Polymeric Reagents. 3. Poly[vinyl(pyridinium chlorochromate)]: A New Recyclable Oxidizing Agent

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Received November 22, 1977

Poly[vinyl(pyridinium chlorochromate)] is prepared easily from cross-linked poly(vinylpyridine) resins by reaction with chromic anhydride and hydrochloric acid. The insoluble reagent, which has a capacity of 3.5–3.9 mmol of chlorochromate per gram, is useful in the oxidation of alcohols to carbonyl compounds. The oxidation has a high efficiency, as less than 1 molar equiv of the reagent is consumed in the reaction. Other advantages of the reagent are associated with its insolubility and that of its byproduct which facilitates the workup of reaction mixtures and allows for the quantitative recovery and regeneration of the spent resin. After several regenerations, the reagent is still as reactive as the original material.

Polymeric reagents[1] have recently been developed for use in simple processes such as epoxidation,[2] oxidation,[3] acylation,[4] halogenation,[5] or Wittig[6] reactions. In all of these applications, advantage is taken of the insolubility of the polymeric reagent and of its byproduct which allows for the easy removal of any excess reagent or spent material from the desired product. In addition to being insoluble, polymeric reagents should be easy to prepare, have a capacity sufficient for use on a practical scale, and be designed in such a way that the spent reagent can be regenerated to its initial activity in an easy fashion. In most cases, the ability of the polymer to be regenerated is critical, since few reactions could justify the use of a custom-made polymer which would be discarded once the reaction has been carried out.

We have recently prepared a cross-linked poly(vinylpyridine) resin[5] by a pearl copolymerization technique, and used this resin to produce a fully regenerable brominating agent which could be used over and over again without deteriorating. This paper describes the application of a similar cross-linked poly(vinylpyridine) resin to the synthesis of a poly[vinyl(pyridinium chlorochromate)] and the application of the polymeric oxidizing agent to the oxidation of various alcohols. A somewhat similar reagent[7] was prepared recently by reaction of Amberlyst A-26 with chromic acid. This reagent was claimed to be regenerable, although little experimental data was given and no mention of its capacity after regeneration was made.

Results and Discussion

The poly[vinyl(pyridinium chlorochromate)] reagent (PVPCC) can be prepared very easily by addition of the stoichiometric amount of chromic anhydride and concentrated hydrochloric acid to a suspension of the cross-linked poly(vinylpyridine) (PVP) in water. The resin, which turns to an orange color, can then be washed free of unbound material and be used directly in oxidation reactions or dried for storage. The capacity of the reagent was measured easily by titration with an appropriate reducing agent, and was usually found to be in the range of 3.5–3.9 mmol of oxidizing agent (expressed as chlorochromate) per gram of dry polymer. Our first attempts to use the reagent were made using conditions similar to those described by Corey and Suggs[8] for pyridinium chlorochromate. However, the reaction in dichloromethane was found to be very sluggish, and a large excess of reagent was required to obtain reasonable rates and yields of carbonyl compounds (Table I). More polar oxygenated solvents such as ether or tetrahydrofuran were found to be even less suitable as a marked decrease in the rate of reaction was observed in these solvents. In contrast, nonpolar hydrocarbons such as benzene, or better, heptane or cyclohexane, gave satisfactory results with the rate of reaction increasing with a decrease in solvent polarity. The results of Table II show the effect of solvent and temperature on the rate of oxidation of 1.7 mmol of cinnamyl alcohol with 1.9 g of PVPCC in 10 mL of the solvent indicated. Best results at room temperature were obtained using the solvent of lowest polarity (cyclopentane). As expected, increases in temperature (Table II) and in molar ratio of resin to substrate resulted in increases in rates of oxidation.[9] As can be seen in Table III, the reaction was rapid with 4.5 or 2.2:1 ratios of chlorochromate to alcohol (entries 1 and 2). When the reaction was attempted with a smaller amount of resin (entry 3), the reaction proceeded rapidly to 50% conversion then slowed down considerably, presumably due to a lack of accessibility of the reactive sites.[10] When a similar reaction was attempted with a partially loaded resin (entry 4) in which only approximately 25% of the vinylpyridine units were transformed into the chlorochromate, the reaction proceeded smoothly to completion due to the greater accessibility of the reactive sites. In this experiment the ratio of oxidizing agent to alcohol was of approximately 1.1:1. The reagent was effective in the oxidation of various types of alcohols: allylic, benzylic, secondary, or primary, as shown in Table IV. Preferred reaction conditions included the use of an excess of PVPCC in cyclohexane at 80 °C to increase the rate of reaction and carry the oxidation to completion to facilitate the work-up procedure. The product isolation and purification steps were made easy by the fact that no products of overoxidation, soluble chromium salts, or other impurities were found in the reaction mixture once the oxidation was complete. Thus, the carbonyl compounds could be obtained by a simple filtration followed by washing of the resin to extract all the product, and finally, evaporation of the solvent. Scheme I summarizes the use of the PVPCC reagent. Although the results reported in Table IV were obtained using a 4.5:1 ratio of oxidizing agent to alcohol, titrations of the resins before and after the oxidations showed that <1 molar equiv of the polymeric reagent was actually consumed in the reaction. Table V shows that a polymer used in the oxidation of an alcohol under the conditions reported for Table IV still

