Indolizines. 3. Oxidation Products of Indolizinols: Radicals, Ions, and Oxidized Dimers

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The oxidation products of 1- and 3-indolizinols have been investigated and characterized. A variety of stabilized indolizinols form stable, crystalline free radicals by one-electron oxidations. Both 7-H and 7-CH_3 substituted indolizinols, when subjected to exhaustive aerial or benzoquinone oxidation, form the oxidatively coupled 1,1'- or 3,3'-dioxo-7,7'-bisindolizines. Two-electron oxidation of indolizinols formed oxoindolizinium ions.

Introduction

In earlier papers[1,2] we described the reactions of diarylcyclopropenones 1 and pyridines that gave either 1- or 3-indolizinols, depending on reaction conditions and substituents (Scheme I). These products were generally isolated and characterized as salts or acetate esters. The free bases of the free alcohols, particularly the 3-isomers, were very prone to air oxidation, leading to deeply colored solutions that exhibited strong ESR signals. We now report studies of the oxidation products of these indolizinols.

Dehydrodimers

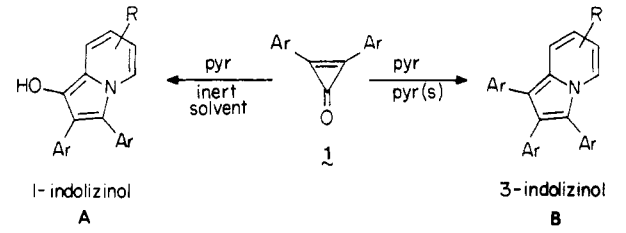
During the preparation of indolizinols unsubstituted at C-7, highly colored, insoluble byproducts were formed when reaction mixtures were exposed to air. The preparation of 1,2-diphenyl-3-indolizinol and 2,3-diphenyl-1-indolizinol, for example, gave a highly insoluble cyan dye (λ_{max} 690, ϵ_{max} 78 000) and a green dye (λ_{max} 790, ϵ_{max} 46 000), respectively, as byproducts. Both dyes showed a m/e of 566, corresponding to a dimer of the 4*H*-indolizinol.

The oxidative dimers of 3-indolizinols were prepared by aerating a solution of an appropriate diarylcyclopropenone in pyridine containing 2.5 mol % cupric acetate (Scheme II), or in lower yield by oxidizing the 3-indolizinol with iodine. The structure of the product from 1,2-diphenyl-3-indolizinol was shown by X-ray crystallography to be **2a** (Figure 1). The crystal structure of **2a** indicates considerable bond delocalization, with all C–N bonds approximately the same length, and the C=O bond longer (1.222 versus 1.189 Å)[3] than normal. The two indolizinone systems are twisted 2.3° from planarity, presumably to relieve 6H, 6'H interactions.

Oxidation of the 3-indolizinol derived from diphenylcyclopropenone and 4-picoline with air–$Cu(OAc)_2$ also led to a dimer-d_2 with spectral properties very similar to those of **2a**. Crystallography revealed that coupling had occurred through the 7-methyl groups, resulting in the ethanediylidenebisindolizine **3a** (Figure 2, Scheme III). The phenyl rings of both dimers are tipped at approximately 65° from the general plane of the molecule. Compound **3a**, with fewer steric interactions at the bridge, is more planar than **2a**, but very similar in all other bond lengths and angles.

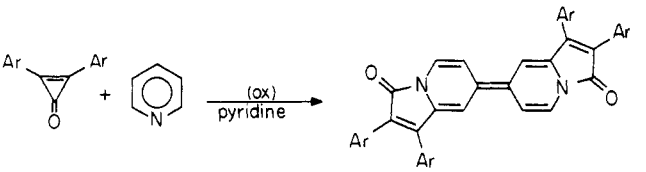
The preparation of 1,1'-oxodimeric dyes from 1 and either pyridine or 4-picoline in dioxane with only air as oxidant was not very successful, producing a mixture of yellow and green compounds (probably indolizinols and radicals) with only a trace of the dimers. With a chemical oxidant such as $Cu(OAc)_2$, benzoquinone, or chloranil, good yields of the 1,1'-dioxodimeric dyes were formed from either pyridine, 4-picoline, bipyridyl, or 1,2-dipyridylethylene and isolated from a nonsolvent such as petroleum ether or methanol (Schemes IV and V). The dyes were near-infrared absorbers (λ_{max} 780–810 nm, ϵ_{max} 45 000–74 000) (Table II). A greater variety of analogues of these 1,1'-dioxodimeric dyes could be realized because of the

Scheme I



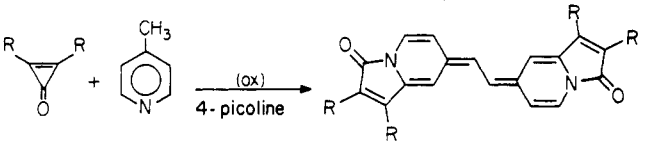
1-indolizinol A — 1 — 3-indolizinol B

Scheme II



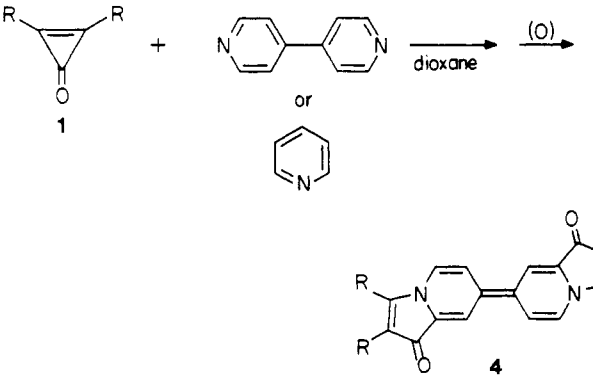
2 a. Ar = C_6H_5
b. Ar = 4-*t*-BuC_6H_4

Scheme III



3 a. R = Ph
b. R = 4-$CH_3OC_6H_4$

Scheme IV



(1) Wadsworth, D. H.; Bender, S. L.; Smith, D. L.; Luss, H. R. *Tetrahedron Lett.* **1981**, *22*, 3569.
(2) Wadsworth, D. H.; Bender, S. L.; Smith, D. L.; Luss, H. R.; Weidner, C. H. *J. Org. Chem.* **1986**, *51*, 4639.
(3) High, D. F.; Kraut, J. *Acta Crystallogr.* **1966**, *21*, 88.

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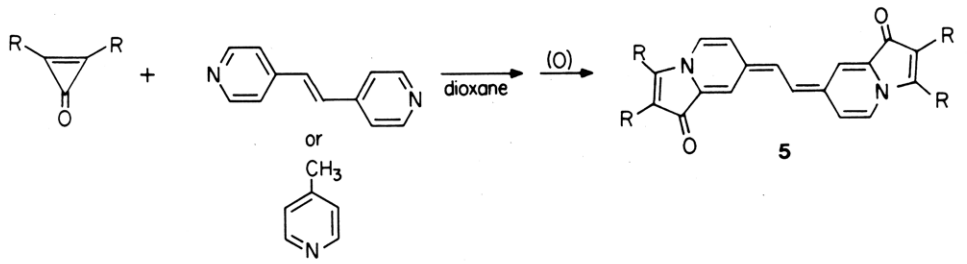
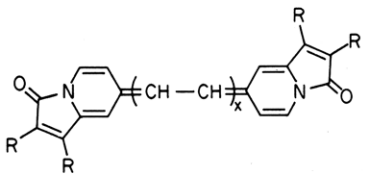
Scheme V



R = C_6H_5 (a); $CH_3OC_6H_4$ (b); 4-*t*-BuC_6H_4 (c); 2,4,6-$(CH_3)_3C_6H_2$ (d); *n*-C_3H_7 (e); $(CH_2)_5$ (f).

