into sp^3. On the basis of the results it can be concluded that **12b**$^-$, **12c**$^-$, and **12d**$^-$ are anionic σ complexes.

^{1}H NMR Spectroscopic Evidence for Anionic σ Complexes. It is well-known that ^{1}H NMR spectroscopy is a useful tool for elucidating the structures of anionic σ complexes.[2] We already reported the time-dependent ^{1}H NMR spectra of the reaction of 1-piperidino-2,4-dinitronaphthalene (**12a**; 1.83×10^{-4} mol) with $NaOCH_3$ (1.83×10^{-4} mol) in 0.62 mL of Me_2SO–CH_3OH (4.2/1, v/v),[16] in which the changes in chemical shifts of aromatic protons from **12a** to **2a**$^-$ were typical for formation of an anionic σ complex.

The results of relevant chemical shifts (**12b,c**, **2b**$^-$,**c**$^-$, **13b,c**, and **12b**$^-$,**c**$^-$) are listed in Table IV[18] [for information about the spectra of **13a** (1-methoxy-2,4-dinitronaphthalene) and **13a**$^-$ (anionic σ complex), see ref 2g]. The changes in chemical shifts of aromatic protons from **12b** and **12c** to **2b**$^-$ and **2c**$^-$ are similar to those from **13b** and **13c** to **13b**$^-$ and **13c**$^-$, respectively.

In addition, in the course of the reactions of **13b** → **13b**$^-$ and **13c** → **13c**$^-$ the signal of the methoxyl protons shifted upfield as a sharp singlet [δ 4.18 (3 H) → 2.78 (6 H) and 4.45 (3 H) → 2.87 (6 H)], indicating the change in hybridization of the C_1 atom of a naphthalene ring (sp^2 → sp^3). These results clearly indicate that the anionic σ complexes are formed in the reactions of **12a–c** or **13a–c** with $^-OCH_3$ in Me_2SO.

(18) Supplementary material.

Registry No. 3b, 61499-36-3; **3c**, 61499-37-4; **3d**, 61499-38-5; **5**, 35462-47-6; **6**, 71436-05-0; **7**, 71436-06-1; **8**, 575-41-7; **9**, 71436-07-2; **10**, 71436-08-3; **11**, 71436-09-4; **12b**, 71436-10-7; **12b**$^-$, 71462-69-6; **12c**, 71436-11-8; **12c**$^-$, 71462-70-9; **12d**, 71436-12-9; **12d**$^-$, 71462-71-0; **13b**, 71436-13-0; **13b**$^-$, 71462-72-1; **13c**, 67122-11-6; **13c**$^-$, 71462-73-2; 1-hydroxy-2-naphthoic acid, 86-48-6; $NaOCH_3$, 124-41-4.

Supplementary Material Available: Table IV, relevant NMR chemical shifts (1 page). Ordering information is given on any current masthead page.

Ipso Nitration. An Efficient Synthesis of Ipso Nitration Products of Aromatic Hydrocarbons

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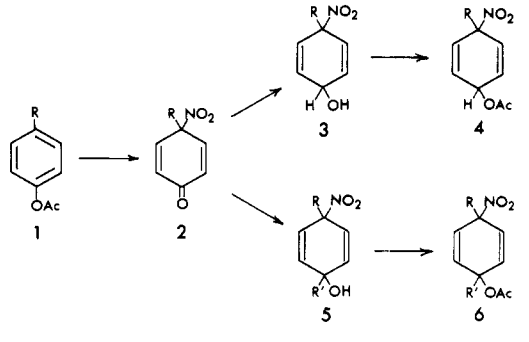
Received February 6, 1979

Ipso nitration products of aromatic hydrocarbons have been synthesized from phenols. Nitration of a number of 4-alkylphenyl acetates gave 4-alkyl-4-nitrocyclohexadienones. Reduction of these nitrodienones with sodium borohydride in methanol gave 4-alkyl-4-nitrocyclohexadienols. These labile nitrodienols were converted to the more easily handled 4-alkyl-4-nitrocyclohexadienyl acetates by low-temperature acylation with acetyl chloride and pyridine. Representative nitrodienyl acetates were synthesized by this three-step sequence in 60% yield from the starting phenyl acetate. The synthesis of 1,4-dimethyl-4-nitrocyclohexadienol from 4-methyl-4-nitrocyclohexadienone illustrates the use of organolithium reagents in 1,2-addition to the carbonyl center of nitrodienones.

In the course of studies of reaction pathways of ipso nitration products it became necessary to develop an indirect procedure for synthesis of certain specifically labeled ipso nitration products.[1,2] The procedure appeared to be an efficient one and one of quite general scope. Further, the method offered distinct advantages over direct methods, particularly for the preparation of ipso nitration products that contain only one alkyl group attached to the carbocyclic ring.[3] We report here a summary of some work directed toward development of this synthetic procedure.

The approach is based on the known reaction, nitration of 4-alkylphenyl acetates, which yields 4-alkyl-4-nitrocyclohexadienones.[4,5] We hoped that methods could be found to effect 1,2-addition at the carbonyl group by metal hydrides or alkyllithium reagents to yield nitrocyclohexadienols. These nitrodienols could be used directly or they could be converted to the more tractable acetate derivatives. This scheme is summarized in Chart I.

Chart I



The potential flexibility of the scheme deserves emphasis. The only formal requirement is the positioning of an alkyl group para to the oxygen substituent.[6] The five remaining positions are subject to considerable structural variation. It should also be noted that a characteristic reaction of 4-alkyl-4-nitrocyclohexadienols and their

(1) C. E. Barnes and P. C. Myhre, *J. Am. Chem. Soc.*, **100**, 975 (1978).
(2) K. S. Feldman, A. McDermott, and P. C. Myhre, *J. Am. Chem. Soc.*, **101**, 505 (1979).
(3) A. Fischer and J. N. Ramsay, *J. Chem. Soc., Perkin Trans. 2*, 237 (1973).
(4) D. J. Blackstock, J. R. Cretney, A. J. Lewis, K. E. Richards, J. Vaughan, and G. J. Wright, *J. Chem. Soc. B*, 1212 (1971).
(5) A. H. Clemens, M. P. Hartshorn, K. E. Richards, and G. J. Wright, *Aust. J. Chem.*, **30**, 113 (1977).