Table I. Reaction of Alcohols with a 12-Fold Excess of PVPCC in Methylene Chloride at Room Temperature

Alcohol	Registry no.	Time, days	% conversion
Cinnamyl alcohol	104-54-1	<0.5	100
1-Phenylethanol	60-12-8	2	78
1-Hexanol	111-27-3	3	91
4-Methyl-4-penten-2-ol	2004-67-3	3	61
3-Hexanol	623-37-0	4	86
Cyclopentanol	96-41-3	3.5	100
2-Octanol	123-96-6	4	76

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Table II. Oxidation of Cinnamyl Alcohol with PVPCC:[a] Influence of Solvent and of Temperature on the Extent of Reaction as a Function of Time

Time, min	Dichloromethane, 25 °C	Cyclopentane, 25 °C	Tetrahydrofuran		Benzene		Cyclohexane		Heptane 80 °C
			25 °C	80 °C	25 °C	80 °C	25 °C	80 °C	
16	15%	56%	9%	15%	38%	80%	52%	97%	96%
36	32%	82%	15%	26%	54%	86%	74%	100%	100%
60	46%	91%	18.5%	31%	65%	92.5%	85%		
110	64%	96%	23.5%	39%	80%	96.5%	98%		
180	79%		26.5%	45%	86%		100%		

[a] Reaction of 1.7 mmol of alcohol with 1.9 g of PVPCC in 10 mL of the solvent indicated.

Table III. Determination of the Reactivity as a Function of the Amount of PVPCC

Entry	Wt of PVP,[a] g	mmol of chlorochromate	mmol of alcohol[b]	% conversion			
				16 min	36 min	56 min	90 min
1	1	7.7	1.7	96	99+		
2	0.5	3.8	1.7	87	95	97	99+
3	0.25	1.9	1.7	51	53	55	55
4[c]	1	1.9	1.7	38	61	71	81

[a] Amount of PVP used in the preparation of PVPCC. [b] All the reactions were carried out with cinnamyl alcohol in 5 mL of cyclohexane at 75 °C. [c] Reaction with partially loaded (25%) PVP; this reaction reached completion in 20 h.

Table IV. Reaction of PVPCC with Various Alcohols

Alcohol	mmol	PVPCC, g	Solvent, mL	Temp,	Time	% conversion
Cinnamyl alcohol	1.7	1.9	Cyclohexane, 10	80	36 min	100
Cyclohexanol[a]	1.7	2.0	Cyclohexane, 4	75	24 h	94
1-Butanol[b]	1.7	2.0	Cyclohexane, 4	75	4.5 h	90
					24 h	100
Benzyl alcohol[c]	1.7	1.9	Cyclohexane, 4	75	15 min	95
					36 min	100
1-Phenylethanol	1.7	2.0	Cyclohexane, 10	80	3.5 h	96
Cyclopentanol	1.7	1.9	Cyclohexane, 4	77	3.5 h	82
					12 h	99

[a] Registry no.: 108-93-0. [b] Registry no.: 71-36-3. [c] Registry no.: 100-51-6.