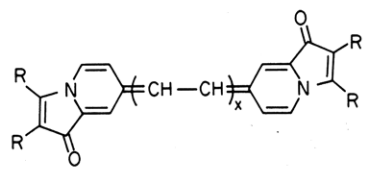
Table I. Preparation of 3,3′-Dioxo-$\Delta^{7,7'}$(3*H*,3′*H*)-bisindolizines



compd	method	R	*x*	yield, %	ϵ_{max}	λ_{max}, nm
2	B-1	C_6H_5	0	50	78 000[a]	695
2	B-2	C_6H_5	0	37		
2	B-3	C_6H_5	0	28		
2	B-1	4-tBuC_6H_4	0	32		
3b	C-1	4-$CH_3OC_6H_4$	1	1	72 000	
3a	C-1	C_6H_5	1	39	72 400	680
3a	C-2	C_6H_5	1	61		

[a] Value obtained from supersaturated solution. Difficult to repeat due to extreme insolubility of compound.

Table II. Preparation of 1,1′-Dioxo-$\Delta^{7,7'}$(3*H*,3′*H*)-bisindolizines



compd	method	R	*x*	mp, °C	yield, %	ϵ_{max}	λ_{max}, nm
4a	D-1	C_6H_5	0	>300	76	46 200	800
4a	D-2	C_6H_5	0		35		
4a	D-3	C_6H_5	0	>300	78		
4a	D-4	C_6H_5	0		71		
4c	D-3	tBuC_6H_4	0	>300	57	54 000	806
4d	D-1[a]	2,4,6-$(CH_3)_3C_6H_2$	0		41	51 400	785
4e	D-1[a]	*n*-C_3H_7	0	>270			
4b	D-1[a]	4-$CH_3OC_6H_4$	0		63	58 600	790
5a	E-1	C_6H_5	1	>300	57	68 200	783
5a	E-4	C_6H_5	1		85		
5c	E-5[b]	tBuC_6H_4	1	>300	78	70 000	790
5d	E-2[c]	2,4,6-$(CH_3)_3C_6H_2$–	1		53		
5d	E-3	2,4,6-$(CH_3)_3C_6H_2$	1		47	73 900	765

[a] Pyridine solvent. [b] Air only. [c] Mass spectral analysis showed only small amounts of impurities; however, microanalyses were poor, indicating probably solvent or water contaminants.

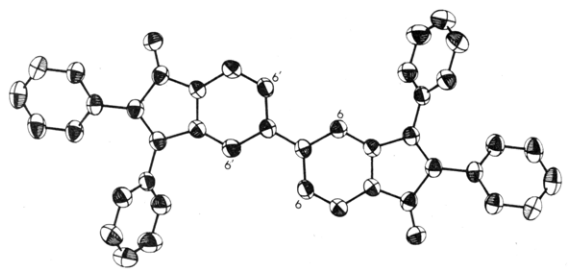


Figure 1.

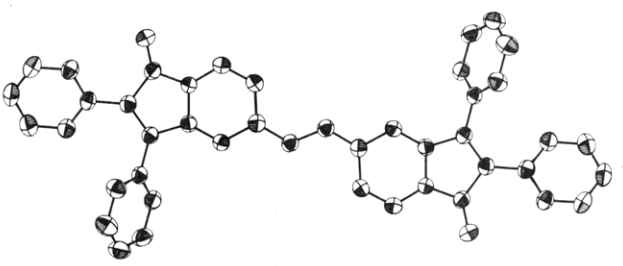


Figure 2.

greater ease of forming 1-indolizinols. The tetraphenyl (**4a**, **5a**), tetra-*p*-anisyl (**4b**, **5b**), tetra-*p*-*tert*-butylphenyl (**4c**, **5c**), and tetramesityl (**4d**, **5d**) analogues exhibited similar spectral properties but varying solubilities. The formation

Scheme VI

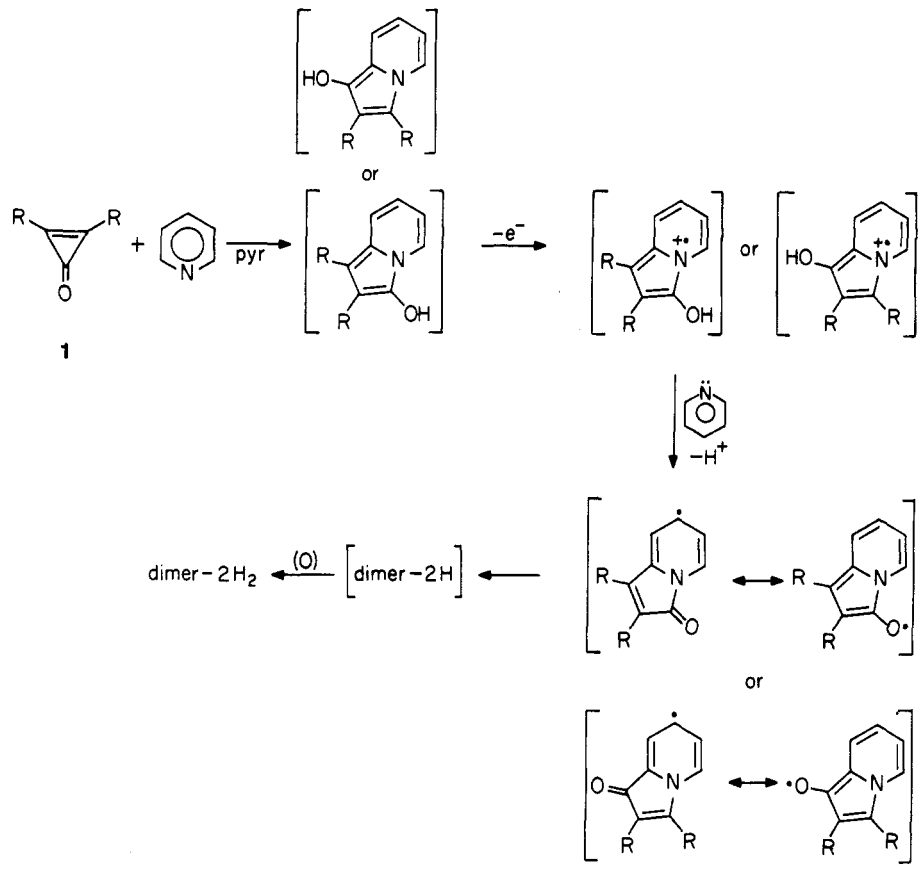
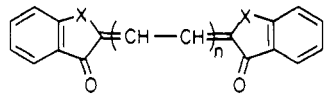


Table III. Comparison of λ_{max} of Several Indigoid Dyes with Their Vinylogues



compd	x	n	λ_{max}, nm
a	NH	0	595
b	NH	1	600
c	S	0	545
d	S	1	508
e	S	2	528

of compound **4a** either by oxidative dimerization of 2,3-diphenyl-1-indolizinol prepared in dioxane solvent or by reaction of **1a** with 4,4′-bipyridyl with subsequent oxidation, confirmed the position of dimerization (Scheme IV). Similarly, compound **5a** could be formed either from 1,2-di-4-pyridylethylene and **1a** or by oxidative dimerization of 2,3-diphenyl-7-methyl-1-indolizinol (Scheme V), confirming structure **5**. All 1,1′-dioxodimeric dyes were most conveniently prepared from bipyridyl or dipyridylethylene and cyclopropenones in dioxane with benzoquinone as oxidant.

