An Investigation of Stereochemistry and Migratory Aptitude in the Reductive Cyclization of β,β-Disubstituted o-Nitrostyrenes to 2,3-Disubstituted Indoles[1]

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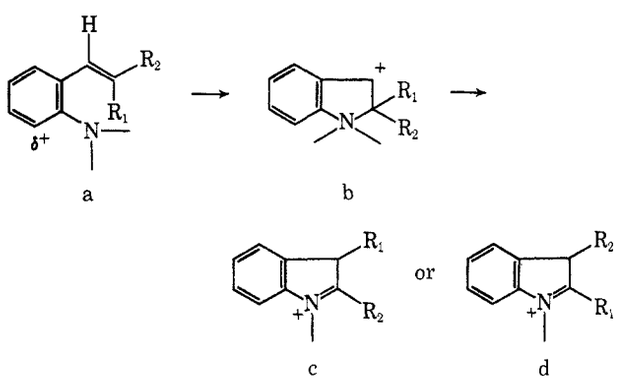
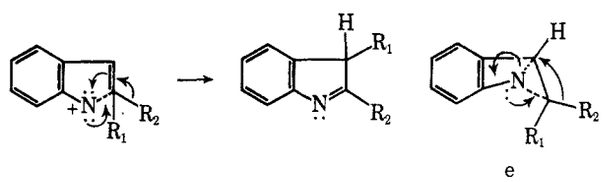
The syntheses of *cis*-α-methyl-2′-nitrostilbene (**2**) and *trans*-2-methyl-1-(*o*-nitrophenyl)-1-propene-3-d_2 (**3**) are reported. Deoxygenation of **2** in refluxing triethyl phosphite gives a 50% yield of 2-methyl-3-phenylindole and about 10% 1-ethyl-2-methyl-3-phenylindole. The product distribution in the deoxygenation of *trans*-α-methyl-2′-nitrostilbene (**1**) is almost identical under similar conditions. Deoxygenation of **3** gives a 20% yield of 2,3-dimethylindole consisting of equal parts of 2-methyl-3-methyl-d_2-indole and 2-methyl-d_2-3-methylindole. These results indicate that the configurational identity of the olefin substituents in the nitrostyrenes is lost before migration commences in these reductive cyclizations.

Deoxygenation of *o*-nitrostyrenes by trivalent phosphorus compounds leads to the formation of indoles.[2] β,β-Disubstituted *o*-nitrostyrenes cyclize with rearrangement of one of the β substituents to give 2,3-disubstituted indoles.[3] Three mechanisms[2,3] have been suggested for these reductive cyclizations and these are summarized, as they apply to the β,β-disubstituted *o*-nitrostyrene to 2,3-disubstituted indole transformation, in Scheme I. The electrophilic nitrogen atom which initiates cyclization could be a nitrene,[2] or the nitrogen atom of a nitroso group[3] or of a cyclic adduct of the nitro group and triethyl phosphite.[2b] No evidence which completely excludes any of these possibilities has been reported to date.[4]

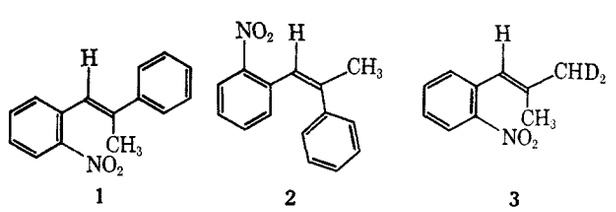
SCHEME I



The β substituents labeled R_1 and R_2 are clearly in different stereochemical environments in the starting *o*-nitrostyrene, but, if structure b represents an intermediate or transition state in the reaction, R_1 and R_2 will become stereochemically equivalent and relative migratory aptitude would determine the extent to which each group migrates. On the other hand, if migration is concerted with cyclization as represented by transition state e, R_1 and R_2 could remain stereochemically unique throughout the course of the cyclizative rearrangement. Such a concerted migration seems feasible if the unshared pair on nitrogen were to promote migration as cyclization proceeded. Stated in another way the question posed is essentially this: does R_2 (or R_1) begin to interact preferentially with the developing electron deficiency at C-3 before the symmetrical transition state b is reached?