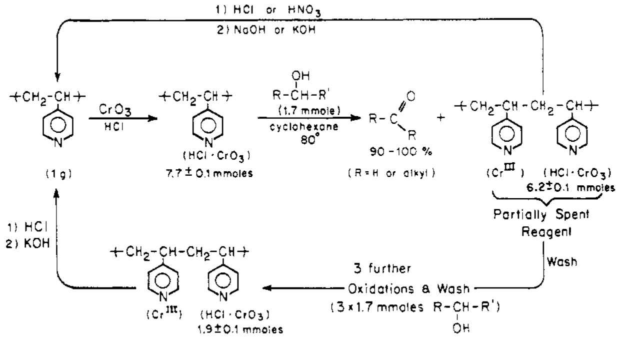
Table V. Determination of the Consumption of Oxidizing Agent and Reactivity of Partially Spent[a] PVPCC

Reaction cycle[b]	mmol of PVPCC	mmol of alcohol	% conversion				
			16 min	36 min	56 min	120 min	420 min
1	7.7	1.7	96	99+			
2	6.2[c]	1.7	92	99+			
3		1.7	57	83	92	99	
4		1.7	32	47	59	83	99
5	1.9[d]						

[a] Reaction of PVPCC prepared from 1 g of PVP with successive portions of cinnamyl alcohol. [b] Each cycle consists of an oxidation followed by a wash with cyclohexane then water. [c] Data obtained in a parallel experiment. [d] Amount of chlorochromate remaining on the resin after four successive oxidations.

contains enough active reagent to be reused without regeneration in further oxidation reactions. Thus, when the oxidation of 1.7 mmol of cinnamyl alcohol was carried out with 7.7 mmol of PVPCC, the reaction was complete within 36 min, and the partially spent reagent still contained 6.2 mmol of chlorochromate. After washing to remove the cinnamaldehyde, three further oxidations were carried out as shown on Scheme I. After four successive oxidations involving a total of 6.8 mmol of alcohol, the resin still contained 1.9 mmol of chlorochromate for a net consumption of 5.8 mmol. This indicates that the actual consumption of oxidizing agent is of the order of 0.85 molar equiv. It should be noted, however, that the rate of the oxidation reaction decreased in the third and fourth oxidations. The spent polymeric reagent, which turned black during the first oxidation, could be regenerated easily to poly(vinylpyridine) (Scheme I) by complete removal of the chromium salts using consecutive washings with hydrochloric acid and sodium or potassium hydroxide. The recycled poly(vinylpyridine), which was slightly darker than the starting PVP resin, could then be treated with chromic anhydride and hydrochloric acid to produce a PVPCC resin with an activity comparable to that of the original material.[11] The reagent recycled four times was found to be as effective an oxidant as the original material (Table VI). It is expected that the polymeric reagent could withstand many more reaction cycles, since no chemical degradation of the polymer was observed. The limitating factor, as in the case of all macroreticular resins, is the mechanical stability of the polymer beads as repeated handling may result in the slow formation of fine particles which, although reactive, are much harder to handle

Scheme I



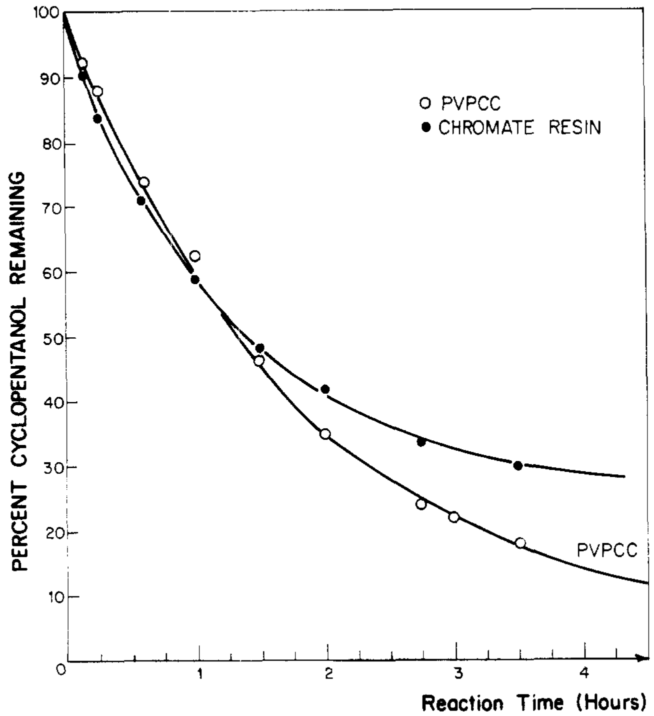


Figure 1. Oxidation of cyclopentanol (1.7 mmol) in 4 mL of cyclohexane at 77 °C using 2 g of resin: comparison of PVPCC with chromate ion exchange resin.