Precedent for the surprising similarity of the spectral properties of **2** and **4** with their respective vinylogues **3** and **5** is found in comparison with the indigoid and thioindigoid vinylogues[4] (Table III).

A probable reaction path for dimer-d_2 formation (Scheme VI) involves initial oxidation of the indolizinol to a radical, dimerization in the 7-position to the corresponding bis(dihydrooxoindolizine), and eventual oxidation directly to the product or preliminary enolization to the bisindolizinol and subsequent oxidation to product.

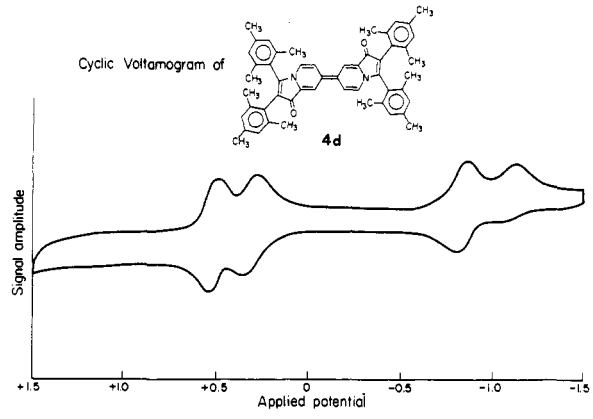
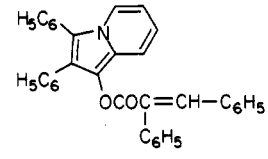


Figure 3.

The dimerization of 2,3-diphenyl-7-methyl-1-indolizinol may proceed by a similar radical dimerization or, alternatively, by a pathway analogous to the dimerization of 4-methylpyrylium salts[5] via a cation radical intermediate (Scheme VII). The product mixture consists of 57% **3** contaminated with a small amount of a soluble isomer (*m/e* 592) and substantial amounts of the diphenylacrylate ester **6** (*m/e* 505).

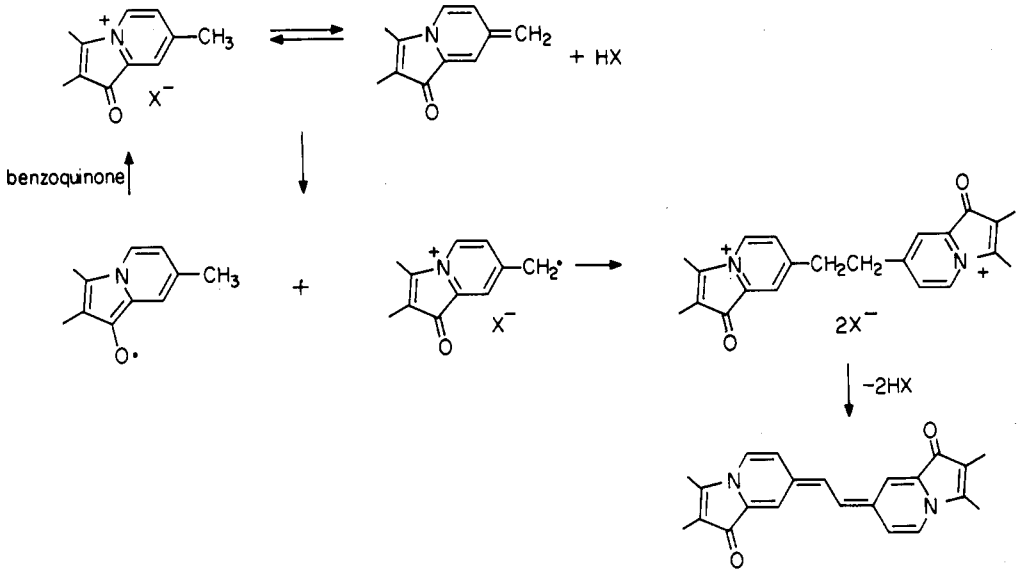


6

(4) Freedlander, P.; Risse, F. *Chem. Ber.* **1919**, *47*, 1914.

(5) VanAllen, J. A.; Reynolds, G. A. *Tetrahedron Lett.* **1969**, *25*, 2047.

Scheme VII



Cyclic voltammetry of **4d** reveals two reversible one-electron oxidations and two reversible one-electron reductions (Figure 3). The tabulated dimers (Tables I and II) were prepared by the indicated preparative schemes. Variations of the aromatic substituents on the dimeric nucleus cause only minor changes in the IR–visible spectra, since steric crowding forces the aromatic rings out of the chromophore plane (see discussion of X-ray crystallography).

It was apparent that the reactive intermediates before dimerization should be valuable synthons for the formation of asymmetrical, highly conjugated materials with interesting spectral and electrical properties.

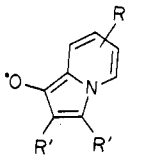
Indolizinyl Radicals

As noted in a previous publication, aeration of indolizinol solutions gave species exhibiting long-lasting EPR signals.[2] We have now investigated the one-electron oxidation products of a variety of indolizinols and isolated a family of crystalline radical species that exhibit a remarkable stability at room temperature, even in the presence of air and moisture (Table IV).

Neutral radicals with varying degrees of stability have been described, most belonging to the aminoxyl class. Other examples of air-stable free radicals include the highly chlorinated 9-phenylfluorenyls, diphenylpicrylhydrazyl (DPPH), phenoxy radicals, pyridinyls, and several organometallic species.[6-10] The indolizinyl radicals listed in Table IV were prepared by several one-electron oxidation procedures. Chemical oxidation was conveniently accomplished with a slight excess (0.6 molar equiv) of benzoquinone in dioxane at room temperature. The products could be precipitated from ether, water, or petroleum ether, water-washed to remove hydroquinone, and recrystallized from toluene, acetonitrile, or dichloroethane.

Although iodine and chloranil were also suitable oxidants, both required strict attention to stoichiometry to avoid overoxidation to the oxoindolizinium ion. Radicals were also conveniently prepared by redox equilibrium of appropriate indolizinols and the corresponding oxo-

Table IV. Preparation and Properties of Indolizinyls



compd	R	R′	method	mp, °C/crystal solvent
7	7-CN	C_6H_5	A, B, C, D	217–18/ toluene
8	7-CN	2,4,6-$(CH_3)_3C_6H_2$	A	109–10/cyclo-hexane
9	7-CN	n-C_3H_7	A	91–2/cyclo-hexane
10	7-CN	4-C_6H_5O-C_6H_4	A	227–8/toluene
11	6-CN	C_6H_5	A, B	–
12	8-CN	C_6H_5	A, B	–
13	7-CHO	C_6H_5	A, D	195–6/toluene
14	7-CO_2CH_3	C_6H_5	A, B, C	179–80/aceto-nitrile water
15	7-$CONH_2$	C_6H_5	A, B	263/dichloro-methane toluene
16	7-$COCH_3$	C_6H_5	A, D	162–3/toluene

indolizinium salt (see below). Two radicals (**9**, **13**) were prepared coulometrically by reduction of the corresponding cations at 0 volts; however, isolation was impractical because of difficulty in separating the product from the electrolyte.

The important structural requirement for stable indolizinyl radicals is an electron-withdrawing substituent such as cyano or carbonyl at C-7 (only 1-indolizinyls with this feature were available for study[2]). The one-electron oxidation of indolizinols without such stabilizing features, while indeed producing long-lived radical species, gave complex mixtures containing dimeric products, oxygen-containing materials, and acrylate esters such as **6**. The character of the substituents in the 5-membered ring does not noticeably affect radical formation or stability (Table IV, 8–10).