In order to determine whether the original configuration of the *o*-nitrostyrene has any influence on the identity of the group which migrates during the cyclization, we have examined the deoxygenation of compounds **1**, **2**, and **3**.



Synthesis

The *trans*-*o*-nitrostilbene **1** was prepared by the literature procedure.[5] The *cis* isomer **2** was obtained from ethyl *trans*-*o*-nitro-α-phenylcinnamate (**5**) by the route outlined in Scheme II. Careful control of the reaction conditions permitted selective reduction of the carbethoxy group in **5** and of the alkyl bromide **8** without extensive reduction of the nitro group. The cinnamyl iodide (**9**) derived from **8** by halogen exchange was of no advantage in the reduction. The aldehyde **7** is a by-product of the reduction of **5**. Reduction of **5** at −10° gives mainly an azo coupling product.

The synthesis of **3** is outlined in Scheme III. The starting material is the cinnamaldehyde **10** which is expected to have the *trans* configuration by virtue of its preparation from *o*-nitrobenzaldehyde and propionaldehyde *via* aldol condensation and dehydration.[6]

Unlabeled **3**, prepared by Scheme III using sodium borohydride and lithium aluminum hydride in the reductions, was identical with a sample of **3** prepared from

(1) (a) Supported by NIH Grant GM-14344 and, in part, by National Science Foundation Grant GP-5292. (b) From the M. S. Thesis of G. S. Kotchmar, Jr., University of Virginia, Sept 1968.

(2) (a) J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Searle, *J. Chem. Soc.*, 4831 (1965); (b) R. J. Sundberg, *J. Org. Chem.*, **30**, 3604 (1965); (c) R. J. Sundberg, *ibid.*, **33**, 487 (1968).

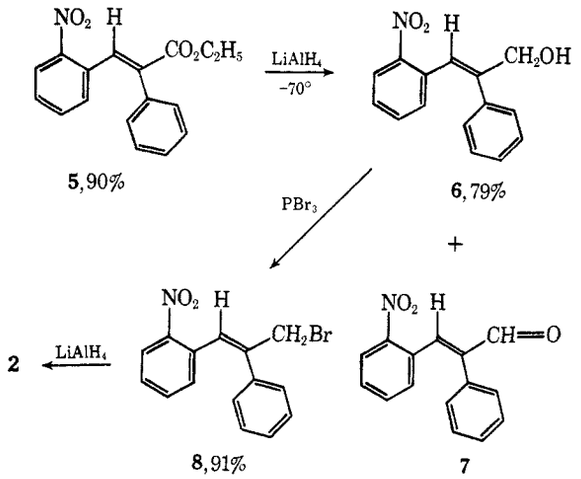
(3) R. J. Sundberg and T. Yamazaki, *ibid.*, **32**, 290 (1967).

(4) J. I. G. Cadogan, *Quart. Rev.* (London), **22**, 222 (1968).

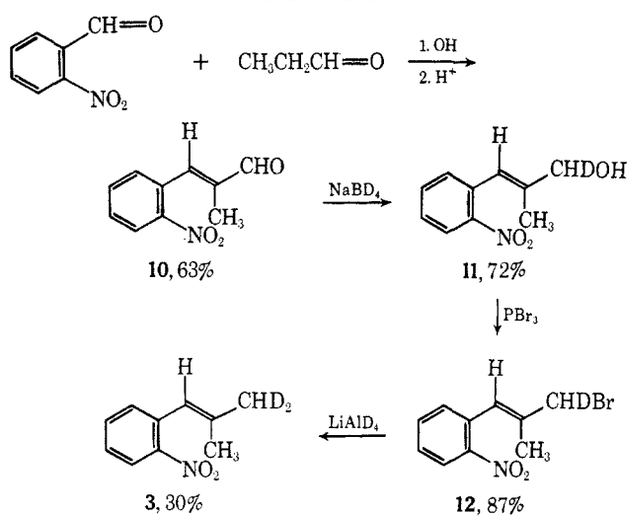
(5) A. V. Dombrovskii, Ya. G. Bal'on, and K. G. Tashchuk, *J. Gen. Chem. USSR*, **32**, 592 (1962).