(6) Possible use of o-alkylphenols and substituent groups other than alkyl would increase the flexibility of the scheme.

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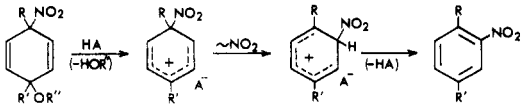
acetate derivatives is the acid-induced elimination of water (or acetic acid) with concomitant 1,2-shift of the nitro group to an open position (eq 1). Thus a combination of



(1)

3,4,5 or 6

R' = H or R

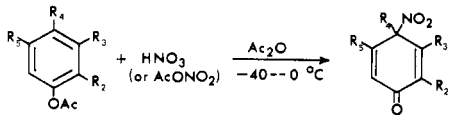
R'' = H or Ac

the reactions shown in Chart I and eq 1 represents not only the formal reduction of an aromatic carbon–oxygen bond but also a useful synthesis of certain classes of *o*-nitroalkylbenzenes that are free of contamination by structural isomers.

While simple in conception, the scheme shown in Chart I suffers from the extreme lability of the intermediates. The nitrocyclohexadienones are not thermally stable. Half-lives of these intermediates in hydrocarbon solvents are as short as 20 min at room temperature.[7] Further, the decomposition of nitrocyclohexadienones is strongly catalyzed by concentrated acids.[7,8] The nitrocyclohexadienols are both thermally labile and solvolytically reactive with half-lives in water of about 10 s or less.[2] Hence the major synthetic problems involved the development of mild but effective reaction conditions and similar conditions for isolation.

Results

Several 4-alkyl-4-nitrocyclohexa-2,5-dienones were prepared in good yield by low-temperature nitration of the appropriate 4-alkylphenyl acetate with 90% nitric acid or acetyl nitrate in acetic anhydride (eq 2). Attempts to



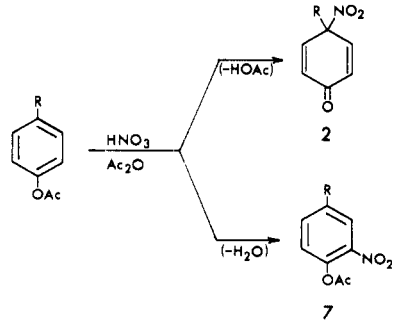
(2)

1 2

a, R_4 = Me; R_2, R_3, R_5 = H; b, R_3, R_4 = Me; R_2, R_5 = H; c, R_3, R_4, R_5 = Me; R_2 = H; d, R_2, R_3, R_4 = Me; R_5 = H; e, R_4 = Et; R_2, R_3, R_5 = H; f, R_4 = *i*-Pr; R_2, R_3, R_5 = H

prepare 4-*tert*-butyl-4-nitrocyclohexadienone and 4-chloro-4-nitrocyclohexadienone from the parent phenyl acetates under these reaction conditions were not successful. The only products detected in the ^{1}H NMR spectra of crude reaction mixtures with these substrates were the 2-nitro substitution products.

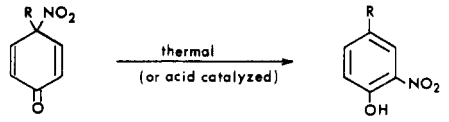
Several factors were important in the optimization of reaction yields for eq 2. At least 2 equiv of nitric acid were necessary to effect complete conversion of reactants. Minimizing the reaction temperature appeared to maximize the nitrodienone–nitrophenyl acetate ratio (eq 3).



(3)

2 7

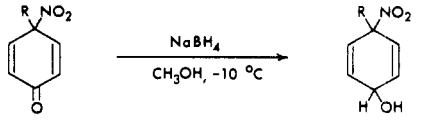
A lower reaction temperature also minimizes the thermal and possible acid-catalyzed decomposition of the nitrodienone products (eq 4).



(4)

2 8

The reduction of several of the nitrodienones **2** to the corresponding nitrodienols **3** could be effected by the action of sodium borohydride in methanol at −15 to 0 °C (eq 5). Products of reduction were isolated with minimum



(5)

2 3

thermal or solvolytic loss by addition of acetic acid followed by vacuum evaporation of the volatiles at −10 °C to yield a crude product as a glassy solid. The crude product was dissolved in cold methylene chloride or chloroform and extracted with cold brine to remove soluble borates and other salts. Subsequent removal of solvent provided the nitrodienols **3** as pale yellow oils or low-melting solids which were characterized by low-temperature ^{1}H NMR spectroscopy. Because of the sensitivity of the nitrodienols, they were used directly or transformed to the more stable nitrodienyl acetates **4**.

Acylation of the nitrodienols was accomplished by dropwise addition of a methylene chloride solution of acetyl chloride to a methylene chloride–pyridine solution of the nitrodienol held at −40 °C. Again, careful temperature control and short contact times with aqueous solutions used for extraction were necessary to achieve good yields of the nitrodienyl acetates.

A standard procedure for the preparation of representative nitrodienyl acetates from phenyl acetates (Chart I) without isolation of intermediates was developed. Repeated trials of this method indicate that **4a**, **4b**, or **4c** can be prepared from the appropriate phenyl acetate in about 60% overall yield (see Experimental Section and Table II).[9]

The use of alkyllithium reagents for 1,2-addition to the carbonyl group of nitrodienones is illustrated by the conversion of **2a** to 1,4-dimethyl-4-nitrocyclohexadienol by reaction of methyllithium in ether. As in other syntheses of nitrodienols, care in workup was crucial to successful isolation of product. Acylation with acetyl chloride and pyridine gave the corresponding nitrodienyl acetate.

^{1}H NMR analyses of the nitrodienols formed by the synthetic route described indicate from 65 to 85% stereoselectivity. Conversion of the nitrodienols to nitroacetates provided a means of correlation. In all of the examples studied, the major diastereoisomeric nitrodienyl acetate formed by this indirect route was the diastereoisomer formed in minor amount by direct reaction of the aromatic hydrocarbon with acetyl nitrate in acetic anhydride.