The tabulated indolizinyls are air-stable, crystalline compounds that give intense EPR signals both as solids or solutes. A broad, visible–IR absorption (λ_{max} 592 nm, ϵ_{max} 2000) imparts a green color; no NMR spectrum or

(6) Lawton, W. R. U.S. Patent 3,600,168.
(7) Ballester, M.; et al. *J. Org. Chem.* **1984**, *49*, 770.
(8) Goldschmidt, S.; Renn, K. *Ber.* **1922**, *55*, 628.
(9) Kochi, J. R. *Organometallic Mechanisms and Catalysts*; Academic Press: New York, 1978.
(10) Kosower, E. M.; Poziomek, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 5515.

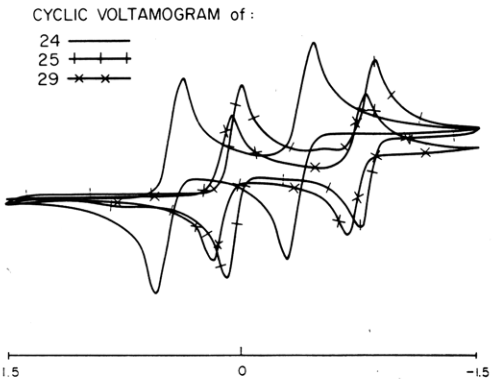


Figure 4.

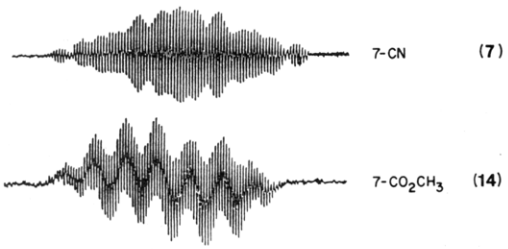


Figure 5.

characteristic IR carbonyl band was observed. Mass spectra of the radicals are compatible with proposed structures showing little, if any, contaminant; however, combustion analyses were poor, consistently showing low carbon values.

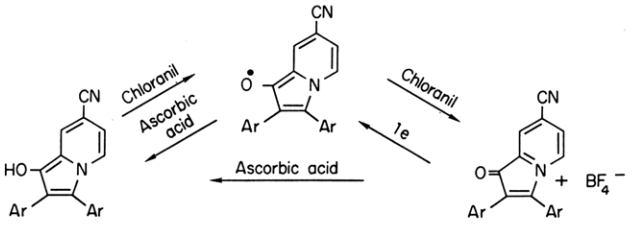
Cyclic voltammetry of oxoindolizinium ions (see below) showed two reversible, one-electron reductions (Figure 4), the radical being the oxidatively stable species at 0 volts. Unsubstituted indolizinyls, while showing typical CV's indicating long-lived radicals (Figure 4), in fact, rapidly formed complex mixtures that eventually gave oxidized dimers.

Thin-layer chromatography (silica gel) of purified radicals always showed a leading yellow edge and trailing red edge to the green radical zone, suggesting a redox equilibrium in the advancing solvent front.

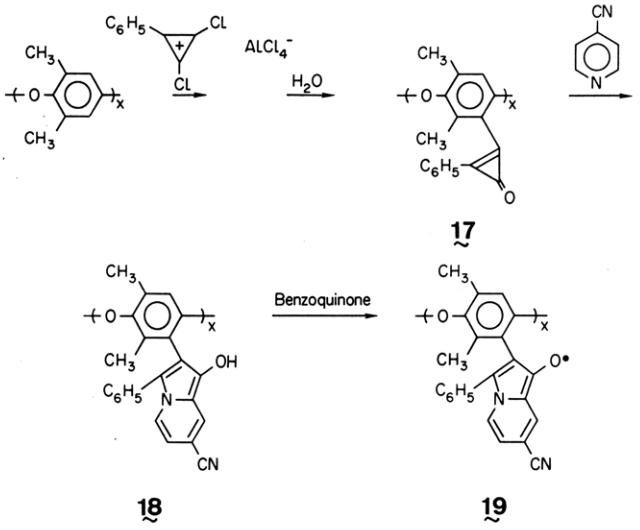
EPR measures on solid **7** and **14** showed a signal of similar magnitude to that of a DPPH standard. Spectra from fresh and old (one month/room temperature) samples were identical. Spectra of deoxygenated methylene chloride solutions of **7** and **14** show many resolved hyperfine lines, indicating considerable delocalization of the unpaired electron into the ring structure (Figure 5). Although the observed spectra did not change in shape, line width, or intensity/mole over a concentration range of 0.003–1.4 molar, indicating absence of a radical–dimer equilibrium, they decay significantly on standing, suggesting a reaction with the solvent. Indolizinol anions, radicals, and oxoindolizinium ions could be quantitatively interconverted either electrochemically or by chloranil or iodine as oxidants and ascorbic acid as reductant (Scheme VIII).

In an attempt to directly measure radical content in two samples (**7**, **13**), the concentric NMR tube method of Evans,[11] a Guoy balance,[12] and a vibrating sample magnetometer were employed. While the Guoy balance indicated the samples to be nearly 100% radical, the NMR method and the magnetometer showed only about 50% radical

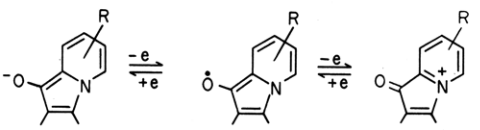
Scheme VIII



Scheme IX



Scheme X



content. Without a more detailed study of the magnetic properties of these radicals regarding diamagnetic contributions, temperature dependency, spin states, quenching, etc., which is outside the scope of this paper, only the most general conclusions can be drawn concerning radical content.

An interesting extension of this chemistry involves the formation of polymeric radicals from the easily prepared polymeric cyclopropenones. As described earlier,[13] many polymers, such as polystyrene and copolymers thereof, and polyphenylene oxides are easily substituted with arylcyclopropenones at any substitution level up to one on each unit. These polymers can in turn be converted in high yield to the desired polymeric indolizinols and subsequently to radicals by treatment with an excess of an appropriate pyridine and oxidation with a suitable oxidizing agent (Scheme IX). Such coatable or castable, paramagnetic materials may be of interest for conductive or antistatic applications.

Oxoindolizinium Ions

Upon further oxidation, indolizinyl radicals formed stable oxoindolizinium ions (Scheme X). Such ions were most conveniently prepared in good yield (70–95%) by direct two-electron oxidation of the desired 1-indolizinol with bromine, iodine, or chloranil (Table V) and were

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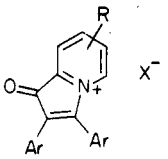
(14) Breslow, R.; Altman, L. J.; Krebs, A.; Mohocsi, E.; Murata, I.; Peterson, R. A.; Posner, J. *J. Am. Chem. Soc.* **1965**, *87*, 1328.
(15) Pohjala, E. *Acta Chem. Scand. B* **1974**, *28*, 582.