Table VI. Activity of Recycled PVPCC: Oxidation of Cinnamyl Alcohol in Cyclohexane at 80 °C^a

Resin cycle^b	Capacity^c	% conversion 16 min	% conversion 36 min
1	3.58^d	97	>99
2	3.60	93	98
3	3.86	96	>99
4	3.70	93	>99
5	3.65	95	>99

^{a} 1.7 mmol of alcohol with 1.9 g of PVPCC in 10 mL of cyclohexane. ^{b} Each cycle consists of: preparation of PVPCC, oxidation, and regeneration to PVP. ^{c} Capacity expressed in millimoles of chlorochromate per gram of resin. ^{d} In other runs, the initial capacity of PVPCC varied from 3.5 to 3.95 mmol/g.

than spherical beads of well defined sizes. In the case of our PVPCC resin, only a small amount of powdery material was produced in five reaction cycles, and the only losses which were observed were mechanical due to the repeated transfers of the polymer. In most cases, these mechanical losses amounted to less than 2% per cycle.

A comparison of the PVPCC resin with the chromate ion exchange resin described by Cainelli and co-workers[7] was made using 2 g of each resin[12] for the oxidation of 1.7 mmol of cyclopentanol at 77 °C. As can be seen in Figure 1, the two reagents were comparable in their initial reactivity but the reaction with PVPCC required much less time to reach completion than that with the chromate ion exchange resin. Both resins are, however, quite similar in their ease of preparation and their handling. The major difference between the two reagents is probably the better efficiency of the PVPCC, which consumes less CrO_3 and is fully regenerable.

Experimental Section

4-Vinylpyridine was purified by distillation under reduced pressure immediately before use. Divinylbenzene (55–60%) was obtained from Polysciences, Inc., and was used without further purification. The oxidation reactions were monitored by withdrawing small aliquots at regular time intervals for analysis by gas chromatography on a 6-ft column of 15% Carbowax 20M on Chromosorb P.

Preparation of the Cross-Linked Poly(vinylpyridine) Resin (PVP). Poly(vinyl alcohol) (2.4 g) was dissolved in 550 mL of boiling distilled water and the solution was placed in a 2-L resin kettle equipped with Teflon seals, a reflux condenser, a nitrogen inlet, and a mechanical stirrer. The solution was stirred under nitrogen at 80 °C and a solution of 25 g of 4-vinylpyridine and 1.5 g of divinylbenzene in 50 mL of toluene was added rapidly. After addition of 1 g of azobisisobutyronitrile (AIBN) the polymerization was allowed to proceed under constant vigorous stirring. Polymer beads started to appear very rapidly, but the mixture was left at 80 °C overnight. The resin beads were collected by filtration through cloth and were washed extensively with water, acetone, ether, dichloromethane, and finally methanol. After drying under vacuum, 25.1 g of almost white PVP resin beads were obtained. A suitable 2% cross-linked vinylpyridine–divinylbenzene resin is also available commercially from Polysciences, Inc.

Preparation of PVPCC. To 10 g of cross-linked PVP resin (50–100 mesh) suspended in 20 mL of water was added 9 g of chromic anhydride and 10 mL of concentrated hydrochloric acid. The mixture was stirred at room temperature for 1 h and filtered and the resin was washed with distilled water until the filtrate was clear. Freshly prepared PVPCC has a bright orange color which turns to brown upon drying in vacuo (60 °C, 5 h). The resin can be used directly without drying or can be stored in dry form. Titration of the chlorochromate resin was done in two ways: indirectly by titration of the filtrate and wash liquid collected during the preparation of PVPCC, or directly by titration of the chromate displaced from the resin by reaction with aqueous 2 N potassium hydroxide overnight. In a typical titration, a freshly prepared solution of ferrous ammonium sulfate was used to reduce the chromate after acidification with phosphoric acid and using diphenylamine sulfonate as indicator. Both methods gave comparable results; however, the results reported in this text are those which were obtained in the direct titrations. Thus, the PVPCC resin (19.3 g) obtained above from 10 g of PVP contained 3.6 mmol of chlorochromate per gram of dry reagent. The PVPCC resins obtained in similar preparations contained up to 3.95 mmol of chlorochromate per gram. In most cases the PVPCC resins were not dried thoroughly before use, but were simply air dried after washing with water. Typically, a PVPCC resin prepared from 1 g of PVP, 0.92 g of CrO_3, and 1 mL of concentrated HCl contained 7.5–7.9 mmol of chlorochromate after thorough washing with water and air drying.

