloxazolium 5-oxide (**2a**) from the reaction of *N*-methyl-*N*-benzoyl-*C*-phenylglycine (**3a**)[14] with acetic anhydride in the presence of 1,4-benzoquinone (**4a**) gave 1,2,4-triacetoxybenzene. Presumably, acetic acid produced in the dehydration step acted as a catalyst for Thiele acetylation[15] of the quinone, destroying its dipolarophilic character. We proceeded to isolate **2a** by a method described by Huisgen.[14] Treatment of 1,4-benzoquinone (**4a**), 1,4-naphthoquinone (**4b**), 2-methyl-1,4-benzoquinone (**4c**), or 2-methyl-3-methoxy-1,4-benzoquinone (**4d**)[16] with **2a** at 20–55 °C in a nonpolar solvent for periods of 2–6 h gave the yellow to orange 2*H*-isoindole-4,7-diones **5**, **6a**, **1a**, and **1b**, respectively, in 29–45% yields (Table I, method A). Each of the isoindolequinones revealed a conjugated carbonyl absorption in the infrared spectrum at 1640–1660 cm^{-1} and an *N*-methyl singlet at δ 3.15–3.37 in the NMR spectrum.

One proposed sequence of steps for these reactions (Scheme I) shows the initial adduct a losing carbon dioxide in a retrocycloaddition reaction to give dipole b which rearranges to c. Oxidation of c would give the observed



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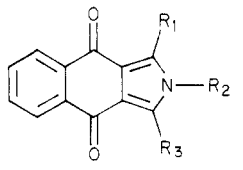
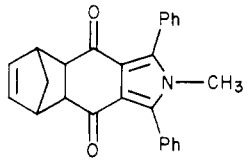


6

	R_1	R_2	R_3
6a	Ph	CH_3	Ph
6b	Ph	CH_3	CH_3
6c	$-CH_2CH_2CH_2-$		Ph

product d. Another possible route is rearrangement of the initial adduct a to hydroquinone structure e. Oxidation of e to quinone f could be followed by loss of carbon dioxide, again giving d. Regardless of the order of steps, loss of two hydrogens has occurred, giving the isoindolequinone structure. The chemical shifts of the *N*-methyl singlets in the NMR spectra at δ 3.15–3.37 for the products support this conclusion. The *N*-methyl chemical shifts at δ 3.29 and 3.13 observed for the pyrrole structures **7** and **8** are comparable and quite distinct from the chemical shifts at δ 2.47 and 2.41 for the N-methyl grouping in 2-pyrrolidine derivatives **9** and **10**.[3]



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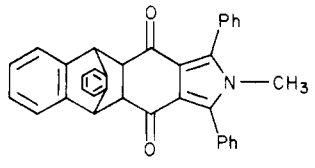

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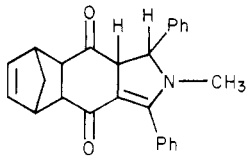

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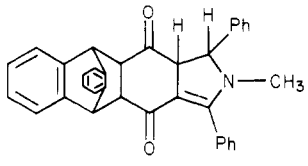


10

In further studies, generation of **2a** in solution and subsequent reaction with 1,4-quinones was accomplished in two ways. *N*-Methyl-*N*-benzoyl-*C*-phenylglycine (**3a**)[14] was warmed to 55–60 °C with an equimolar amount of acetic anhydride in a nonpolar solvent under nitrogen for 20–30 min, giving a bright yellow solution of the oxazolium 5-oxide **2a**. Sodium carbonate and sodium sulfate were added to neutralize the acetic acid produced and absorb any water formed. 1,4-Quinone **4** was then added at room temperature. Alternatively, an equimolar amount of dicyclohexylcarbodiimide was added to a suspension of **3a** in methylene chloride. The mixture was heated to reflux for 30–45 min, and then white solid *N*,*N*′-dicyclohexylurea was filtered from a yellow solution of **2a** and washed with small amounts of warm solvent. 1,4-Quinone **4** was added at room temperature. Dicyclohexylurea was removed in the latter reaction to facilitate the isolation of the product isoindolequinones.

Use of an equimolar amount of the cyclodehydration agent, acetic anhydride or dicyclohexylcarbodiimide, apparently decreases the probability of side reactions of these reagents with the 1,4-quinone. Either method gave yields of the isoindolequinones comparable with that observed with isolated **2a** as shown in Table I, methods B and C.