Table V. Preparation and Properties of Oxoindolizinium Ions



compd	R	Ar	x	method	mp, °C/solvent	^{1}H NMR[b] 5	6	7	8	9
20	H	C_6H_5	Br	A	236–9 dec/CH_3OH					
			BF_4	A	255–7/CH_3OH–H_2O	8.64	8.17	8.77	8.40	
			I_3	A	150–1/CH_3CN–H_2O					
21	7-$(CH_3)_3C$	C_6H_5	BF_4	A	248–9/CH_3OH	8.5	8.1	–	8.4	2.3
		C_6H_5	I_3	A	218–20/$CH_3C_6H_5$[a]					
22	7-$(HO)_2CH$	C_6H_5	Br	B						
		C_6H_5	BF_4	D, B	(112–20) 188–9 dec/dioxane	8.57	8.2	–	8.37	6.1
23	6,8-$(CH_3)_2$	C_6H_5	I_3	A	167–8/CH_3COCH_3–H_2O	8.35	–	8.42	–	2.6
						(8.42?)		(8.35?)		2.87
24	6-CN	C_6H_5	BF_4	D	243–5/dioxane[a]	8.97	–	9.1	8.48	–
25	7-CN	C_6H_5	Br	B	232–5/DMF–H_2O	8.8	8.54	–	8.67	–
			BF_4	D	254–64 dec/dioxane[a]					
			I_3	C	180–2/$(CH_3)_2COH_2O$					
26	8-CN	C_6H_5	BF_4	D	130–5 dec/dioxane[a]					
27	7-CH_3CO	C_6H_5	BF_4	D	204–5/dioxane[a]	8.75	8.45	–	8.6	4.0
		C_6H_5	I_3	C	141–2/$(CH_3)_2CO$–H_2O					
28	7-CH_3OCO	C_6H_5	Br	B	180 dec/THF[a]					
		C_6H_5	BF_4	B	237–8/$(CH_3)_2CO$–H_2O	8.75	8.45	–	8.6	2.75
		C_6H_5	I_3	C	161–2/$(CH_3)_2CO$–H_2O					
29	7-H_2NCO	C_6H_5	Br	B	260–2 dec/THF[a]					
			BF_4	B	278–80 dec/THF[a]	8.85	8.55	–	8.7	–
			I_3	C	210–11/$(CH_3)_2CO$–H_2O					
30	H	p-$CH_3OC_6H_4$	I_3	A	148–9/CH_3CN–H_2O	8.65	8.31	8.71	8.17	–
31	H	o,p-$(CH_3O)_2C_6H_3$	I_3	A	149–50/$(CH_2)_2CO$–H_2O	(8.05	8.9M)			

[a] Reaction solvent; product precipitates from the medium as it is formed. [b] CD_3CN, Me_4Si as internal standard.

Table VI. Redox Potentials of Oxoindolizinium Ions[a]

compd	$E_{1/2}^{I}$	$E_{1/2}^{II}$
20	0.041	–0.697
21	–0.065	–0.785
25	0.480	–0.345
27	0.230	–0.420

[a] All potentials arre in volts versus SCE, using CH_3CN as solvent and tetra-n-butylammonium perchlorate (0.1 M) as electrolyte.

isolated as fluoborate or halide salts.

Bromides and fluoborates were prepared in fair-to-good yields by treatment of the appropriate indolizinol in a suitable solvent with 2 equiv of bromine. The resulting precipitate was collected by filtration and washed with water. Bromide salts could be converted to fluoborates by treating aqueous or solvent–water solutions with excess 49% fluoboric acid. Although simple iodides could not be prepared pure, good yields of pure triiodides could be formed by using 4 equiv of iodine for oxidation.

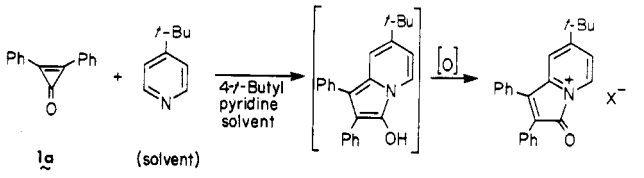
Alternatively, solutions of an indolizinol in dioxane containing a slight excess of fluoboric acid were treated with molar amounts of chloranil, and the resulting precipitates were collected and washed with hot dioxane.

2,3-Diphenyl-7-methyl-1-indolizinol, however, as in the one-electron oxidation, showed anomolous behavior in the bromine oxidation, forming substantial amounts of compound **5a**. Even a quick-precipitation technique (Experimental Section, A-1) could not avoid the copious oxidized dimer formation.

7-Acyl-2,3-diphenyl-1-oxoindolizinium fluoborate was also prepared electrochemically. Table VI summarizes several representative redox potentials.

The preparation of 3-oxoindolizinium ions posed several problems. Since 3-isomers were formed only by using the reactive pyridine as solvent (Scheme I), oxidations of the

Scheme XI



3-indolizinols in their preparative media were attempted. With the 3-indolizinol, B (R = Ph), oxidation with bromine gave primarily the cyan dye **2a**. A technique that might precipitate the 3-oxoindolizinium bromide as it formed gave only 1-oxoindolizinium bromide **20** (from the 1-indolizinol contaminant) and the aforementioned dimeric product. Although 1,2-diphenyl-7*H*-3-oxoindolizinium ions can be trapped by a reactive substrate, isolation has been impossible.[16] The oxidation of 7-*tert*-butyl-1,2-diphenyl-3-indolizinol in its 4-*tert*-butylpyridine solution with 2.2 equiv of bromine (Scheme XI, [O] = Br_2), proceeded smoothly, furnishing the corresponding 3-oxoindolizinium bromide, albeit in low yield. As with the corresponding isomeric 1-indolizinol, however, bromine or chloranil oxidation of 1,2-diphenyl-7-methyl-3-indolizinol in 4-picoline also proved anomolous, giving large amounts of the cyan dimer **3a**. All oxoindolizinium ions could be reduced to their corresponding indolizinols with ascorbic acid, demonstrating the maintenance of structural integrity during the oxidations.

Table VI lists redox potentials of several representative oxoindolizinium ions. The formal resemblance of oxoindolizinium ions to pyridinium and pyrylium salts suggests considerable chemistry that may be possible with

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these interesting materials. Indeed, the oxoindolizinium ions react with many nucleophilic species such as active methylenes,[16] phenols, naphthols, etc., producing highly colored products. Subsequent publications will deal with these reactions and products.

In summary, reactive oxyindolizinyl radicals, oxoindolizinium ions, and dimeric dyes are easily prepared from cyclopropenones and pyridines. Many of these materials react with various substrates to form a wide variety of dyes. Functional group reactions produce other interesting new compounds that will be described in future publications.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390 (90 MHz) or an IBM-WP270SY (270 MHz) spectrometer. Infrared spectra were recorded on a Beckman 4250 spectrophotometer. UV–visible spectra were obtained on a Perkin-Elmer 330 or a Cary 17 spectrophotometer. Total magnetic moments were measured on a Princeton Applied Research vibrating sample magnetometer. Magnetic susceptibilities were determined with a Guoy balance. Field desorption mass spectra (FDMS) were obtained on a MAT 23C mass spectrometer. Elemental analyses were obtained on a Perkin-Elmer C, H, and N analyzer by Analytical Sciences, Research Laboratories, Eastman Kodak Co. Iodine and bromine analyses were done by neutron activation. All microanalyses except those indicated were within established limits. The insolubility of some of the compounds and their tendency to incorporate solvents of crystallizaton made acceptable chemical analyses difficult to obtain. Field desorption mass spectrometry in all cases showed only the correct mass with no contaminants. Compounds **4e**, **5e**, and **5f** all gave the correct FDMS molecular ions, showing few, if any, contaminants, but were far-off in chemical analyses.

Neutral radicals were confirmed by ESR, mass spectroscopy, thin-layer chromatography, and electrochemistry but failed to give satisfactory combustion analysis, even when appearing to be chromatographically pure.

Solvents, reagents, and pyridines were used as received from Eastman Chemicals or Aldrich.

A Princeton Applied Research Model 173 potentiostat and Model 175 universal programmer were used in the standard three-electrode configuration to obtain redox potentials by cyclic voltammetry. A platinum-inlay electrode was used as the working electrode, along with a platinum auxiliary electrode and a standard calomel electrode. Solutions were $\sim 10^{-4}$ M in CH_3CN dried over CaH_2 with 0.1 M tetra-*n*-butylammonium fluoborate (Southwestern Analytical Chemicals, Inc.) recrystallized from ethyl acetate/pentane as the supporting electrolyte. All scans were performed at 100 mV/s scan rate.