Oxidation of Alcohols: General Procedure. Best results in the oxidation reactions were obtained using wet PVPCC resins. Thus, in instances where the dry resin was used, it had to be soaked briefly (5–10 min) in water prior to filtration to remove the excess water and before use in oxidation reactions. Alternately, the PVPCC could be prepared immediately before use by reaction of the required amounts of PVP, CrO_3, and HCl, followed by thorough washing with water and filtration. The second procedure was often preferred over the first as it eliminated the lengthy drying step. In a typical oxidation, the PVPCC obtained by reaction of 1 g of PVP with CrO_3 and HCl as described above (or 1.9–2 g of dry reagent soaked in water and filtered) was used in 4–10 mL of cyclohexane at 75–80 °C (Table IV). After addition of 1.7 mmol of the alcohol, the mixture was stirred at 75–80 °C and small aliquots were withdrawn at regular time intervals for chromatographic analysis. The percent conversion was calculated directly from the chromatograms after calibration. Some reactions were also carried out using less PVPCC for the same amount of alcohol (Table III). Reactions were also carried out on a larger scale using, for example, the PVPCC prepared above from 10 g of PVP to oxidize 2.4 g of cinnamyl alcohol in 50 mL of cyclohexane at 60 °C. The reaction was monitored by GLC and had essentially reached completion in 60 min. After 105 min, the reaction mixture was filtered and the resin washed with ether and dichloromethane to extract the cinnamaldehyde. After evaporation of the solvent, 2.0 g of pure cinnamaldehyde (84%) was obtained.

Reactions with Partially Spent PVPCC. PVPCC (7.7 mmol) was prepared from 1.03 g of PVP and the required amounts of CrO_3 and HCl as described above. The resin was used immediately after washing with water for the oxidation of 1.7 mmol of cinnamyl alcohol in 5 mL of cyclohexane at 75 °C. The reaction was followed by GLC and was complete in 36 min. The resin, which had turned almost completely black in this first oxidation, was filtered and washed with cyclohexane to remove all the cinnamaldehyde. After rinsing with water and air drying on filter, the resin was transferred quantitatively to a flask containing 1.7 mmol of cinnamyl alcohol in 5 mL of cyclohexane at

75 °C. This second oxidation proceeded rapidly and was complete in 36 min. After washing and rinsing the resin with cyclohexane and water as above, a third oxidation of another 1.7 mmol of cinnamyl alcohol was carried out. The reaction required 2 h to reach completion. The resin was again filtered and washed as above, then used in a fourth oxidation using another 1.7 mmol of cinnamyl alcohol. This fourth oxidation reached completion in 7 h. After washing with cyclohexane, the resin was soaked in 2 N potassium hydroxide overnight, and the filtrate was titrated with standard ferrous ammonium sulfate in acidic medium. The titration showed that the resin still contained 1.9 mmol of chlorochromate after four successive oxidations of 1.7-mmol portions of cinnamyl alcohol (Table V).

Recycling of the Resin. The spent reagent, which was black after filtration of the desired product, was easily regenerated by washing with 2 N hydrochloric acid (or 2 N nitric acid) followed by 2 N aqueous sodium or potassium hydroxide and rinsing with water. This treatment effectively removed the chromium salts from the polymer and regenerated the PVP resin. The regenerated PVP was usually slightly darker than the original material, but was unaffected in its ability to produce a satisfactory PVPCC reagent (Table VI). After regeneration with CrO_3 and HCl, the recycled PVPCC, which was dark red, had an activity comparable to that of the fresh reagent, and its activity remained essentially constant through repeated oxidation–reduction cycles. The only losses which were observed were mechanical, due to the numerous transfers of wet polymers at the different stages of reaction or recycling. In a typical run these losses amounted to 1–2%.