Two unstable oxazolium 5-oxides, **2b** and **2c**, were generated in solution from *N*-methyl-*N*-acetyl-*C*-phenylglycine (**3b**)[5a] and *N*-benzoylproline (**3c**),[17] respectively. Subse-

(14) H. O. Bayer, R. Huisgen, R. Knorr, and F. C. Schaefer, *Chem. Ber.*, **103**, 2581 (1970).

(15) (a) L. F. Fieser, *J. Am. Chem. Soc.*, **70**, 3165 (1948); (b) L. F. Fieser and M. I. Ardao, *ibid.*, **78**, 774 (1956).

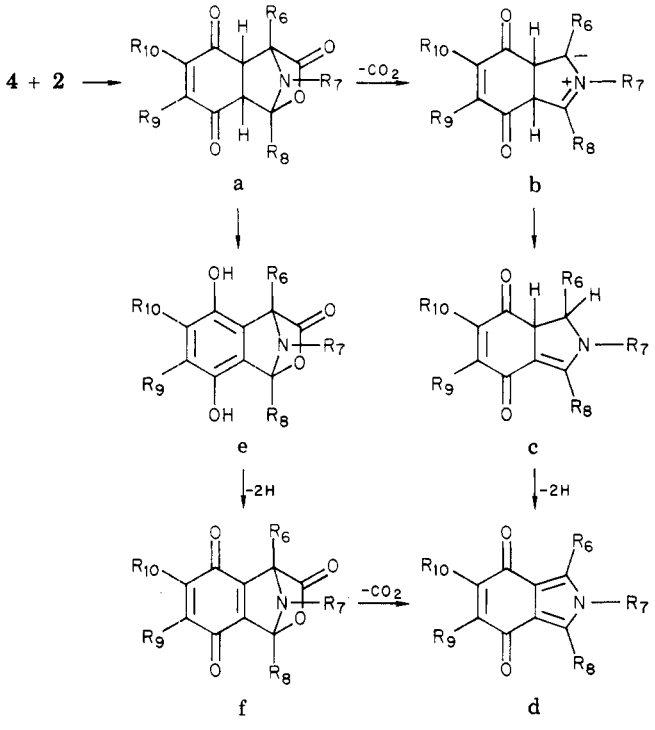
(16) L. Mandell and E. C. Roberts, *J. Heterocycl. Chem.*, **2**, 479 (1965).

(17) B. R. Barker, M. V. Querry, A. F. Kadish, and J. H. Williams, *J. Org. Chem.*, **17**, 52 (1952).

Table I. Isolated Yields (%) of Selected 2*H*-Isoindole-4,7-diones

quinone	product	method A	method B	method C
4a	5	29	6	14
4b	6a	44	30	35
4c	1a	29	37	26
4d	1b	36		

Scheme I



quent reaction of **2b** and **2c** with 1,4-naphthoquinone gave the 2*H*-benz[*f*]isoindole-4,9-diones **6b** and **6c**, respectively. Again, the presence of conjugated carbonyl absorptions at 1660 and 1645 cm^{-1} in the IR spectra and a singlet for the *N*-methyl hydrogens at δ 3.40 and a triplet for the *N*-methylene hydrogens at δ 4.04 in the respective NMR spectra are in agreement with the assigned isoindolequinone structures.

Reaction of 2,3-dimethyl-4-phenyloxazolium 5-oxide (**2b**), generated in solution, with 2-methyl-1,4-benzoquinone (**4c**) was nonregiospecific, giving a mixture of isomers, 1,2,5-trimethyl-3-phenyl-2*H*-isoindole-4,7-dione (**1c**) and 1,2,6-trimethyl-3-phenyl-2*H*-isoindole-4,7-dione (**1d**). An NMR spectrum of the mixture revealed separate doublets at δ 1.98 and 2.04 for the hydrogens in the quinone methyl groups, slightly overlapping quartets at δ 6.43 and 6.50 for the vinylic hydrogens, and two singlets at δ 2.62 and 2.64 for the pyrrole methyl hydrogens. One isomer was less soluble than the other in 2-propanol and could be conveniently separated from the other by repeated crystallizations. The less soluble isomer had the upfield methyl doublet and the downfield vinylic quartet.