A. Preparation of Starting Materials. 1. Diarylcyclopropenones were prepared from trichlorocyclopropenium ions by standard literature procedures. 2. Di-*n*-propylcyclopropenone was prepared by the method of Breslow[14] from 4-octyne and sodium trichloroacetate. 3. Indolizinols were prepared according to ref 1.

B. Preparation of 3,3′-Dioxo-1,1′,2,2′-tetraaryl-$\Delta^{7,7'}$-(3*H*,3′*H*)-bisindolizines (2). 1. In a typical preparation, 0.82 g (0.004 mol) of diphenylcyclopropenone was dissolved in 20 mL of argon-purged pyridine, and the mixture was heated at 100 °C for 15 min to effect the formation of the 3-indolizinol. After cooling to room temperature, the reaction mixture was treated with 20 mg (2.5 mol %) of cupric acetate and purged with air for 1 h. After standing overnight, the resulting brownish precipitate was filtered off, washed thoroughly with water and acetone, and air-dried to give 0.56 g of product (50% yield) of good purity (analytical and *E* values of crude dye were within experimental error of ϵ of purified dye). Purification of a sample was accomplished by vapor sublimation using an inert entrainer/carrier gas. The crude sample, about 0.5 g, was placed in an open quartz boat, which was then inserted into the middle of a Pyrex tube (1 in. i.d., 2 ft long). Argon gas was let in from one end by a needle valve, passed over the crude sample, and let out into a rotary pump. The pressure inside the tube was regulated to about 5 mTorr and the flow rate to about 20 scc/min. The source (boat) temperature was maintained at 380 °C by a tube furnace. The crystal was collected downstream in a temperature zone of about 250–300 °C. Dark green crystals as long as approximately 0.5 cm were formed in about 3 h. Solutions of product in toluene or methylene chloride were a bright cyan color. The crystals were examined by X-ray crystallography and the data furnished in Table VII (supplementary material).

2. A solution of an appropriate cyclopropenone in argon-flushed pyridine was heated on the steam bath for 10 min. After cooling, the solution was treated with 1 molar equiv of benzoquinone and warmed at 50 °C for 60 min. The resulting product was filtered off, washed with several portions of pyridine and then water, and air-dried to furnish only 3–5% yield of product. The majority of the product was a bright-green compound that was not identified.

3. Procedure B-2 was followed except that 2 equiv of iodine dissolved in 20 mL of pyridine were used as oxidant. The precipitate was filtered off, washed with acetone and water, and air-dried to furnish 28% yield of product.

C. Preparation of 3,3′,7,7′-Tetrahydro-3,3′-dioxo-1,1′,2,2′-tetraaryl-7,7′-(1,2-ethanediylidene)bisindolizines (3). 1. 4-Picoline (15 mL) was flushed with argon, and the appropriate diarylcyclopropenone (4 mmol) was added. The mixture was stirred at room temperature for 15 min and heated briefly on the steam bath, cooled, treated with cupric acetate (20 mg, 2.5 mol %), and purged with air for 1 h. After standing overnight, the brownish precipitate was filtered and washed with acetone to furnish 30–40% yield of product. The product from diphenylcyclopropenone (>90% pure based on spectral comparison with purified material) was sublimed for X-ray crystallography as described in B-1. The resulting large crystals were red-purple and gave bright cyan solutions in methylene chloride.

2. Diphenylcyclopropenone (2.06 g, 10 mmol) was dissolved in 4-picoline and stirred at room temperature until reaction was complete. The resulting green solution was cooled to 0 °C and treated with a solution of 1.62 g (15 mmol) of benzoquinone dissolved in 10 mL of dioxane, while the temperature was maintained below 10 °C with cooling. After the reaction mixture was allowed to come to room temperature, the product was filtered off, washed with acetone until the green color was gone, water, and acetone, and air-dried to furnish 1.8 g (61% yield) of product.

D. Preparation of 3,3′,7,7′-Tetrahydro-1,1′-dioxo-2,2′,3,3′-tetraaryl-$\Delta^{7,7'}$-bisindolizines (4). 1. A solution of pyridine (0.32 g, 4 mmol) and an appropriate cyclopropenone (2 mmol) in 20 mL of deaerated *p*-dioxane was refluxed under argon for 1 h, treated with benzoquinone (0.22 g, 2 mmol) in 10 mL of *p*-dioxane, and allowed to stand overnight. The resulting precipitate was filtered and dried to furnish 70–80% yield of product. With di-*p*-anisyl- and dimesitylcyclopropenones, the reaction could be run in pyridine solvent and treated as in B-2 to furnish 63% of **4b** (precipitated from ethyl ether) and 41% of **4d** (precipitated from water), respectively, as ~90% pure products (estimated from ϵ values). Both were thoroughly washed with ether and methanol to remove traces of byproducts at considerable sacrifice of product. The tetramesityl analogue was recrystallized from methylene chloride to give a bright green microcrystalline product, mp >300 °C, which was chromatographically pure (TLC); *m/e* 734 (no observable impurities).

2. Method D-1 was followed, but instead of oxidizing with benzoquinone, the reaction mixture was treated with 2.5 mol % $Cu(OAc)_2 \cdot H_2O$ and purged with air for 60 min. If the air oxidation was attempted without the copper acetate catalyst, only 3% yield of product was obtained, even after 3-h aeration.

3. A solution of 0.77 g (5 mmol) of 4,4′-bipyridyl in 20 mL of dioxane was treated with 2.06 g (10 mmol) of diphenylcyclopropenone at 100 °C under argon until the reaction was complete. The green solution was purged with air for 180 min, allowed to stand at room temperature overnight, and filtered to furnish crude product. After being washed thoroughly with ether to remove any unreacted starting materials, the solid was air-dried to furnish 2.2 g (78% yield) of product.

4. Method D-3, but with 0.54 g (5 mmol) of benzoquinone/5 mL dioxane as oxidant to furnish 2.0 g (71% yield) of product, was followed.

E. Preparation of 3,3',7,7'-Tetrahydro-1,1'-dioxo-2,2',3,3'-tetraaryl-7,7'-(1,2-ethanediylidene)bisindolizines (5). 1. A solution of 4-picoline (2.8 g, 30 mmol) in 20 mL of *p*-dioxane was flushed with argon, treated with diphenylcyclopropenone (2.06 g, 10 mmol), and refluxed under argon for 30 min. A solution of benzoquinone (1.62 g, 15 mmol) in 10 mL of *p*-dioxane was added to the green solution, which was then warmed at 50 °C for an additional hour. The resulting solid was filtered off, washed with *p*-dioxane and water, and dried to furnish 1.7 g, 57% yield, of product. The filtered reaction mixture was flooded with water to furnish an additional 0.7 g of product, which was shown by FDMS to be a crude mixture consisting mostly of the diphenylacrylate ester **6** and soluble isomers of **5** (mass 592).

2. A solution of 1.45 g (5 mmol) of dimesitylcyclopropenone in 15 mL of 4-picoline was heated on a steam bath until reaction was complete (4 h). The reaction mixture was cooled to 0 °C and oxidized with 0.81 g (75 mmol) of benzoquinone/10 mL of dioxane. After being warmed to room temperature, the solution was poured into petroleum ether and filtered, and the precipitate was thoroughly washed with methanol to remove starting materials and hydroquinone. Air-drying furnished 1.0 g (53% yield) of **5d**.

