was decolorized with activated charcoal and recrystallized several times from ether–pentane, yielding 10.5 g (51%) of fine orange needles: mp 92–93°; nmr (CCl_4) δ 6.8–7.7 (m, Ar H's, 8), 4.46, 4.16 (t's C_5H_4, 4), 3.90 (s, C_5H_5, 5), 2.86 (s, C-2 H's, 2), 2.37 (s, CH_3, 3).

Anal. Calcd for $C_{25}H_{22}D_2O_3SFe$: C, 64.94; H and D, 5.63. Found: C, 64.22; H and D, 5.50.

Solvolysis Reactions. All solvents were deoxygenated by several hours of refluxing while a stream of N_2 was bubbled through the liquid. The reactions were carried out under N_2 using 0.50 g of 1-OTs-*1*-d_2 and 50 ml of solvent under the conditions given in Table I. Each reaction mixture was worked up by pouring into ice–H_2O, extraction with ether, washing with $NaHCO_3$ solution and then with H_2O, and chromatographing the residue from the extract through alumina which separated any unreacted tosylate from the product. In preliminary trials, it was noted that, while 1-OH and 1-OAc from solvolyses in acetone–H_2O and in HOAc were stable over alumina, passage of the formolysis product through the alumina column resulted largely in cleavage of the formate to the alcohol. Consequently, after separation of any unreacted tosylate, the acetolysis and formolysis products were hydrolyzed by refluxing for 8 hr in 50 ml of dioxane–20 ml of 10% NaOH and all D scramblings were measured using the resulting 1-OH-d_2.

Acknowledgment. The financial support given by the National Research Council of Canada is gratefully acknowledged.

Registry No. Methyl *p*-ferrocenylphenylacetate, 12290-33-4; 2-(*p*-ferrocenylphenyl)ethyl-*1,1*-d_2 tosylate, 43225-00-9; 2-(*p*-ferrocenylphenyl)ethanol-*1,1*-d_2, 43189-89-5; *p*-aminophenylacetic acid, 1197-55-3.

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Metal Ion Catalysis of Oxygen-Transfer Reactions. IV. The Molybdenum-Catalyzed Oxidation of Substituted Azobenzenes[1a]

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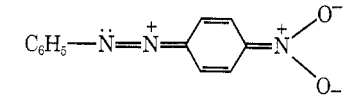
The scope of hydroperoxide oxidations, as catalyzed by molybdenum compounds, has widened perceptibly in recent years. Such oxidations have been used to convert alkenes to epoxides,[2] imines to imine oxides,[3] tertiary amines to amine oxides,[4] and substituted anilines to nitrobenzenes.[5] We here report extension of the use of the molybdenum–hydroperoxide combination to the oxidation of substituted azobenzenes to azoxybenzenes, a conversion which is generally carried out with peroxycarboxylic acids. In comparing the two methods, we find that the yields of azoxy compounds from the metal-catalyzed reactions compare favorably with those from the peroxy acids, but reactions with the RO_2H–Mo systems are considerably slower. In favorable cases, the catalyzed oxidations exhibit significant regiospecificity; moreover, we would anticipate them to be useful for azo oxidations in cases where a peracid-sensitive group (such as keto) lies elsewhere in the molecule. The catalyzed oxidations have not been effective in the oxidation of azobenzonitriles.

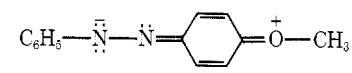
In conjunction with *tert*-butyl hydroperoxide, we have used, as catalysts, molybdenum hexacarbonyl [$Mo(CO)_6$] and the dipivaloylmethane chelate of molybdenum(VI) [$MoO_2(dpm)_2$],[6] both of which are soluble in hydrocarbon solvents. Reaction conditions, yields, and conversions are summarized in Table I.

The marked similarity between the $MoO_2(dpm)_2$-catalyzed oxidations here described and the $MoO_2(acac)_2$-catalyzed epoxidation of olefins (for which kinetic evidence points to a nonradical path[2b]) suggests a polar mechanism featuring the transfer of electron-deficient oxygen to one of the azo nitrogens, and the observed catalytic ineffectiveness of those metal centers which promote homolysis of hydroperoxides[6] may be taken as further evidence for the heterolytic character of the catalyzed azo oxidations. Moreover, with each of the unsymmetrically substituted azobenzenes, the distribution of isomeric azoxy products from the $MoO_2(dpm)_2$-catalyzed reaction corresponds closely to that from the oxidation with peroxyacetic acid.[7] Note that, in the one case where we find a difference, the $MoO_2(dpm)_2$-catalyzed oxidation of the monomethoxy derivative is significantly more regiospecific than the oxidation with CH_3CO_3H.