In a similar manner, a mixture of isomers, 1,2,5-trimethyl-6-methoxy-3-phenyl-2*H*-isoindole-4,7-dione (**1e**) and 1,2,6-trimethyl-5-methoxy-3-phenyl-2*H*-isoindole-4,7-dione (**1f**), was isolated from the reaction of **2b** with 2-methyl-3-methoxy-1,4-benzoquinone (**4d**). In this case, the NMR spectrum revealed two singlets for the methoxy hydrogens and two singlets for the quinone methyl hydrogens.

Conversion of *N*-benzoylproline (**3c**) to 2-phenyl-3,4-trimethyleneoxazolium 5-oxide (**2c**) with acetic anhydride in toluene at 70–80 °C and subsequent additions of **4c** and of **4d** were accomplished, giving a mixture of two isomers in each case. Reaction of **2c** with **4c** afforded 5-methyl- and 6-methyl-1-phenyl-2,3-trimethylene-2*H*-isoindole-4,7-dione (**1g** and **1h**) as bright orange crystals in 28% yield. As in the case of **1c** and **1d** the presence of separate doublets for the quinone methyl hydrogens in the NMR spectra of **1g** and **1h** gave evidence of the two isomeric structures. Addition of **2c** to **4d** produced 5-methyl-6-methoxy- and 6-methyl-5-methoxy-1-phenyl-2,3-trimethylene-2*H*-isoindole-4,7-diones (**1i** and **1j**) as yellow crystals in 39% yield. Two singlets for the quinone methyl hydrogens and two singlets for the methoxy hydrogens were observed in the NMR spectrum of the product.

Finally, certain observations should be mentioned. The formation of tricyclic quinone **5** in the reaction of **2a** with 1,4-benzoquinone (**4a**) represents the first 2:1 adduct reported of an oxazolium 5-oxide with a dipolarophile,[18] although 1:2 adducts have been observed.[19] The fact that some 1,4-naphthohydroquinone was isolated from the reaction of **2a** with **4b** may be evidence that the 1,4-quinones can act as oxidizing agents in these syntheses and may explain the relatively low yields of isoindolequinones. In each synthesis, dark, colored residues which have not been characterized were obtained from the filtrates. The structure of tricyclic quinone **6** was verified by an independent synthesis.[20]

A preliminary collaborative investigation of the 5-methyl-2*H*-isoindole-4,7-diones as potential radiosensitizers for the radiotherapeutic treatment of cancerous tissues in mice will be presented elsewhere.[21]

Experimental Section

General Methods. Melting points were taken on a Laboratory Apparatus Mel-Temp and are uncorrected. Infrared spectra (IR) were determined as Nujol mulls on sodium chloride plates on a Beckman IR-10 or IR-18 spectrophotometer. Proton magnetic resonance spectra (^1H NMR) were determined on a Varian EM-360A NMR spectrometer relative to tetramethylsilane as internal standard. Certain ^1H NMR spectra were obtained from a Varian XL-100 instrument on samples submitted to the Center for NMR Spectroscopy at the University of North Carolina at Chapel Hill. Mass spectra were run by the Center for Mass Spectrometry at the Research Triangle Institute on an AEI MS-902 mass spectrometer. Elemental analyses were performed by Integral Microanalytical Laboratories. Cycloaddition reactions were performed under a stream of nitrogen gas.

2,6-Dimethyl-1,3,5,7-tetraphenyl-2*H*,6*H*-pyrrolo[3,4-*f*]-isoindole-4,8-dione (5). Method A. Five grams (0.020 mol) of 3-methyl-2,4-diphenyloxazolium 5-oxide (**2a**)[14] was added to a solution of 2.16 g (0.020 mol) of 1,4-benzoquinone (**4a**) dissolved in 50 mL of dry tetrahydrofuran under nitrogen. After the mixture was stirred for 10–15 min at room temperature, a yellow suspension was observed in the reaction vessel. The mixture was stirred an additional 2 h and filtered. Recrystallization from methylene chloride gave 1.5 g (29%) of yellow solid **5**: mp >350 °C; IR (Nujol) 1645 (C=O), 1090 (C—O), 755 (Ar) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.15 (s, 6, NCH_3), 7.40 (s, 20, ArH): mass spectrum, *m/e* (relative intensity) 518 (100), 517 (98), 259 (15), 258 (12). Anal.

(18) For a related 2:1 adduct of 3-phenylsydnone with 1,4-benzoquinone, see D. L. Hammick and D. J. Voaden, *Chem. Ind. (London)*, 739 (1956).

(19) See ref 6a where **2a** was added to *N*-phenylmaleimide.