3. Method E-2, but with air used as the oxidant (bubbled through the mixture for 90 min/room temperature) instead of benzoquinone, was used to furnish 0.9 g (47% yield) of **5d**.

4. A solution of 1,2-di-4-pyridylethylene (0.9 g, 5 mmol) and diphenylcyclopropenone (2.06 g, 10 mmol) in 20 mL of dioxane was refluxed until reaction was complete. The reaction mixture was treated with 0.54 g (5 mmol) of benzoquinone and allowed to stand at room temperature overnight. The reaction mixture was poured into ether and filtered, and the precipitate was washed with ether and water to give 2.51 g (85% yield) of **5**.

5. Same preparation as E-4, but with the indicated cyclopropenones, was followed.

Preparation of Oxyindolizinyls 7–16. Method A. The formation of **13** illustrates a typical radical preparation by this method. A solution of 1.56 g (0.005 mol) of 2,3-diphenyl-7-formyl-1-indolizinol in 5 mL of *p*-dioxane was treated with a dioxane solution of 0.30 g (0.0028 mol) of *p*-benzoquinone. The resulting bright green solution was warmed at 50 °C for 5 min, poured into excess petroleum ether, and filtered to give 1.5 g (96% yield) of green solid. Crystallization from hot toluene gave green crystalline needles, mp 195–6 °C. Water and ether were also effective precipitation solvents for the various radicals.

Method B. Pyridine solutions (10%) of equimolar amounts of an indolizinol and its oxoindolizinium ion were mixed and warmed briefly at 50 °C. The solvent was stripped off in vacuo, and the residue was extracted with hot toluene to separate the pyridine salt. Reduction of the toluene volume in vacuo and cooling gave recrystallized product.

Method C. A solution of an indolizinol bearing an electron-withdrawing group in the 7-position was dissolved in a minimum of pyridine and treated with 1 equiv of bromine or iodine. The resulting green solution was evaporated to dryness in vacuo at 50 °C and triturated with hot toluene to extract the radical from the pyridinium halide. Cooling the toluene triturate gave good yields of crystalline radical.

Method D. Solutions of an appropriate oxoindolizinium ion in dry acetonitrile (ca. 5×10^{-4} M) containing 0.1 M TBAF were reduced at an appropriate voltage (0.00 for electronegatively substituted ions, +0.20 for electropositively substituted ions) until the theoretical number of coulombs were passed. Although such solutions were useful for spectral examination, it was impractical to isolate the radical from the electrolyte contaminant.

Radical Content of 7 and 13. Sample weights of **7** and **13** in and out of a magnetic field (Δw) were determined with a Guoy balance. Samples were weighed five times, and the average Δw determined. For **7**, $\Delta w = 1.53 \times 10^{-4}$ g; for **13**, $\Delta w = 1.64 \times 10^{-4}$ g. Magnetic susceptibilities were then calculated for each sample from the equation

$$X = K_2V + (g\Delta w)/HdH/dz/w$$

HdH/dz was determined to be 1.124×10^6 by use of the standard $CoHg(CNS)_4$. With the constants for the particular instrument ($K_2V = 1.64 \times 10^{-9}$, $g = 981$, $HdH/dz = 1.124 \times 10^6$) and the weight differential Δw, the molar magnetic susceptibility X_m was calculated to be 1.33×10^{-3} cgs units/mol for **7** and 1.28×10^{-3} cgs units/mol for **13**. The magnetic susceptibility in Bohr magnetons μ_B was calculated to be 1.72 for **7** and 1.69 for **13**. Consequently, the number of unpaired electrons/molecule is determined from the equation $\mu_B^2 = [n(n+2)]^{1/2}$ to be 0.989 for **7** and 0.960 for **13**.

Preparation of Polymeric 7-Cyanoindolizinyl Radicals. A. Preparation of Poly[2,6-dimethyl-3-[1-(3-oxo-2-phenylcyclopropenyl)]phenyleneoxy] 17. A 1.20-g sample of 2,6-dimethylpolyphenylene oxide (mw 2000 → 15 000), dissolved in dry dichloromethane, was cooled to 0 °C and treated with an equivalent amount of phenyldichlorocyclopropenium tetrachloroaluminate (prepared in dichloromethane as described above). The reaction mixture was allowed to come to room temperature and stirred for 1 h. After recooling to 0 °C, the solution was treated sequentially with 5 mL of water and 10 mL of methanol and warmed to reflux for several minutes. The reaction mixture was washed thoroughly with water, the organic layer was separated and concentrated, and the dissolved polymer was precipitated from methanol to furnish 2.4 g, 95% yield, of product **17**.

B. A 10% solution of **21** in deoxygenated dioxane and a 3-equiv excess of 4-cyanopyridine was warmed on the steam bath under argon for 60 min until an IR spectrum of the reaction mixture indicated the disappearance of the characteristic 1850-cm^{-1} cyclopropenone absorption. Precipitation of the resulting product from methanol gave quantitative yields of the polymeric indolizinol **18**.

C. Product **18** was dissolved in dioxane and treated with a dioxane solution of 1 equiv of benzoquinone. The reaction solution was poured into petroleum ether and filtered, and the resulting precipitate was water-washed to remove the hydroquinone. The resulting polymeric radical **19** was obtained as a green solid in quantitative yield. Alternatively, the dioxane solution described in **2** could be treated with benzoquinone directly without isolation of the intermediate polymeric indolizinol.

Oxidation of 7 to 7-Cyano-1,7-dihydro-2,3-diphenyl-1-oxoindolizinium Tetrafluoroborate (25). A solution of 0.31 g (1 mmol) of **7** in 10 mL of dioxane was treated sequentially with 0.13 g (0.5 mmol) of chloranil and 4 mL (2 mmol) of 49% fluoboric acid. The resulting solution was stirred for 60 min and filtered, and the precipitate was air-dried to furnish 0.40 g (100% yield) of product, mp 254–64 °C dec.

Reduction of 7 to 7-Cyano-2,3-diphenyl-1-indolizinol. A solution of 0.31 g (1 mmol) of **7** in methanol was treated with 0.5 g of L-ascorbic acid dissolved in water. The resulting yellow solution was diluted with water and filtered, and the precipitate was dried to furnish 0.30 g of product. Acetylation with acetic anhydride gave 1-acetoxy-2-cyano-2,3-diphenylindolizine, mp 198–9 °C (lit.[2] 198–9 °C).

Coulometry and Optical Spectroscopy. 7-Cyano-1,7-dihydro-2,3-diphenyl-1-oxoindolizinium tetrafluoborate (6.13 mg) was dissolved in 25 mL of dry CH_3CN containing 0.1 M TBAF to give a solution concentration of 6.2×10^{-4} M in indolizinium ion. The UV–visible spectrum of this solution was recorded prior to reduction. The solution was then reduced at 0.00 V SCE to generate the neutral radical species. After the theoretical number of Coulombs were passed, an aliquot of the solution was put into a cell and the UV–visible spectrum taken. This aliquot was replaced, and the solution was oxidized at 0.40 V versus SCE to regenerate the original species. A UV–visible spectrum was identical with that of the starting ion, confirming the reversible nature of the redox cycle.

This reduction–oxidation cycle was repeated three times with no change in the absorption characteristics of the radical solution (±4%). The ϵ value for neutral radical solution from this experiment ($\lambda_{max} = 592$ nm, $\epsilon \simeq 1850$) compared well with the value for ϵ of isolated **1b** ($\epsilon \simeq 2000$). In addition, after the final cycle to neutral radical, additional electrons were introduced into the solution by varying the current amplitude. The UV–visible spectrum of this solution did not change, indicating that all the indolizinium ion had already been reduced to neutral radical.