Acknowledgment. Financial support of this work by the National Research Council of Canada in the form of a research grant and a graduate scholarship (to M.J.F.) is gratefully acknowledged.

Registry No.—Cinnamaldehyde, 104-55-2; 1-phenylethanone, 122-78-1; hexanal, 66-25-1; 4-methyl-4-penten-2-one, 3744-02-3; 3-hexanone, 589-38-8; cyclopentanone, 120-92-3; 2-octanone, 111-13-7; cyclohexanone, 108-94-1; butanol, 123-72-8; benzaldehyde, 100-52-7; PVPCC, 66212-21-3.

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(9) Cainelli et al. (ref 7) claim to observe an increase in rate for higher substrate to resin ratio; this is unlikely.

(10) The data shown on Table V suggest that the active sites may become coated with the oxidized material, thus slowing down the reaction. This is supported by the observation that, after washing with solvent, the partially spent resin can react again at a normal rate.

(11) An alternate regeneration procedure aimed at the selective removal of the spent chromium salt after reaction was not successful, as some CrO_3 leached from the polymer at the same time as the reduced chromium salt.

(12) Reference 7 shows that the recommended ratio of resin to alcohol for most reactions with the chromate ion exchange resin is of 3.5 g of resin per mmol of alcohol. However, such a high ratio is not well-suited for practical applications.

Effects of Structure on the Ease of Electron Removal from *o*-Phenylenediamines

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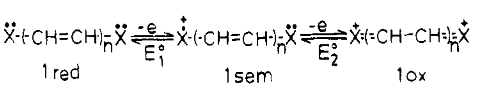
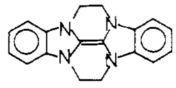
Received December 5, 1977

Cyclic voltammetric (CV) data are reported for 23 alkyl-substituted *o*-phenylenediamine derivatives, including examples with *N,N′*-alkyl bridging and bis bridging. The ^{13}C NMR shift at C_4,C_5 of the aromatic ring appears to be a good criterion for the average amount of lone pair, aromatic ring overlap in the neutral materials. For several examples, both $E°_1$ and $E°_2$ were measured by CV. $E°_1$ varies by over 1.1 V (25 kcal/mol) in the series investigated and is discussed in terms of electronic and steric effects. The dications are argued to be significantly nonplanar from the observed $E°$ values, and the 1,4,5,8-tetramethyl-1,2,3,4-tetrahydroquinoxaline dication was found to have nonequivalent CH_2 hydrogens at −88 °C by ^{1}H NMR.

Electrochemical studies allow measurement of the standard oxidation potential ($E°$) for electron-transfer reactions, providing that these reactions are electrochemically reversible, which requires both chemical reversibility and that electron transfer is rapid on the time scale of the experiment. $E°$ values are of particular interest because they are a measure (relative to the reference electrode used, or of one compound relative to another[1]) of the free energy difference between oxidized and reduced forms. More than 1 electron can be reversibly added to or removed from some compounds. Hünig[2] has suggested the term "violene" to designate radical cations of systems which have lone pair bearing heteroatoms flanking a π system (symbolized by **1red** below), so that the radical cation has $2n + 3$ electrons shared by $2n + 2$ atoms (**1sem**). For violenes, all three oxidation states are frequently long lived,[2] allowing both $E°_1$ and $E°_2$ to be measured electrochemically and other physical and chemical methods to be used to characterize these redox-related species. Hünig and co-workers[3] have carried out extensive studies of a variety of violenes. The difference in standard potentials for the two oxidations, $\Delta E° = E°_2 - E°_1$, is a measure of the disproportionation constant for the sem form, because $K_d = (\text{sem})^2/(\text{red})(\text{ox}) = \exp C\Delta E°$, where $C = (23.06 \times 10^3)/(1.987T)$, where $\Delta E°$ is in V, and T is in K. The K_d values observed for violenes vary tremendously with structure. An unusually large K_d was observed for **2**, $K_d = 2.6 \times 10^{14}$ ($\Delta E° = 0.85$ V), while at the other extreme, **3** has a negative $\Delta E°$,[4] the second electron being easier to remove than the first, in spite of the electrostatic problem in going to a dication. Fritsch and co-workers[4] pointed out that only the sem form of **3** has a strong requirement of planarity for the two



1red 1sem 1ox



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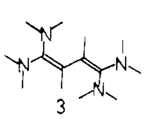

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