(20) Addition of **2a** to dimethyl acetylenedicarboxylate[5a] followed by hydrolysis gave 1-methyl-2,5-diphenylpyrrole-3,4-dicarboxylic acid. Treatment of the diacid with thionyl chloride at reflux gave the corresponding anhydride. Friedel–Crafts acylation of benzene with the anhydride in the presence of aluminum chloride gave a small amount of **6a** in the neutral fraction.

(21) G. A. Infante, C. Camacho, E. Pagan, A. Santos, D. Cruz, R. Perez, and J. Correa (Catholic University of Puerto Rico) and J. A. Myers, L. D. Moore, and W. Whitter (NCCU), unpublished results.

Calcd for $C_{36}H_{26}N_2O_2$: C, 83.37; H, 5.05; N, 5.40. Found: C, 82.87; H, 4.83; N, 511.

Method B. To 5.38 g (0.020 mol) of *N*-methyl-*N*-benzoyl-*C*-phenyglycine (**3a**)[14] in 50 mL of benzene was added 2.0 mL (0.020 mol) of acetic anhydride. The mixture was warmed to 55–60 °C in a water bath for 30 min. To the resulting bright yellow solution was added 1 g each of sodium sulfate and sodium carbonate. After the mixture was stirred another 10 min, 2.16 g (0.020 mol) of **4a** was added, and stirring was continued for 2 h. Attempts to filter the dark brown mixture were not successful, and the mixture was evaporated to dryness. The residue was taken up in acetone and heated to boiling. Filtration gave 0.3 g (6%) of yellow solid, mp >350 °C. The IR and NMR spectra matched those of **5**. The reddish brown filtrate did not yield further evidence of **5**.

Method C. A suspension of 5.38 g (0.020 mol) of *N*-methyl-*N*-benzoyl-*C*-phenylglycine (**3a**)[14] and 4.12 g (0.020 mol) of *N*,*N*′-dicyclohexylcarbodiimide (DCC) in 50 mL of methylene chloride was heated to reflux for 30–40 min. A white solid, *N*,*N*′-dicyclohexylurea (DCU), was collected from a yellow solution. To the solution was added 2.16 g (0.020 mol) of **4a**, and stirring was continued for 3 h at room temperature. A yellow solid mixture with gray particles was collected by filtration. Recrystallization from methylene chloride gave 0.7 g (14%) of yellow solid, mp >350 °C. The IR and NMR spectra were identical with those of **5**.

2-Methyl-1,3-diphenyl-2*H*-benz[*f*]isoindole-4,9-dione (6a). Method A. Replacement of **4a** with 1,4-naphthoquinone (**4b**) in the reaction with **2a** described above resulted in a 44% yield of yellow crystals of **6a**: mp 286–290 °C; IR (Nujol) 1660 (C=O), 1055 (C—O), 755 (Ar) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.37 (s, 3, NCH_3), 7.5–7.8 (m, 12, ArH), 8.26 (m, 2, ArH); mass spectrum, *m/e* (relative intensity) 363 (100), 362 (68), 181.5 (8.5). Anal. Calcd for $C_{25}H_{17}NO_2$: C, 82.62; H, 4.72; N, 3.85. Found: C, 82.86; H, 4.56; N, 3.61.

Method B. A 30% yield of bright yellow crystals of **6a**, mp 284–285 °C, was isolated from the reaction of **4b** with **2a** generated in acetic anhydride solution from **3a** as described above.

Method C. Conversion of **3a** to **2a** by reaction with DCC as described above and subsequent addition of **4b** resulted in a 35% yield of **6a**, mp 279–283 °C.

2,5-Dimethyl-1,3-diphenyl-2*H*-isoindole-4,7-dione (1a). Method A. To a dark brown solution of 2.44 g (0.020 mol) of 2-methyl-1,4-benzoquinone (**4c**) in 15 mL of xylene was added with stirring 5.01 g (0.020 mol) of **2a** in portions. Vigorous gas evolution was observed, and the dark brown solution slowly became a yellow-brown suspension. Filtration could not be accomplished, so the mixture was evaporated to dryness under reduced pressure. A brown residue was triturated with 2-propanol, and an orange solid was collected in two crops. Recrystallization from 2-propanol yielded 1.88 g (29%) of orange crystals: mp 172-174 °C; IR (Nujol) 1640 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (d, J = 1.5 Hz, 3, quinone CH_3), 3.32 (s, 3, NCH_3), 6.51 (q, J = 1.5 Hz, 1, quinone H), 7.53 (s, 10, ArH); mass spectrum, *m/e* 327 (M^+). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.24; N, 4.27. Found: C, 80.44; H, 5.08; N, 4.14.