The *p*-Cl substituent appears to have little directive effect in reactions of this kind, for oxidations of the 4-chloro compound yield mixtures of azoxy products with the α isomer only slightly predominant.[8] In the oxidation of the nitro and monomethoxy compounds, the sites at which attack preferentially occurs, both with *t*-BuO_2H–$MoO_2(dpm)_2$ and with CH_3CO_3H, are consistent with significant contributions of structures 1 (N_β deactivated)[8] and 2 (N_α activated). The reaction of the methoxy derivative in acetic acid is, however, complicated by the partial conversion of this azo compound to its conjugate acid,[9] with protonation principally at N_α, which is the more nucleophilic nitrogen. In the latter oxidation the ratio of the two possible azoxy products will depend not only on the mode of partition of the azo compound between two acidic and one basic forms, but also on the rate of oxidation of each form. The oxidation with *t*-BuO_2H–$MoO_2(dpm)_2$, which is carried out in a nonacidic medium, is free from this complexity and yields only the α product.



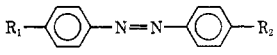
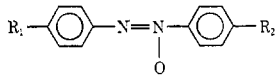
1



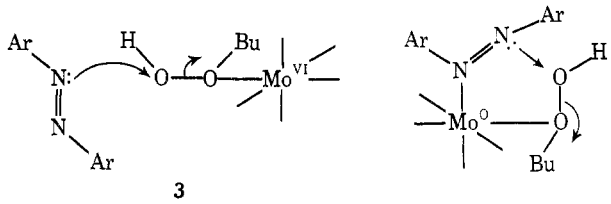
2

With $Mo(CO)_6$ as catalyst, the hydroperoxide oxidation of the monomethoxy compound yields a mixture of nearly equal quantities of α and β azoxy products. This striking change in selectivity argues strongly that substantial alteration in mechanism has resulted from variation in the oxidation state and the ligand environment of molybdenum. The $MoO_2(dmp)_2$-catalyzed reaction may be reasonably assumed to proceed through the same type of Mo(VI)–hydoperoxide complex which has been shown[2b] to intervene in the $MoO_2(acac)_2$-catalyzed epoxidation of cyclohexene. For the $Mo(CO)_6$-catalyzed reaction, in which the active catalytic species[10] features molybdenum in one of its lower oxidation states, reaction through a ternary complex of metal, substrate, and oxidant, such as those characterized in oxidation catalyzed by the lower oxidation states of rhodium and iridium,[11] remains a clear possibility. Suggested transition states for the two types of catalyzed oxidation are shown schematically as **3** and **4**.

Table I
Oxidations of Substituted Azobenzenes[a]

Reactant			Products							
										
Registry no.	R_1	R_2	Registry no.	R_1	R_2	%	Oxidant[b]	Time, hr	Total yield, %	Conversion, %
21650-55-5	OCH_3	OCH_3	21650-70-4	OCH_3	OCH_3		A	4	78	95
21650-49-7	OCH_3	H	43187-18-4	OCH_3	H	100	A	4	81	95
				OCH_3	H	47	B	24	88	95
			43187-52-6	H	OCH_3	53				
				OCH_3	H	74	C	20	75	100
				H	OCH_3	26				
				OCH_3	H	62	D	1	86	100
				H	OCH_3	38				
6141-95-3	Cl	H	43187-53-7	Cl	H	60	A	24	73	76
			43187-54-8	H	Cl	40				
				Cl	H	60	C	20	50	100
				H	Cl	40				
20488-61-3	NO_2	H	43187-19-5	NO_2	H	100	A	24	73	30
				NO_2	H	100	C	20	84	100
				NO_2	H	100	D	24	86	100

[a] Reaction temperature 60°. [b] Oxidants: A, *t*-BuO_2H–$MoO_2(dpm)_2$, benzene; B, *t*-BuO_2H–$Mo(CO)_6$, benzene; C, CH_3CO_3H, HOAc; D, *m*-$ClC_6H_4CO_3H$, $CHCl_3$.