(6) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 220, and references therein.

SCHEME II



SCHEME III



acetone and diethyl *o*-nitrobenzylphosphonate *via* a Wittig reaction.[3]

The nmr spectrum of **3** shows doublets in the nmr spectrum at δ 1.69 and 1.91 with integration ratios of 3:1, confirming the specific introduction of deuterium. Nonplanarity of the styrene system is indicated by the fact that the methyl group *cis* to the *o*-nitrophenyl group is more shielded than the *trans* group.[7] The nmr spectra of **1** and **2** show analogous behavior. The methyl group of **1** appears at δ 2.07 while the methyl signal in **2** is found at δ 2.24.

Deoxygenations

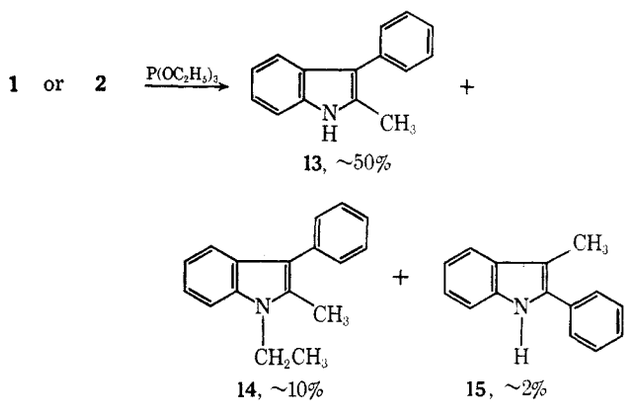
Deoxygenations of **1** and **2** were accomplished under comparable conditions in refluxing triethyl phosphite (6 hr). The major product from both nitrostyrenes was 2-methyl-3-phenylindole (**13**). Minor products included 1-ethyl-2-methyl-3-phenylindole (**14**), 3-methyl-2-phenylindole (**15**), and, probably, 1-ethyl-3-methyl-2-phenylindole (**16**). The yields as determined by isolation after column chromatography are summarized in Table I. The deoxygenation of **1** has been reported previously.[3] Compounds **13** and **14** were identified by spectral comparison with authentic samples.[3] The results of this work are in qualitative agreement with the previous work although the yields of **13** and **14** were found to be somewhat less than previously reported. The product of methyl migration, 3-methyl-2-phenylindole, has been identified as a component of the deoxygenation product by thin layer chromatography but it is present in too small an amount to permit isolation or detection by nmr. Nmr spectra of mixtures of **13** and **15** indicate that **15** would have been detectable by nmr if formed in a yield of 2% or more. Trace amounts of an oil having spectral properties in accord with expectation for **16** have been isolated. Phenyl migration appears to predominate by at least 25:1 over methyl migration in the deoxygenation of both **1** and **2** and the product mixture from both starting compounds is quite comparable.

TABLE I

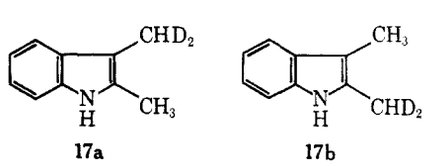
PRODUCT YIELDS FROM DEOXYGENATION OF *cis* AND *trans*-2-METHYL-2′-NITROSTILBENE

	Yield, %			
	13	**14**	**15**	**16**[a]
cis	54 (49)[b]	12 (12)[b]	<2	<1
trans	53 (53)[b]	9 (7)[b]	<2	<1

[a] Identification of this product is tentative. [b] Yield from duplicate experiment.



Deoxygenation of the deuterated β,β-dimethyl-*o*-nitrostyrene **3** gave a mixture of 2,3-dimethylindole (**17**, 22% yield) and 2,2-dimethyl-3-indolinone (**18**, 21% yield). These products have previously been characterized when isolated from undeuterated **3**.[3] The distribution of deuterium in **17** was investigated by nmr and by mass spectrometry. The nmr spectrum in benzene-d_6 shows the two methyl signals to be of equal intensity indicating that equal amounts of **17a** and **17b** have been formed by nonselective migration of the methyl and dideuteriomethyl groups. The parent peak in the mass spectrum of undeuterated **18** is shifted to 147 in the **17a**–**17b** mixture. The strong M − 15 peak[8] splits into peaks at 130 and 132 of nearly equal intensity in the dideuterated sample, again indicating that the deuterium is present in dideuteriomethyl groups equally distributed between C-2 and C-3.