Method B. With 2.44 g (0.020 mol) of **4c** in place of **4a**, the procedure with acetic anhydride and **3a** was followed to afford 2.45 g (37%) of orange solid, mp 172–174 °C. The IR and NMR spectra were identical with those given above for **1a**.

Method C. With 2.44 g (0.020 mol) of **4c** in place of **4a**, the procedure with DCC and **3a** was followed, yielding 1.7 g (26%) of orange crystals, mp 160–168 °C. The IR and NMR spectra were identical with those of **1a**.

2,5-Dimethyl-1,3-diphenyl-6-methoxy-2*H*-isoindole-4,7-dione (1b). Reaction of **2a** with 2-methyl-3-methoxy-1,4-benzoquinone (**4d**)[16] afforded a 36% yield of yellow-orange solid **1b**: mp 180–182 °C; IR (Nujol) 1660 and 1640 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (s, 3, quinone CH_3), 3.29 (s, 3, NCH_3), 3.93 (s, 3, OCH_3), 7.53 (s, 10, ArH); mass spectrum, *m/e* 357 (M^+). Anal. Calcd for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 77.14; H, 5.05; N, 3.75.

1,2-Dimethyl-3-phenyl-2*H*-benz[*f*]isoindole-4,9-dione (6b). Conversion of *N*-methyl-*N*-acetyl-*C*-phenylglycine (**3b**)[5a] to the oxazolium 5-oxide **2b** in solution by reaction with DCC as described above for **3a** was followed by addition of quinone **4b**. A 10% yield of yellow crystals of **6b** was collected: mp 245–246 °C; IR (Nujol) 1655 and 1645 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.75 (s, 3, pyrrole CH_3), 3.43 (s, 3, NCH_3), 7.15–8.50 (m, 9, ArH). Anal. Calcd for $C_{20}H_{15}NO_2$: *m/e* 301.1102. Found: *m/e* 301.1105.

1-Phenyl-2,3-trimethylene-2*H*-benz[*f*]isoindole-4,9-dione (6c). *N*-Benzoylproline (**3c**;[17] 2.19 g, 0.010 mol) was heated in 3 mL (0.030 mol) of acetic anhydride until a clear, yellow-orange solution was obtained. Benzene (40 mL) was added to the solution followed by 0.5 g each of sodium carbonate and sodium sulfate. After the mixture was stirred for 10 min, 1.58 g (0.010 mol) of 1,4-naphthoquinone (**4b**) was added, and the mixture was refluxed for 2.5 h. Upon standing overnight, the mixture solidified. A mixture of brown solid and bright yellow crystals was separated by filtration. The solid material was taken up in hot benzene, and the mixture was filtered. Beige crystals began to separate from the filtrate first, and when yellow crystals appeared, the remaining solution was decanted. Yellow crystals were obtained from the decanted liquid and recrystallized from benzene to afford 1.25 g (40%) of **6c**: mp 226–228 °C dec; IR (Nujol) 1645 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.60 (p, 2, J = 7.2 Hz, CH_2), 3.27 (t, 2, J = 7.2 Hz, pyrrole CH_2), 4.04 (t, 2, J = 7.2 Hz, NCH_2), 7.35–7.80 (complex m, 7, ArH), 8.10–8.34 (m, 2, ArH); mass spectrum, *m/e* (relative intensity) 313 (100, M^+). Anal. Calcd for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.83; N, 4.47. Found: C, 80.43; H, 4.68; N, 4.22.

Mixture of 1,2,5-Trimethyl- and 1,2,6-Trimethyl-3-phenyl-2*H*-isoindole-4,7-diones (1c and 1d). Conversion of **3b** to oxazolium 5-oxide **2b** by reaction with acetic anhydride as described above and subsequent addition of **4c** resulted in a 33% yield of a bright yellow-gold solid mixture of **1c** and **1d**: mp 196–198 °C; IR (Nujol) 1645 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 and 2.04 (2 d, J = 1.8 Hz, 3, quinone CH_3), 2.62 and 2.63 (2 s, 3, pyrrole CH_3), 3.39 (s, 3, NCH_3), 6.43 and 6.50 (2 q, J = 1.8 Hz, 1, quinone H), 7.44 (br s, 5, ArH); mass spectrum, *m/e* (relative intensity) 265 (88, M^+), 264 (100, $M^+ - 1$). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.07; H, 5.61; N, 5.20.