(7) C. E. Barnes and P. C. Myhre, *J. Am. Chem. Soc.*, **100**, 973 (1978).
(8) R. G. Coombes and J. G. Golding, *Tetrahedron Lett.*, 3583 (1978).

(9) Nitrocyclohexadienols **3** and nitrocyclohexadienyl acetates **4** with different alkyl group substitution patterns are designated by the letter code defined in eq 2. Thus **3a** and **4a** refer to 4-methyl-4-nitrocyclohexadienol and 4-methyl-4-nitrocyclohexadienyl acetate, respectively.

Table I. Product Distributions from Nitration of Some Phenyl Acetates in Acetic Anhydride

reactant	temp, °C	% product ortho	meta	para or ipso
phenyl acetate[a]	20	27	<1	72
1a	−40	14		86
	0	15		85[b]
1b	−40	14		86
	0	13		87
1c	−40	22		78
	30	33		67
1e	−15	15		85

[a] Reference 12. [b] Includes 15% nitrophenol from decomposition of the dienone.

Discussion

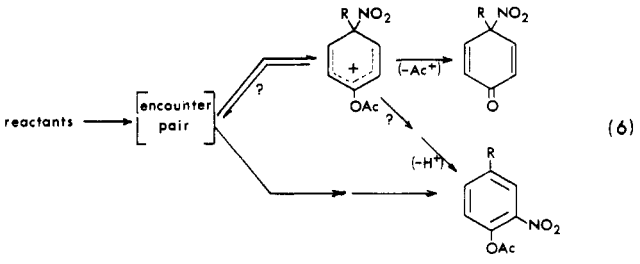
The preparation of the various 4-alkyl-4-nitrocyclohexadienones (2) follows directly from previously described procedures.[4,5] There is good evidence for the formation of 1,4-adducts in the initial stage of the synthesis of nitrodienones from related 4-alkylanisole derivatives.[10,11] However, the detailed mode by which the acetoxyl group at C-1 in 4-alkylphenyl acetates is transformed to the carbonyl group is not known at present. We have not detected adducts of acetyl nitrate in these reactions. More sensitive tests of this and other aspects of the transformation are in progress.

The preparations of the nitrodienones described in the Experimental Section illustrate some of the many minor variations in experimental procedure that have been used. These variations do not appear to affect the primary course of the reaction. The variations do, however, affect the degree of conversion and the extent to which the thermally stable nitrodienones decompose to yield nitrophenol products.[7] We conclude on the basis of optimization studies that the most generally useful procedure is that described as part of the multistep synthesis of **4a**, **4b**, and **4c**. Variations that involve precipitation of nitrodienone product have distinct advantages when ease of preparation rather than yield is of prime importance.

Where overlap exists, our results are in reasonable agreement with those reported by the Canterbury group.[4,5] There is, however, one exception. Nitration of **1a** at 0 °C in acetic anhydride was reported to yield 20 ± 5% 4-methyl-3-nitrophenyl acetate.[5] We have been unable to detect this product in the ^{1}H NMR spectra of either crude reaction mixtures or mother liquors. Since more sensitive analytical procedures have not been applied to this question, a conservative upper bound for the yield of this product is placed at 3–5%, on the basis of our results.

It is interesting to compare the yields of the nitrodienone product obtained in this work with those predicted by application of the additivity principle, under the assumption that nitration at the positions meta to the acetoxyl group is negligible. Given this assumption, distribution data for the nitration of phenyl acetate in acetic anhydride,[12] and derived partial rate factors for the nitration of toluene in the same medium,[13,14] one predicts 86% **2a**, 82% **2b**, and 78% **2c** upon nitration of the respective reactants. As indicated by the data collected in Table I, these predictions agree suprisingly well with the yield data observed.

One additional qualification must be noted. The yields of nitrodienone products represent minimum estimates of the fraction of ipso attack, since the possibility remains that some migration of the nitro group will occur before the ipso ion is converted to the nitrodienone by formal loss of the acyl group (eq 6).



(6)

Reduction of the carbonyl group of more stable cyclohexadienones has been carried out by various procedures.[15,16] Vitullo and co-workers have recently prepared 4,4-dimethylcyclohexadienol and 4-methyl-4-(trichloromethyl)cyclohexadienol by reduction with aluminum isopropoxide in 2-propanol, sodium borohydride in ethanol, and lithium aluminum hydride in ether.[17] We found that nitrodienones (**2a–c** and **2e**) could be efficiently reduced by sodium borohydride in methanol at temperatures ranging from −15 to 0 °C. The critical feature of the reduction was the processing of the very labile nitrodienol products in order to minimize base-induced, thermal, and solvolytic decomposition. Our experimental procedure relied in part on the use of a solvent that could be removed easily under reduced pressure and low temperature. Hence the sodium borohydride–methanol system was studied in greatest detail. The use of other alcohols to minimize alcoholysis of the borohydride proved to be less useful because of greater difficulties in the isolation step. More selective reducing agents, sodium cyanoborohydride and 9-borobicyclononane, were not useful because degradation proved to be competitive with reduction. The use of more reactive metal hydride reducing agents was not explored.

A moderate degree of stereoselectivity (65–85%) was achieved in the borohydride reductions. The stereoselection was such that the major products (as the nitrodienyl acetates) were identical with the minor products formed in direct nitration of the parent hydrocarbon in acetic anhydride. On the basis of steric and field effects of the nitro group, we anticipated that the hydride would be preferentially delivered to the carbonyl group from the opposite ring face, leading to the formation of the *Z* isomer as the major product. In each case the dominant product from the route outlined in Chart I was identical with the dienyl acetate that has been assigned the *Z* configuration.[18] Similarly, addition of methyllithium gave evidence of a similar pattern of stereoselection, yielding what is believed to be the *Z* isomer as the major product.