3

In our view, the most interesting facet of this study relates to the directive effects encountered. In virtually all other cases in which an activating group is substituted for a deactivating group on a conjugated system, the effects of the two groups, although of opposite character, are transmitted to the same site or sites. Aromatic azo compounds appear to be unique in that conjugative deactivation by a ring substituent operates on one nitrogen, whereas conjugative activation affects the other, with the net result that either a strongly electron-attracting or a strongly electron-donating substituent at one para position directs electrophilic attack to that nitrogen adjacent to the unsubstituted ring.[12]

Experimental Section

Melting points were taken in open capillary tubes and are uncorrected. Ultraviolet spectra in ethanol were recorded on a Cary 14 spectrophotometer. Mass spectra of azoxy derivatives were measured with an A.E.I. MS 12 mass spectrometer operating at 70 eV with the source at 200°; the spectra were additionally determined at 80° to show that no thermal migration of oxygen had occurred. Both ultraviolet and mass spectra were taken on materials crystallized from aqueous ethanol, for noncrystallized material gave unsatisfactory spectra. It is thus possible that the isomer distributions in the analyzed azoxy products differed slightly from those in the crude products.

Materials. *tert*-Butyl hydroperoxide[13a] and *m*-chloroperoxybenzoic acid[13b] were purified and analyzed as described. *p*-Nitroazobenzene (Aldrich) was purified by chromatography on neutral alumina (Merck), eluting with CH_2Cl_2, then recrystallized from ethanol. *p*-Chloroazobenzene[14a] and azodianisole,[14b] both prepared as described, were purified by recrystallization from ethanol, as was *p*-phenylazoanisole (Pfaltz and Bauer). Metal chelates were prepared as described.[6] Benzene (Matheson Spectroquality) was dried over 4A molecular sieve before use.

Molybdenum-Catalyzed Oxidations. The substituted azobenzene (1.2 mmol), $MoO_2(dpm)_2$ (8 mg, 0.016 mmol), and *tert*-butyl hydroperoxide (0.45 g, 5 mmol) were dissolved in 10 ml of benzene, and the reaction mixture was heated in a stoppered flask at 60°. Reaction times are listed in Table I. The mixture was cooled and filtered, the solvent was evaporated under vacuum, and the oily residue was chromatographed on W200 neutral alumina (Waters). Two bands were eluted: the first, with CH_2Cl_2, yielded unreacted starting material; the second, with 97:3 CH_2Cl_2–acetone, yielded the azoxy compound, which was crystallized from aqueous ethanol.

Oxidation of azodianisole yielded 4,4′-dimethoxyazoxybenzene in 78% yield: mp 115–116° (nematic), 135° (isotropic) (lit.[15] mp 118°, 135°); nmr (CCl_4) A_2B_2 aromatic δ 8.16 (d, 4, J_{AB} = 9.5 Hz) and 6.84 (d, 4, J_{AB} = 9.5 Hz), 3.78 (s, 6); λ_{max} (EtOH) 355 nm (ϵ 2.47×10^4).

Oxidation of *p*-phenylazoanisole yielded 4′-methoxy-*NNO*-azoxybenzene (the α isomer[8]) in 72% yield: mp 68–69° (lit.[16] mp 66.5–67.5°); mass spectrum *m/e* (rel intensity) 228 (42), 212 (21), 135 (16), 121 (47), 107 (60), 77 (100). For comparison, the β isomer[16] was isolated from the peroxy acid oxidation, described below, by fractional crystallization from hexane at constant melting point, mp 41–42° (lit.[16] mp 42–43°).

Oxidation of *p*-chloroazobenzene yielded a mixture of the α and β-azoxy derivatives[8] (3:2) with total yield 73%, mp 61–62°. Recorded melting points are 81–82° for the pure α and 69–70° for the pure β isomer.[17]

Oxidation of *p*-nitroazobenzene yielded only the α-azoxy compound: mp 150–151° (lit.[16] mp 152–153°); mass spectrum *m/e* (rel intensity) 243 (14), 122 (10), 105 (17), 91 (13), 77 (100).

The oxidation of the *p*-methoxy compound, as catalyzed by $Mo(CO)_6$, was performed under similar reaction conditions but yielded a mixture of the isomeric azoxy derivatives.

Oxidations with Peroxy Acids. For oxidations with peroxyacetic acid, the azo compound (1.2 mmol) was treated with 2.0 ml of 30% hydrogen peroxide in 15 ml of glacial HOAc for 20 hr at 60°. The cooled reaction mixture was added to 100 ml of water, and the solution was extracted with two 25-ml portions of CH_2Cl_2. The combined extracts were washed with 5% $NaHCO_3$, dried over anhydrous Na_2SO_4, and concentrated under vacuum. Subsequent work-up was as described for the catalyzed oxidations.