Mixture of 5-Methoxy-1,2,6-trimethyl- and 6-Methoxy-1,2,5-trimethyl-3-phenyl-2*H*-isoindole-4,7-diones (1e and 1f). Reaction of **2b**, generated from **3b** and acetic anhydride as described, with **4d** afforded a 41% yield of yellow crystals of **1e** and **1f**: mp 170–171 °C; IR (Nujol) 1640 and 1620 (C=O) cm^{-1}; ^1H NMR NMR ($CDCl_3$) δ 1.92 and 2.00 (2 s, 3, 3, quinone CH_3), 2.64 (s, 3, pyrrole CH_3), 3.39 (s, 3, NCH_3), 3.95 and 4.01 (2 s, 3, OCH_3), 7.47 (br s, 5, ArH); mass spectrum, *m/e* (relative intensity) 295 (100, M^+), 280 (31, $M^+ - CH_3$). Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.21; H, 6.03; N, 4.62.

Mixture of 5-Methyl- and 6-Methyl-1-phenyl-2,3-trimethylene-2*H*-isoindole-4,7-diones (1g and 1h). Reaction of **4c** with the oxazolium 5-oxide generated from *N*-benzoylproline (**3c**) as described above gave a 28% yield of bright orange crystals of **1g** and **1h**: mp 178–179 °C: IR (Nujol) 1640 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03 and 2.05 (overlapping d, J = 1.5 Hz, 3, quinone CH_3), 2.52 (apparent p, J = 7 Hz, 2, $CH_2CH_2CH_2$), 3.13 (t, J = 7 Hz, 2, pyrrole CH_2), 3.98 (t, J = 7 Hz, 2, NCH_2), 6.49 and 6.52 (overlapping q, J = 1.5 Hz, 1, quinone H), 7.25–7.70 (complex m, 5, ArH); mass spectrum, *m/e* (relative intensity) 277 (100, M^+), 276 (55, $M^+ - 1$). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.04; H, 5.17; N, 4.81.

Mixture of 5-Methoxy-6-methyl- and 6-Methoxy-5-methyl-3-phenyl-1,2-trimethylene-2*H*-isoindole-4,7-diones (1i and 1j). To 4.16 g (0.020 mol) of **3c** in 50 mL of tetrahydrofuran was added 2.0 mL (0.020 mol) of acetic anhydride, and the mixture was refluxed for 30 min. A pale yellow-green solution resulted and was treated with 1 g each of sodium carbonate and sodium sulfate for 10 min at room temperature. Three grams (0.020 mol) of **4d** was added, and stirring was continued for 2 h at reflux. Following reflux the yellow-green mixture was filtered under reduced pressure, and the white precipitate was washed twice with 25-mL portions of methylene chloride. The filtrate and methylene chloride washings were combined and concentrated to an oil under reduced pressure. The oil was stirred with 100 mL of petroleum ether for 30 min, and then the petroleum ether was decanted. The residual oil was triturated with ethanol, giving 1.25 g of yellow crystals. The filtrate was concentrated to an oil, which was treated with a mixture of ethanol and water to afford 1.23 g of yellow-green crystals. Recrystallization of both crops together from absolute ethanol gave 2.39

g (39%) of yellow crystals: mp 202-204 °C; IR (Nujol) 1635 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 and 2.01 (2 t, J = 7.4 Hz, 2, pyrrole CH_2), 3.99 (t, J = 7.4 Hz, 2, NCH_2), 3.96 and 4.04 (2 s, 3, OCH_3), 7.35-7.75 (complex m, 5, ArH); mass spectrum, m/e (relative intensity) 307 (100, M^+), 292 (30, $M^+ - CH_3$). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.55. Found: C, 73.98; H, 5.49; N, 4.38.

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Registry No. **1a**, 72726-02-4; **1b**, 72749-06-5; **1c**, 72726-03-5; **1d**, 72726-04-6; **1e**, 72726-05-7; **1f**, 72726-06-8; **1g**, 72726-07-9; **1h**, 72726-08-0; **1i**, 72749-07-6; **1j**, 72726-09-1; **2a**, 13712-75-9; **2b**, 72726-10-4; **2c**, 72726-11-5; **3a**, 28544-45-8; **3b**, 2392-54-3; **3c**, 5874-58-8; **4a**, 106-51-4; **4b**, 130-15-4; **4c**, 553-97-9; **4d**, 2207-57-0; **5**, 65022-42-6; **6a**, 72726-12-6; **6b**, 72726-13-7; **6c**, 72726-14-8.