The synthetic utility of this indirect approach to nitrodienyl acetates is perhaps best illustrated by the optimization studies of the three-step sequence. By conducting this sequence without purification of intermediates, one could prepare the nitrodienyl acetates **4a**, **4b**, and **4c** in better than 58% yield based on the starting material,

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(11) R. B. Moodie, K. Schofield, and G. D. Tobin, *J. Chem. Soc. Chem. Commun.*, 180 (1978).
(12) T. A. Modro and J. Pioch, *Can. J. Chem.*, **54**, 560 (1976).
(13) S. R. Hartshorn, R. B. Moodie, and K. Schofield, *J. Chem. Soc. B*, 1256 (1971).
(14) A. Fischer and G. J. Wright, *Aust. J. Chem.*, **27**, 217 (1974).
(15) H. Pleininger, *Angew. Chem., Int. Ed. Engl.*, **1**, 367 (1962).
(16) A. J. Waring, *Adv. Alicyclic Chem.* **1**, 197 (1966).
(17) V. P. Vitullo, M. J. Cashen, J. N. Marx, L. J. Caudle, and J. R. Fritz, *J. Am. Chem. Soc.*, **100**, 1205 (1978).
(18) Configurational assignments rest on the results of NMR shift reagent studies.

on the average a yield of better than 85% in each step.

Experimental Section

4-Methylphenol, 4-ethylphenol, 4-isopropylphenol, 4-*tert*-butylphenol, 3,4-dimethylphenol, and 3,4,5-trimethylphenol were obtained from commercial sources. 2,3,4-Trimethylphenol was available from an earlier study.[19] These phenols were converted to phenyl acetates by standard methods, and they were characterized by their physical and spectral properties. Purities of the phenyl acetates were determined by GLC analyses. All melting points were taken on a Mel-Temp apparatus and are corrected. Routine ^{1}H NMR spectra were recorded on an A-60 or a HA 100 spectrometer. Deuteriochloroform was the solvent for all NMR spectra, and chemical shifts are referenced to Me_4Si. The lability of new compounds precluded elementary analysis.

4-Methyl-4-nitrocyclohexa-2,5-dienone (2a). A 500-mL three-necked flask equipped with a mechanical stirrer and dropping funnel was charged with *p*-methylphenyl acetate (30 g, 0.20 mol), acetic anhydride (76 ml, 0.80 mol) and methylene chloride (200 mL). The contents were cooled to 0 °C, and cold 90% nitric acid (18.5 mL, 0.40 mol) was added dropwise with stirring and efficient cooling over 20 min. Stirring at 0 °C was continued for 10 min, at which time the temperature was lowered to −78 °C. A ^{1}H NMR spectrum of an aliquot recorded at −15 °C indicated complete conversion of reactants with a product distribution as follows: nitrodienone **2a**, 75%; 4-methyl-2-nitrophenol, 7%; 4-methyl-2-nitrophenyl acetate, 15%. There was no evidence of formation of 4-methyl-3-nitrophenyl acetate or the corresponding phenol.

Ammonia (26 g, 1.53 mol) was slowly condensed in the reaction flask (−78 °C) over a 3-h period. The resulting mixture was allowed to warm slowly (0 °C maximum), and the residual ammonia was removed at the aspirator. The residue was treated with 500 mL of ice–water to dissolve ammonium salts, and the layers were separated in a prechilled 1-L separatory funnel. The aqueous layer was counterextracted with 50 mL of methylene chloride, and the combined organic layers were washed successively with cold water (100 mL), 5% sodium bicarbonate (150 mL), and water (100 mL). Prechilled solvents and glassware were used throughout. The methylene chloride layer was dried over sodium sulfate at reduced temperature, and evaporation of the methylene chloride (−10 °C, 1 torr final pressure) gave 38.5 g of an orange oil that solidified in the freezer. The solid was twice triturated with methanol at −78 °C and twice recrystallized from methanol by dissolving the material in the minimum amount of methanol at 0 °C (ca. 3 mL/g) and cooling to −78 °C. The resulting colorless, well-formed crystals were collected in the cold and dried at −10 °C at 1 torr to yield 15.3 g (50%) of product: mp 43–45 °C dec; NMR δ 1.96 (s, 3 H, 4-Me), 6.35 (d, J_{app} = 10 Hz, 2 H, 2,6-H), 7.15 (d, J_{app} = 10 Hz, 2 H, 3,5-H). The ^{1}H NMR spectrum of the concentrated mother liquors from trituration revealed mainly 4-methyl-2-nitrophenol and 4-methyl-2-nitrophenyl acetate with less than 10 mol % of **2a**. Similar spectral examination of pooled mother liquors from recrystallizations indicated ca. 60% **2a**.

A more convenient method of isolation of **2a** was direct precipitation from the reaction mixture. Nitration of *p*-methylphenyl acetate in the manner described but with the omission of methylene chloride cosolvent was followed by cooling the reaction mixture to −78 °C and slow addition of methanol. The colorless crystalline crop that formed was collected by suction filtration in the cold, and recrystallization from methanol gave a 50% yield of colorless, crystalline product.

3,4-Dimethyl-4-nitrocyclohexadienone (2b). 3,4-Dimethylphenyl acetate was nitrated by addition of 2 molar equiv of 90% nitric acid to an acetic anhydride solution of the reactant held at −15 to −0 °C. The progress of the reaction was monitored by NMR spectra. These spectra indicated 85% **2b** with about 15% 3,4-dimethyl-6-nitrophenyl acetate. Isolation of the product was accomplished by one of three methods: (1) ammonolysis of the acetic anhydride, (2) vacuum evaporation of the volatiles at reduced temperature (ca. 10 °C) and recrystallization from methanol, (3) precipitation of the dienone from the reaction mixture by slow addition of methanol at −78 °C followed by filtration. The latter procedure was most convenient and gave yields in the 80% range. This crystalline product was contaminated with 3,4-dimethyl-6-nitrophenyl acetate which could be removed efficiently by crystallization from methanol (7 mL/g) over the temperature range 0 to −40 °C to give fine colorless needles: mp 76 °C dec (lit.[5] mp 76 °C); NMR ($DCCl_3$) δ 1.88 (s, 3 H, 4-Me), 2.01 (d, J_{app} = 1 Hz, 3 H, 3-Me), 6.23 (m, 1 H, 2-H), 6.36 (m, 1 H, 6-H), 6.90 (d, J_{app} = 10 Hz, 1 H, 5-H).