For oxidations with *m*-chloroperoxybenzoic acid, 1.2 mmol of the azo compound and 530 mg of the peroxy acid were dissolved in chloroform and allowed to react for 1 hr at 60°. The reaction mixture was cooled, washed with aqueous Na_2SO_3, dried over Na_2SO_4, and concentrated under vacuum. Subsequent work-up was as described above.

Analyses of Mixtures of Isomeric Azoxy Compounds. The fractions of α and β isomers in the azoxy products derived from oxidation of the 4-chloro and 4-nitro azo compounds were determined mass spectrometrically.[18] Analyses of the mixtures from the oxidation of the 4-methoxy compound were by uv spectroscopy, using the ratio of absorbances at 300 and 250 nm. The ratio A_{300}/A_{250} (EtOH) was found to be 0.584 for the pure α isomer and 1.435 for the β.

Attempts to study the kinetics of reactions catalyzed either by $MoO_2(dpm)_2$ or $Mo(CO)_5$ were unsuccessful, owing to partial and gradual deactivation of the catalyst and small amounts of precipitation during the course of the reaction. No complex could be ob-

served between $MoO_2(dpm)_2$ and *p*-phenylazoanisole, either in the visible or the ultraviolet spectra.

Acknowledgments. The authors are indebted to Mr. David Mattern for mass spectrometric analyses and to Dr. John Gordon for valuable discussions.

Registry No. *t*-BuO_2H, 75-91-2; $MoO_2(dpm)_2$, 34872-98-5; $Mo(CO)_6$, 13939-06-5; CH_3CO_3H, 79-21-0; *m*-$ClC_6H_4CO_3H$, 937-14-4.

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(1) (a) This work was sponsored by the National Science Foundation (Grant GP-23136). Support is gratefully acknowledged. (b) Postdoctoral Research Associate.
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(6) The dipivaloylmethane derivatives, $Co(dpm)_2$, and $VO(dpm)_2$, as well as the acetylacetone chelate, $Mn(acac)_3$, each of which has been shown to decompose *t*-BuO_2H with production of *t*-BuO· and *t*-BuO_2· radicals [see, for example, N. A. Johnson and E. S. Gould, *J. Amer. Chem. Soc.*, **95**, 5198 (1973)], exhibited no catalytic activity in the oxidation of azobenzenes.
(7) All azo and azoxy compounds in the present study are assumed to be trans, rather than the considerably less stable cis forms. See, for example, G. M. Badger, R. G. Buttery, an G. E. Lewis, *J. Chem. Soc.*, 2143 (1953); D. L. Webb and H. H. Jaffe, *J. Amer. Chem. Soc.*, **86**, 2419 (1964).
(8) Current usage designates the α isomer of a substituted azoxybenzene as that with the NO group adjacent to the less substituted aryl ring; see, for example, G. G. Spence, E. C. Taylor, and O. Buchart, *Chem. Rev.*, **70**, 231 (1970). In an extension of this convention, we here indicate that nitrogen adjacent to the less substituted ring in the parent azo compound as N_α, and the other as N_β.
(9) The H_0 value for anhydrous acetic acid has been estimated as 0.00 [N. M. Milyaeva, *Russ. J. Inorg. Chem.*, **3**, 2011 (1958)], and the pK_a for the monomethoxy azo compound as −0.02 [H. H. Jaffe and R. W. Gardner, *J. Amer. Chem. Soc.*, **80**, 319 (1958)]. Note, however, that the latter value was determined in 20% ethanolic sulfuric acid.
(10) Both Baker[2a] and Su[2b] have presented evidence that $Mo(CO)_6$ must lose at least one CO molecule before becoming catalytically active in the epoxidation of olefins.
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(12) Although there are several levels at which the orientation effects associated with azobenzenes can be rationalized, we prefer to regard them merely as reflections of the peculiar structure of the azo group, which has two chemically similar atoms connected by a double bond, with each atom having, in addition, an unshared pair of electrons. None other of the usual organic structural units fit this description.
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(17) T. E. Stevens, *J. Org. Chem.*, **29**, 311 (1964).
(18) Both E. T. McBee, G. W. Calundann, M. T. Hodgins, and E. P. Wessler [*J. Org. Chem.*, **37**, 3140 (1972)] and J. H. Bowie, R. G. Cooks, and G. E. Lewis [*Aust. J. Chem.*, **20**, 1601 (1967)] have shown that the base peaks in the mass spectra of azoxybenzenes are produced by C–N cleavage adjacent to N–O. Evidence of the latter group of authors suggests, however, that this generalization breaks down for azoxy compounds having strongly electron-donating substituents.