Addition of Selenium Tetrachloride to (*E*)- and (*Z*)-2-Butenes[1]

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The addition of $SeCl_4$ to (*Z*)-2-butene in methylene chloride at 25 °C forms bis((2*RS*,3*RS*)-3-chloro-2-butyl) and (2*R*,2′*S*,3*R*,3′*S*)-3-chloro-2-butyl 3′-chloro-2′-butyl selenide dichloride. Similarly, addition of $SeCl_4$ to (*E*)-2-butene yields a mixture of bis((2*SR*,3*RS*)-3-chloro-2-butyl) selenide dichloride and (2*S*,2′*R*,3*R*,3′*S*)-3-chloro-2-butyl 3′-chloro-2′-butyl selenide dichloride. Their relative configurations were assigned from their ^{13}C and ^1H magnetic resonance spectra. A mechanism involving a stepwise addition of two molecules of alkene to $SeCl_4$ is proposed. Both steps of the addition process involve stereospecific anti addition.

Selenium tetrachloride, $SeCl_4$, reacts with carbon-carbon double bonds in a facile manner.[2-5] For example, 2 mol of an alkene such as 2-butene reacts per mole of $SeCl_4$ to yield bis(3-chloro-2-butyl) selenide dichlorides (eq 1).

$$SeCl_4 + CH_3CH{=}CHCH_3 \rightarrow (CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH(CH_3))_2SeCl_2 \qquad (1)$$

Little is known about the mechanism or the stereochemistry of this reaction. In fact there are a number of abnormalities with respect to reaction conditions and yields in the earlier literature. This is probably due to the incomplete characterization of the selenium reagent.[6-12]

As part of a continuing study of the mechanism and stereochemistry of the additions of selenium reagents to alkenes and alkynes, we wish to report the stereochemistry of this addition reaction.

Results and Discussions

The addition of $SeCl_4$ to 2 equiv of 2-butene can form 10 stereoisomers: two meso isomers and four *dl* pairs. We have found that the reaction of $SeCl_4$ with 2 equiv of (*Z*)-2-butene at 25 °C in anhydrous methylene chloride gives only two products, **1** and **2**, in approximately 90 and 10% yields, respectively. Addition of $SeCl_4$ to (*E*)-2-butene under the same conditions gives two different products, **3** and **4**, in 90 and 10% yields, respectively. The product ratios are based upon integration of nonoverlapping resonances in the ^1H NMR spectra. Elemental analyses, obtained for each product mixture, are in agreement with the formation of bis(3-chloro-2-butyl) selenide dichlorides.

The identity and stereochemistry of these four adducts are assigned from their ^1H and ^{13}C NMR spectra. The NMR assignments are based upon the observation that, in general, the $SeCl_2R$ group deshields both carbons and protons relative to the effect of a chlorine atom. The exception is a nucleus situated geminal to the selenium, where one observes a shielding interaction. Assignments in Table I were aided by the observation of $^{77}Se^{13}C$ and $^{77}SeC^1H$ spin-spin coupling interactions.

The ^1H NMR spectra of adducts **1** and **2** show doublets of quartets with vicinal proton-proton coupling constants of 4.2 and 3.7 Hz, respectively. In contrast, the spectra of adducts **3** and **4**, derived from (*E*)-2-butene, show asymmetric "quintets" with $^3J_{H,H}$ couplings of 6.7 Hz each. The relative configurations were assigned by observing the variations of $^3J_{H,H}$ with solvent dielectric as shown in Table II.[13-15] For the bis-threo compounds $^3J_{H,H}$ should increase with increasing solvent dielectric, whereas for the bis-erythro species a decrease should be observed. Further, $^3J_{H,H}$(threo) is generally less than $^3J_{H,H}$(erythro).

Configurational assignments distinguishing between the *dl*-racemate and meso forms of the bis-threo and bis-erythro adducts were based on the ^{13}C NMR parameters of the methyl carbons geminal to the $SeCl_2R$ moiety and the known δ-syn-1,5 interaction with regard to ^{13}C NMR chemical shifts.[16,17]

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