4-Nitro-3,4,5-trimethylcyclohexadienone (2c). Dropwise addition of 90% nitric acid (13 mL, 0.28 mol) to a mechanically stirred, cold (0 °C) solution of 3,4,5-trimethylphenyl acetate (35 g, 0.20 mol) in 70 mL of acetic anhydride led to a temperature increase to 30 °C and then a slow decrease to 5 °C. At the end of the 30-min addition period the flask was chilled to −78 °C. NMR analysis of the crude reaction mixture indicated complete conversion of starting material with 67% **2c** and 33% 2-nitro-3,4,5-trimethylphenyl acetate. Cold methanol (150 mL) was added to the reaction flask, and the crystalline crop that formed after 1 h at −78 °C was collected by suction filtration to yield 18.6 g that analyzed for 41% **2c** and 59% nitrophenyl acetate. Evaporation of the mother liquor under vacuum (1 torr, 25 °C) left 19 g of solid that analyzed for 82% **2c** and 18% nitrophenyl acetate. Further fractional recrystallization of this sample from methanol gave pure crystalline **2c**: mp 63–64 °C; NMR ($DCCl_3$) δ 1.84 (s, 3 H, 4-Me), 1.94 (d, J = 1 Hz, 6 H, 3,5-Me), 6.11 (br s, 2 H, 2,6-H). The mixture of components in the mother liquors from fractional crystallizations could be separated by column chromatography over deactivated alumina.

4-Nitro-2,3,4-trimethylcyclohexadienone (2d). A solution of 90% nitric acid (1.7 mL, 36 mmol) in 5 mL of acetic anhydride was added dropwise (30 min) to a cold (−40 °C), mechanically stirred solution of 2,3,4-trimethylphenyl acetate (1.68 g, 9.43 mmol) in a mixture of acetic anhydride (7.5 mL) and methylene chloride (10 mL). After the addition, the reaction mixture was warmed to −15 °C for 15 min and then cooled to −78 °C. An NMR spectrum indicated complete conversion of reactant. Additional methylene chloride (25 mL) was added, and ammonia (10 g) was slowly distilled (60 min) into the stirred reaction flask. Excess ammonia was removed at the aspirator, cold brine solution was added, and the methylene chloride layer was separated. This solution was extracted two times with cold (0 °C) 5% sodium hydroxide to remove nitrophenols. The methylene chloride layer was then washed with cold pH 7 buffer, dried over sodium sulfate, and evaporated at reduced temperature and pressure to yield 1.92 g of dark oil. Colorless cubic crystals formed slowly upon dilution of the oil with methanol and cooling of the solution to −78 °C. Separation of the mother liquor from the crystalline product and recrystallization from methanol gave 0.51 g of **2d**: mp 27–30 °C; NMR δ 1.85 (s, 3 H, 4-Me), 1.90 (s, 3 H), 1.91 (s, 3 H), 6.60 (quartet, J = 10 Hz, 2 H, 5- and 6-H).

4-Ethyl-4-nitrocyclohexadienone (2e). Cold 90% nitric acid (9.3 mL, 0.20 mol) was added dropwise over a 30-min period to a cold (−15 °C), stirred solution of 4-ethylphenyl acetate (16.7 g, 0.10 mol) in 40 mL of acetic anhydride and 100 mL of methylene chloride. The reaction flask temperature was raised to 0 °C for 10 min following the addition and then cooled to −78 °C. NMR analysis indicated complete conversion of reactant with the formation of 85% **2e**. Ammonia (14 g, 0.82 mol) was slowly condensed in the cold reaction flask, and the products were isolated in the manner described for the preparation of **2a**. Nitrodienone **2e** was isolated as colorless needles (4.5 g, 25%) by dissolving the isolated yellow oil in methanol (0 °C) and cooling the solution to −40 °C: mp ca. 20 °C; NMR δ 0.94 (t, 3 H, Me), 2.33 (quartet, 2 H methylene), 6.41 (d, 2 H, 2,6-H), 7.17 (d, 2 H, 3,5-H).

4-Isopropyl-4-nitrocyclohexadienone (2f). A solution of 90% nitric acid (2.4 mL, 51.4 mmol) in 5 mL of acetic anhydride was added dropwise over 30 min to a cold (−40 °C), mechanically stirred solution of 4-isopropylphenyl acetate (3.81 g, 21.4 mmol) in acetic anhydride (7.5 mL) and methylene chloride (10 mL). The mixture was maintained at −40 °C for 30 min, and then the temperature was raised to −15 °C for 15 min. The mixture was then cooled to −78 °C, and an aliquot was withdrawn for NMR analysis. The spectrum indicated that the mixture was 40% **2f**,

(19) T. Banwell, C. S. Morse, P. C. Myhre, and A. Vollmar, *J. Am. Chem. Soc.*, **99**, 3042 (1977).

45% 4-isopropyl-2-nitrophenol, 10% 4-isopropyl-2-nitrophenyl acetate, and 5% starting material. The crude product was isolated by distilling ammonia (11 g) into the vigorously stirred reaction mixture. Additional methylene chloride was added as necessary to maintain fluidity. The excess ammonia was removed at the aspirator, and cold 10% sulfuric acid was added to dissolve the salts and precipitated acetamide. The methylene chloride layer was separated, extracted twice with brine, and dried over sodium sulfate. Evaporation of the solvent left 3.51 g of brown oil with a product distribution (by NMR) nearly identical with that of the crude reaction mixture. Attempts to induce crystallization failed. The crude product was taken up again in methylene chloride and extracted repeatedly with 5% sodium hydroxide in brine solution at 0 °C. The pale yellow methylene chloride layer was dried over sodium sulfate after extraction with cold pH 7 buffer solution. Removal of the solvent left 2.00 g of yellow oil whose NMR spectrum indicated 70% **2f**, 18% nitroacetate, and 12% starting material. Dilution of the oil with 4 mL of methanol with cooling to −40 °C caused crystal formation. The mother liquor was removed with a filter stick, and the crystalline product was recrystallized twice from methanol to give 0.95 g of colorless crystals: mp 31.5–32.5 °C; NMR δ 0.95 (d, 6 H, Me), 2.78 (septet, 1 H, methine), 6.48 (d, J = 10 Hz, 2 H), 7.15 (d, J = 10 Hz, 2 H).