Azabicyclo Chemistry. IV. A New Route to 2-Azabicyclo[3.3.1]nonanes Containing a Functionalized Carbocyclic Ring[1]

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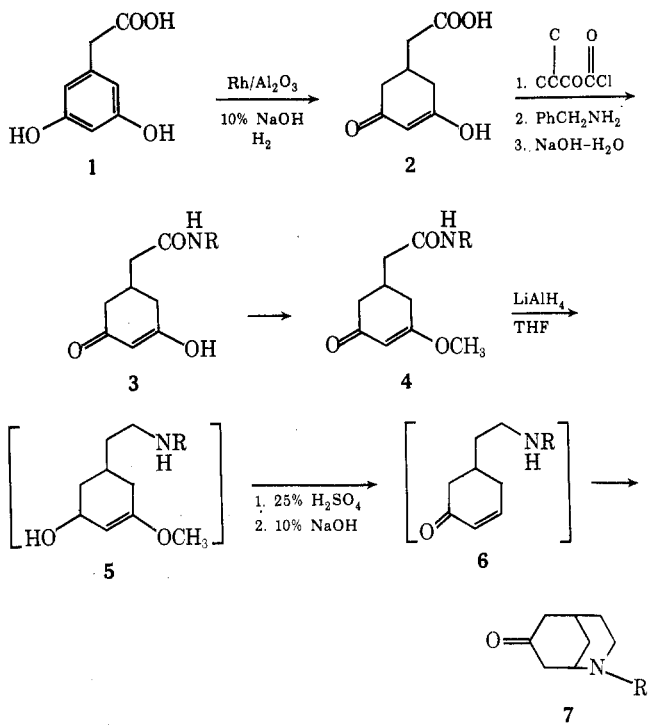
We have been interested in functionalized 2-azabicyclo[3.3.1]nonanes because of their possible elaboration into more complex molecules with potential analgetic activity. An inspection of the literature indicates a paucity of routes to the 2-azabicyclo[3.3.1]nonane skeleton and only a few examples[2] of any derivatives having a functional group in the carbocyclic ring. Our synthetic route was chosen on analogy to that used for another azabicyclo system[3] and was dependent on the success of an intramolecular Michael-type cyclization.

Diethyl 3-oxoglutarate was converted in two steps, by a slight modification of the procedure of Theilacker and Schmid,[4] to crystalline 3,5-dihydroxyphenylacetic acid (**1**), the starting point in the synthesis. The latter authors[4] reported obtaining the dione **2** in a 59% yield by conversion of **1** to its ethyl ester followed by reduction with Pt/H_2. We were able to improve not only the yield, but the time necessary for obtaining **2** by directly reducing **1** in an atmosphere of H_2 (50 psi) with rhodium on alumina in base at elevated temperature, thus affording **2** in a 77% yield. The physical properties were consistent with **2** existing in the expected enolic form, that is, uv max 254 nm (ϵ 14,800) and nmr (DMSO-d_6) δ 5.20 (s, 1, vinyl H).



a, R = $CH_2C_6H_5$
b, R = CH_3

Amide formation directly on **2** is complicated by the fact that primary amines also react with the conjugated enolic system. We were able to overcome this by forming the amide by the mixed carbonic anhydride method used by Anderson, *et al.*,[5] for the synthesis of peptides. When **2** is treated with 2 equiv of isobutyl chloroformate and *N*-methylmorpholine ("inverse addition"[5]), not only is the carboxyl activated for amide formation but the enolic hydroxyl is protected as the carbonate ester. Subsequent treatment with benzylamine or methylamine, followed by hydrolysis of the intermediate carbonate and neutralization, gave the amides **3a** and **3b** in 60 and 64% yields, respectively. A solution of **3a** in refluxing methanol containing *p*-toluenesulfonic acid readily gave the enol ether **4a** in a 89% yield, nmr δ 3.65 (s, 3, OCH_3), uv max 248 nm (ϵ 16,400). The methylamide **3b** was also converted to its methyl enol ether **4b**; however, it apparently was more sensitive to hydrolysis as attempts at crystallization