Preparation of 1-Oxoindolizinium Salts. A. Method 1. A solution of **1a** (2–5%) in either cyclohexane or chlorobenzene (for bromides) or toluene or chlorobenzene (for triiodides) was thoroughly flushed with argon and treated with 1.1 equiv of an appropriate pyridine. The resulting reaction mixture was refluxed

under argon for 40 min (or until IR indicated complete reaction of **1a**). Four equivalents of iodine or 2.2 equiv of bromine dissolved in the reaction solvent were added dropwise at room temperature, and the resulting solution was stirred for 1 h, or until the product precipitated. The triiodide salt was filtered off and washed with an acetonitrile, methanol, water mixture or recrystallized from an appropriate solvent to furnish pure product. The bromides, which occasionally proved to be hygroscopic, were dissolved in methanol directly after filtration and were treated with excess 48% fluoboric acid to furnish pure fluoborate salts.

B. Method 2. A sample of an appropriate indolizinol was dissolved in chlorobenzene, pyridine, THF, or DMF and was treated with 2 equiv of bromine. The solution was stirred for 30 min at room temperature, and the resulting solid was filtered off. Since bromine analyses of the isolated bromides were often high due to the presence of tribromide ion, fluoborates were prepared by treating water or DMF–water solutions of crude bromides with excess 48% fluoboric acid.

C. Method 3. An appropriate indolizinol was dissolved in acetone (10% w/v) and was treated with 1 equiv of pyridine. Four equivalents of iodine dissolved in acetone were added in one portion, and the mixture was stirred at room temperature for 1 h. If no precipitate was formed, the solution was treated with water until the product precipitated. The resulting triiodide salt was recrystallized from an appropriate solvent.

D. Method 4. An indolizinol and 3.1 equiv of 48% aqueous HBF_4 were dissolved in a minimum of dioxane and were treated with 1 equiv of chloranil. The resulting red solution was stirred at room temperature until the product precipitated. Filtration and washing with hot dioxane furnished pure oxoindolizinium fluoborate.

Attempted Preparation of 1,7-Dihydro-2,3-diphenyl-7-methyl-1-oxoindolizinium Bromide. A 5% solution of 0.41 g (2 mmol) of 2,3-diphenylcyclopropenone and 0.37 g (4 mmol) of 4-picoline in chlorobenzene was heated on the steam bath for 30 min. Treatment of the cooled solution with 0.35 g (2.2 mmol) of Br_2 gave a bright magenta solution that rapidly deposited a red solid. Filtration and other washing furnished 0.55 g of a crude product. Mass spectrometry (FDMS) of the crude material revealed a complex mixture containing none of the desired product.

Attempted Preparation of 3-Oxoindolizinium Salts. A. Method 1. All attempts to isolate 7-H- or 7-Me-3-oxoindolizinium salts have been unsuccessful, furnishing only dimers.

1. A 5% solution of 0.41 g (2 mmol) 2,3-diphenylcyclopropenone in 4-picoline was stirred under argon for 15 min at room temperature. The greenish solution was treated with 0.36 g (2.2 mmol) of Br_2, and the resulting red solution was allowed to stir for several minutes at room temperature. Filtration of the reaction mixture in air and washing the precipitate with isopropyl alcohol gave 0.41 g of **3a** (68% yield).

2. A 5% solution of 0.21 g (1 mmol) of 2,3-diphenylcyclopropenone in pyridine was stirred at room temperature under argon for 15 min. Bromine (0.16 g, 2 mg-atoms) dissolved in pyridine was added rapidly at room temperature, and the reaction mixture was stirred at room temperature for 10 min. The resulting solid was removed by filtration, washed with several portions of ether, and dried to furnish 0.30 g of **2a**.

B. Method 2. 3,7-Dihydro-7-*tert*-butyl-1,2-diphenyl-3-oxoindolizinium Bromide (21). A solution of 0.21 g (1 mmol) of 2,3-diphenylcyclopropenone in 5 mL of deoxygenated 4-*tert*-butylpyridine was heated under argon at 120 °C/0.5 h, cooled, and diluted with 25 mL of chlorobenzene. Bromine (0.18 g, 1.1 mmol) was added rapidly, and the solution was allowed to stand at room temperature for 2 h. The resulting orange-red precipitate was filtered off and dried to give 0.15 g (18% yield) of product: mp 283–5 °C dec; ^1H NMR (CD_3CN + 2 drops CF_3SO_3H, Me_4Si as internal standard) δ 8.97 (d, 1 H, J = 6 Hz), 8.06 (dd, 1 H, J = 6 Hz, 1.5 Hz), 7.72 (d, 1 H, J = 1.5 Hz), 7.70–7.20 (m, 10 H), 1.40 (s, 9 H); IR (KBr) 3045, 3020, 2965–2560 (broad, strong), 1710, 1620, 1375, 1205, 1160, 700 cm^{-1}; FDMS m^+/e 340 ($C_{24}H_{22}BrNO$) – (Br). Unable to obtain satisfactory analyses for C. Anal. Calcd for $C_{24}H_{22}BrNO$: C, 68.6; H, 5.3; N, 3.3. Found: C, 65.5; H, 5.4; N, 3.2.

Reduction of 1-Oxoindolizinium Ions. A. Method 1. A dilute solution of 0.10 g of **25** in methanol was treated with 0.10 g of L-ascorbic acid and several drops of water. After warming for several minutes, the yellow solution was flooded with water and filtered, furnishing 0.08 g of product. Spectral data were consistent with authentic 7-cyano-2,3-diphenyl-1-indolizinol.

B. Method 2. A solution of 0.2 g (0.5 mmol) of **20** (BF_4^-) in 2 mL of pyridine was thoroughly flushed with argon and 0.2 g (1.1 mmol) of L-ascorbic acid was added. After heating at 100 °C for 15 min, 0.2 g (2 mmol) acetic anhydride was added, and heating was continued an additional 5 min. The solution was flooded with water and was stirred to give a crude solid that was filtered and dried. Chromatography on Woelm silica gel, eluting with CH_2Cl_2, gave 0.08 g (45%) of bright yellow solid identical with authentic 2,3-diphenyl-1-indolizinyl acetate (NMR, IR).

Supplementary Material Available: X-ray diffraction data for **2a** and **3a** and analyses for **2, 3,** and **21–31** (11 pages). Ordering information is given on any current masthead page.

Indolizines. 4. Dyes Derived from Oxoindolizinium Ions and Active Methylene Compounds

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Dyes of a new class, incorporating the dihydro-1-oxoindolizine structural unit, have been synthesized. Oxoindolizinium ions react with active methylene compounds to give dyes (λ_{max} 560–630 nm) in high yield. The syntheses of the dihydro-1-oxoindolizinium ions and representative dyes from their reactions with active methylene compounds, along with the spectral and physical properties of the intermediates and the dyes, are presented. One example of the preparation of an isomeric dihydro-3-oxoindolizine dye is also described. The preparation of several 5-substituted indolizinols and their coupling reactions with active methylenes is described.

As previously reported,[1] a variety of stable oxoindolizinium salts can be prepared from appropriate cyclopropenones and pyridines. These reactive molecules can be oxidatively coupled in high yield with active methylene compounds to form a new class of dye A (Scheme I).

The dyes absorbed at unexpectedly long wavelengths, as compared with corresponding pyridinium and pyrylium analogues, leaving their structures in some doubt. Since legitimate dye structures can be drawn for substitution at **5**, **6**, **7**, or **8** on A, it was necessary to demonstrate unam-

(1) Wadsworth, D. H.; Weidner, C. H.; Nuttall, R. H.; Bender, S. L. *J. Org. Chem.*, preceding paper in this issue.

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