4-Methyl-4-nitrocyclohexadienol (3a). A sample of recrystallized 4-methyl-4-nitrocyclohexadienone (2.06 g, 13.5 mmol) was suspended in 15 mL of cold (−10 °C) anhydrous methanol, and powdered sodium borohydride (0.269 g, 7.11 mmol) was added in small portions over a 30-min interval to the magnetically stirred mixture. As the reaction proceeded the mixture became homogeneous. Fifteen minutes after the addition the solution was treated with 30 mmol of acetic acid, and the volatiles were removed at 1 torr and 0 °C to yield a solid. This material was dissolved in cold (−10 °C) methylene chloride, extracted twice with cold brine solution, and then dried over sodium sulfate at −10 °C. Removal of the solvent (1 torr, −10 °C) left a crystalline solid, 1.85 g. The NMR spectrum could be interpreted as a 2:1 mixture of diastereoisomers with the dominant form (Z isomer) exhibiting δ 1.67 (s, 3 H, 4-Me), 4.2 (v br s, 1 H, hydroxyl), 4.48 (br s, 1 H, 1-H), and 6.09 (br s, 4 H, 2,3,4,6-H) and the minor form (E isomer) exhibiting δ 1.73 (s, 3 H, 4-Me), 4.16 (v br, 1 H, hydroxyl), 4.53 (br s, 1 H), and 6.09 (br s, 4 H, 2,3,5,6-H). This material could be stored for extended periods at −78 °C, but it rapidly decomposed to a dark brown mass if held at room temperature. Decomposition products detected by GC/MS included 4-methyl-2-nitrophenol and 4-methylphenol.

A similar reduction conducted with 1.64 g of **2a** and sodium borodeuteride gave crystalline (Z)- and (E)-4-methyl-4-nitrocyclohexadienol-d_1 (**3a**-d_1) with a ^{1}H NMR spectrum quite similar to that of **3a** except for the absence of absorptions assigned to the C-1 methine proton.

3,4-Dimethyl-4-nitrocyclohexadienol (3b). Portionwise addition of powdered sodium borohydride (0.11 g, 2.9 mmol) over 40 min to a magnetically stirred suspension of 4-nitro-3,4-dimethylcyclohexadienone (0.479 g, 2.87 mmol) in 5 mL of anhydrous methanol at −10 °C and isolation as described for **3a** gave 0.40 g of pale yellow oil whose NMR spectrum indicated a 75% yield of **3b** as an 80:20 mixture of Z and E isomers: NMR δ 1.65 (br s, 6 H, 3- and 4-Me), 4.50 and 4.64 (br s, 1 H (total), 1-H), 4.8 (v br s, 1 H, hydroxyl, exchanged with D_2O), 5.84 (br d, 1 H, 5-H), 5.88 (br s, 1 H, 2-H), 6.16 (br d, 1 H, 6-H). The remaining bands in the spectrum were identical with those of 3,4-dimethylphenol.

Similar reductions of **2b**-2,6-d_2 with sodium borohydride and **2b** with sodium borodeuteride gave **3b**-2,6-d_2 and **3b**-1-d_1 in 65 and 85% yields, respectively, based on the starting dienone. The ^{1}H NMR spectra of these labeled compounds confirmed assignments made for the unlabeled **3b** reported above. In each case the major contaminant was 3,4-dimethylphenol, presumably formed by elimination during isolation.

4-Nitro-3,4,5-trimethylcyclohexadienol (3c). Reduction of 4-nitro-3,4,5-trimethylcyclohexadienone with sodium borohydride in the manner described for **3a** and **3b** gave **3c** in 85% yield as a pale yellow oil: NMR δ 1.66 (m, 9 H, 3,4,5-Me), 4.45 and 4.7 (br s, 1 H (total), 1-H), 5.86 (br s, 2 H, 2,6-H). Reduction of **2c** with sodium borodeuteride gave **3c**-1-d_1 with an NMR spectrum similar to that found for **3c** except for the absence of signals at δ 4.45 and 4.7 assigned to the C-1 methine protons of the diastereoisomers of **3c**.

4-Methyl-4-nitrocyclohexadienyl Acetate (4a). A suspension of recrystallized **2a** (5.00 g, 32.7 mmol) in 25 mL of anhydrous methanol was cooled to −5 °C, and powdered sodium borohydride (0.70 g, 19 mmol) was added in three portions over a 10-min interval to the mechanically stirred mixture. The temperature of the reaction rose, reached 30 °C momentarily, and then returned to close to 0 °C. After 25 min total time, 37 mmol of acetic acid diluted in 4 volumes of methanol was added dropwise, and the bulk of the solvent was stripped off under vacuum (1 torr at 0 °C) to yield a semisolid. The reaction flask was refitted with a mechanical stirrer and then cooled to −40 °C with a calcium chloride bath. Cold methylene chloride (30 mL) and anhydrous pyridine (30 mL) were added to dissolve the crude nitrodienol. Acetyl chloride (15 mL, 0.21 mol) dissolved in 30 mL of methylene chloride was added dropwise to the cold, stirred mixture over 30 min. After an additional 30 min at −40 °C, the reaction mixture was allowed to warm toward 0 °C and poured into a prechilled funnel partially filled with 10% sulfuric acid and ice. The pyridine-free methylene chloride layer was drawn off, rapidly extracted with ice-cold water, and dried over sodium sulfate. Evaporation of the solvent and acetic anhydride left a crude dark oil (6.21 g) whose NMR spectrum indicated 60% **4a** and nearly equimolar amounts of 4-methyl-2-nitrophenol and 4-methylphenol. The ratio of diastereoisomers of **4a** appeared to be 72:28 on the basis of the integrals of the two 4-methyl signals. Column chromatography gave a pure sample of **4a** as a diastereoisomeric mixture.

A sample of purified **3a**-1-d_1 (0.255 g, 1.63 mmol) was acylated with acetyl chloride and pyridine in methylene chloride to yield 0.271 g of crude product. The NMR spectrum of this sample indicated 90 mol % of **4a**-d_1 (0.256 g, 78% of theory) in a 68:32 ratio of diastereoisomers. The remainder of the mixture was p-cresol. Column chromatography over alumina (deactivated with 10 wt % of 10 vol % acetic acid in water) gave **3a**-1-d_1 in a 67:33 ratio of isomers: NMR ($DCCl_3$) δ 1.69 and 1.75 (2 s, 3 H (total), 4-Me), 2.03 (s, 3 H, acetoxyl), 6.15 (m, 4 H, 2,3,5,6-H).

3,4-Dimethyl-4-nitrocyclohexadienyl-2,6-d_2 Acetate (4b-2,6-d_2). A magnetically stirred suspension of **2b**-2,6-d_2 (1.22 g, 7.2 mmol) in 13 mL of anhydrous methanol was cooled to −15 °C, and powdered sodium borohydride (0.170 g, 4.5 mmol) was added in one portion. The temperature was held at −10 °C for 5 min, raised to 0 °C for 10 min which resulted in initial frothing and dissolution, and then cooled to −15 °C as a pale yellow solution. Acetic acid (1 mL) diluted in methanol was added dropwise. The volatiles were evaporated (1 torr, 0 °C) to yield a glassy solid. This crude product was acylated with acetyl chloride and pyridine in the manner described for **4a** to yield 1.40 g of dark oil. Analysis of the NMR spectrum indicated 75 mol % (68% of theory) of **4b**-2,6-d_2 as a 5:1 mixture of diastereoisomers, 15 mol % of 3,4-dimethylphenyl-2,6-d_2 acetate, and 10 mol % of 3,4-dimethylphenol-2,6-d_2. Column chromatography of the sample over deactivated alumina at 0 °C with elution by 10 vol % ether in pentane gave 190 mg of a mixture of diastereoisomers and 620 mg of a mixture whose isomer ratio was 95:5. This fraction crystallized in large prisms from pentane–ether at −10 °C to yield 520 mg (34% of theory) of the Z isomer: mp 49–50 °C (lit.[20] 38–42 mp °C); NMR ($DCCl_3$) δ 1.74 (s, 3 H, 4-Me), 1.81 (d, J_{app} = 1.7 Hz, 3 H, 3-Me), 2.10 (s, 3 H, acetoxyl), 5.64 (m, 1 H, 4-H), 6.05 (m, 1 H, 6-H).

Unlabeled **4b** and **4b**-1-d_1 were prepared by similar procedures to give crystalline samples of the Z isomer with melting points of 51–52 and 49–50 °C, respectively.

4-Ethyl-4-nitrocyclohexadienyl Acetate (4e). 4-Ethyl-4-nitrocyclohexadienone (**2e**; 0.900 g, 5.39 mmol) was reduced with sodium borohydride (0.129 g, 3.41 mmol) in methanol at −8 °C. After a 10-min reaction period, the solution was acidified with 1 equiv of acetic acid in methanol, and the volatiles were removed at 1 torr and 0 °C to yield a glassy solid residue. This crude product was acylated in the manner previously described to yield 0.81 g of crude product. NMR analysis indicated 89% **4e** (63%

(20) H. W. Gibbs, R. B. Moodie, and K. Schofield, *J. Chem. Soc., Perkin Trans. 2*, 1145 (1979).

Table II. Yields of Products in Direct Syntheses of Nitrodienyl Acetates from Phenyl Acetates at Various Stages[a]

reactant	% after step 1		% after step 3			material balance, %
	2	7	1	4[b]	7	
1a	84	16	9	58 (3:1)	18	85
1b	84	14	18	66 (5:1)	14	98
1c	78	23	11	60 (7:1)	22	94

[a] Yields were determined from the weight of the crude product and NMR determination of the mole fractions of materials in the crude product mixtures. All yields are referenced to starting reactant. [b] Values in parentheses are $Z:E$ isomer ratios.

of theory). Chromatography over deactivated alumina at 0 °C with ether–pentane elution gave a lime green oil that could not be induced to crystallize: NMR ($DCCl_3$) δ 0.87 (t, 3 H, Me), 2.05 (s, 3 H, acetoxyl), 2.09 (quartet 2 H, methylene), 5.65 (m, 1 H, 1-H), 6.23 (m, 4 H, 2,3,5,6-H).

Direct Synthesis of Nitrodienyl Acetates 4a, 4b, and 4c from the Phenyl Acetates. A 100-mL two-necked flask equipped with a mechanical stirrer and an addition funnel was charged with the phenyl acetate (21 mmol), acetic anhydride (7.5 mL), and 10 mL of methylene chloride. The solution was cooled to −45 ± 5 °C with dry ice, and a solution of 90% nitric acid (2.4 mL, 50 mmol) dissolved in acetic anhydride (5.0 mL) was added dropwise over 30 min. The solution was maintained at −45 °C for an additional 30 min, warmed to −15 °C for 15 min, and then cooled in dry ice–acetone to −78 °C. Additional methylene chloride (25 mL) was added, and 10 g of anhydrous ammonia was distilled into the reaction mixture with vigorous stirring over 60 min. Excess ammonia was removed by evaporation at its boiling point and finally by aspiration. The residue was extracted with 50 mL of cold (0 °C) 10% sulfuric acid and three 50-mL portions of aqueous sodium chloride (0 °C). The solvent was removed (1 torr, 0 °C) to give a solid residue. The crude dienone was then suspended in 25 mL of absolute methanol, and powdered sodium borohydride (0.68 g, 18 mmol) was added in ca. 50-mg portions over 60 min to the cold (−15 °C), stirred mixture. The homogeneous solution that resulted was treated with 5 mL of a 1:4 (v/v) solution of acetic acid in methanol, and the volatiles were then removed under vacuum at 0 °C. The yellow oil that resulted was dissolved in cold methylene chloride (50 mL), extracted with three 50-mL portions of cold brine, and dried over sodium sulfate at reduced temperature. A 250-mL three-necked flask equipped with a mechanical stirrer, addition funnel, and drying tube was charged with the dried methylene chloride solution of the crude nitrodienol and pyridine (12 mL). The flask was cooled to −40 °C, and a solution of acetyl chloride (6.5 mL, 91 mmol) in 15 mL of methylene chloride was added dropwise over 40 min. After the addition, the temperature of the mixture was raised to −15 °C for 30 min. The thick, slightly yellow suspension that resulted was then extracted with cold 10% sulfuric acid and three 50-mL portions of cold brine. After being dried, the methylene chloride was removed under vacuum to leave the crude nitrodienyl acetate. Table II summarizes yield data at various stages of the syntheses.

1,4-Dimethyl-4-nitrocyclohexadienol (5). A 250-mL three-necked flask (predried and nitrogen flushed) equipped with a mechanical stirrer, addition funnel, and nitrogen-purging line was charged with **2a** (4.95 g, 32.3 mmol) and 30 mL of anhydrous ether. The flask and contents were cooled to −78 °C, and a solution of methyllithium (21 mL, 1.84 M, 38.6 mmol) was added dropwise with stirring over 30 min. The suspended dienone went into solution while the color of the mixture turned orange. After an additional 10-min reaction period, concentrated hydrochloric acid (3.2 mL, 38.4 mmol) dispersed in anhydrous ether was added dropwise to the rapidly stirred mixture. Pentane (20 mL) was added and following this an additional 50 mL of ether. The temperature was then brought to −20 °C at which time the reaction mixture changed appearance from two phases (liquid and semisolid) to one that indicated suspended solids. The solution was transferred to a prechilled separatory funnel, extracted with aqueous sodium chloride (−10 °C), and dried over sodium sulfate (0 °C) to give a pale yellow solution. Vacuum removal of the solvent (−5 °C) gave 4.94 g (ca. 95%) of crude product as a viscous orange liquid that solidified upon cooling in the freezer (−10 °C). The ^1H NMR spectrum indicated 90 mol % of nitrodienol **5** with a 4:1 ratio of stereoisomers. Column chromatography of 0.90 of this product over 70 g of deactivated alumina at 0 °C with ether–pentane elution (25 vol % ether increased by 15 vol % with each 100-mL portion of eluant added) gave the major stereoisomer (0.374 g, mp 51–53 °C) in fractions 9–22 (63–154 mL): NMR δ 1.25 (s, 3 H, 1-Me), 1.62 (s, 3 H, 4-Me), 3.99 (br s, 1 H, OH), 5.92 (s, 4 H, 2,3,4,5-H). The minor isomer (0.160 g, mp 113–114 °C) was isolated from fractions 24–45 (168–315 mL): NMR δ 1.37 (s, 3 H, 1-Me), 1.73 (s, 3 H, 4-Me), 5.96 (quartet, J_{app} = 9.5 Hz, 4 H, 2,3,4,5-H).

Acknowledgment. We thank the Research Corp. and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for grants supporting this work.

Registry No. **1a**, 140-39-6; **1b**, 22618-23-1; **1b**-*2,6-d*$_2$, 71462-74-3; **1c**, 6719-74-0; **1d**, 58972-38-6; **1e**, 3245-23-6; **1f**, 2664-32-6; **2a**, 62622-59-7; **2b**, 32590-94-6; **2b**-*2,6-d*$_2$, 71486-28-7; **2c**, 32591-49-4; **2d**, 71462-75-4; **2e**, 71462-76-5; **2f**, 71462-77-6; (*E*)-**3a**, 71462-78-7; (*Z*)-**3a**, 69578-17-2; (*E*)-**3a**-*d*$_1$, 71462-79-8; (*Z*)-**3a**-*d*$_1$, 71462-80-1; (*E*)-**3b**, 71462-81-2; (*Z*)-**3b**, 69578-18-3; (*E*)-**3b**-*2,6-d*$_2$, 71462-82-3; (*Z*)-**3b**-*2,6-d*$_2$, 71462-83-4; (*E*)-**3b**-*1-d*$_1$, 71462-84-5; (*Z*)-**3b**-*1-d*$_1$, 71462-85-6; (*E*)-**3c**, 71462-86-7; (*Z*)-**3c**, 69578-19-4; (*E*)-**3c**-*1-d*$_1$, 71462-87-8; (*Z*)-**3c**-*1-d*$_1$, 71462-88-9; (*E*)-**4a**, 40230-41-9; (*Z*)-**4a**, 40230-42-0; (*E*)-**4a**-*d*$_1$, 71462-89-0; (*Z*)-**4a**-*d*$_1$, 71486-29-8; (*E*)-**4b**, 71462-90-3; (*Z*)-**4b**, 69305-43-7; (*E*)-**4b**-*2,6-d*$_2$, 71462-91-4; (*Z*)-**4b**-*2,6-d*$_2$, 71462-92-5; (*E*)-**4b**-*1-d*$_1$, 71462-93-6; (*Z*)-**4b**-*1-d*$_1$, 71462-94-7; (*E*)-**4c**, 63614-92-6; (*Z*)-**4c**, 63614-91-5; **4e**, 71462-95-8; (*E*)-**5**, 54874-33-8; (*Z*)-**5**, 54913-24-5; **7a**, 54646-55-8; **7b**, 71462-96-9; **7c**, 71462-97-0; **7e**, 71462-98-1; **7f**, 71462-99-2; **8a**, 119-33-5; **8f**, 1576-10-9; 3,4-dimethylphenol-*2,6-d*$_2$, 71463-00-8; 4-methylphenol, 106-44-5.