(7) H. Rottendorf, S. Sternhell, and J. R. Wilmhurst, *Aust. J. Chem.*, **18**, 1759 (1965).

(8) J. H. Beynon, "Mass Spectrometry and Its Application to Organic Chemistry," Elsevier Publishing Co., New York, N. Y., 1960, p 399.

Control experiments have established that **1** and **2** are deoxygenated more rapidly than they are interconverted and that **3** is not converted into its geometrical isomer under the conditions of the deoxygenation reaction.

Discussion

The results from the deoxygenation of **3** show that the configuration of the nonequivalent methyl groups in the starting material does not have a measurable effect on the extent to which each of the groups migrates. This suggests that the methyl groups become stereochemically equivalent prior to migration. Similarly, the fact that **1** and **2** give predominantly the product of phenyl migration demonstrates that the configuration of the olefin is not an important factor in determining the identity of the migrating group. The fact that both **1** and **2** give a similar product mixture is consistent with the possibility that **1** and **2** give rise to a common intermediate. These results indicate that a structure such as b (Scheme I) represents an intermediate in the deoxygenation of β,β-disubstituted *o*-nitrostyrenes and rules out the possibility[3] that olefin configuration might play a part in determining which olefin substituent migrates. The relative phenyl–methyl migratory aptitude (>25:1) in **1** and **2** is consistent with mechanisms which involve migration to a carbonium ion site.

Experimental Section

General.—Commercial samples of triethyl phosphite were redistilled at atmospheric pressure under nitrogen. Silica gel H (Brinkmann Instruments) was used for thin layer chromatography and silicic acid powder (Mallinckrodt or Baker and Adamson) was used for column chromatography. Lithium aluminum hydride reductions were run under nitrogen.

Ethyl *trans*-*o*-Nitro-α-phenylcinnamate (5).—*trans*-*o*-Nitro-α-phenylcinnamic acid[9] was esterified with absolute ethanol and sulfuric acid in the normal manner giving **5** (90.6%), mp 57.4–58.4° (lit.[10] mp 59°).

Reduction of 5 with Lithium Aluminum Hydride. *trans*-*o*-Nitro-α-phenylcinnamaldehyde (7) and *trans*-*o*-Nitro-α-phenylcinnamyl Alcohol (6).—A solution of the ester **5** (10.0 g, 0.034 mol) in dry ether (80 ml) was cooled to about −70° with Dry Ice and ethanol. Lithium aluminum hydride (0.64 g, 0.017 mol) was refluxed in ether (150 ml) for 30 min and the resulting suspension was added to the ester solution through a dropping funnel over a period of 1 hr. The reaction mixture was stirred for 15 min and excess hydride was destroyed by successive addition of ethanol (20 ml), moist ether (40 ml), and water (40 ml). The temperature of the reaction mixture was allowed to rise to −5° and then 10% sulfuric acid (300 ml) was added. The reaction mixture was extracted with ether and the crude product was chromatographed on silicic acid (200 g). Benzene eluted unreacted **5** (3.3 g, 0.011 mol) and *trans*-*o*-nitro-α-phenylcinnamaldehyde (**7**, 0.6 g, 0.0024 mol, 10.5%): mp 92–94° after crystallization from ethanol; $\nu_{C=O}$ 1680 cm^{-1}; ν_{NO_2} 1515, 1340 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 222 mμ (log ε 4.27), 268 (4.07); nmr peaks ($CDCl_3$) at δ 6.8–8.3 (9 H, multiplet), 7.8 (1 H, s), 9.88 (1 H, s).

Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.30; H, 4.38; N, 5.54. Found: C, 71.25; H, 4.50; N, 5.38.

Later benzene fractions contained *trans*-*o*-nitro-α-phenylcinnamyl alcohol (**6**), a yellow oil (4.6 g, 0.018 mol, 80%) which was purified by short-path distillation: bp 198–200° (0.3 mm); ν_{OH} 3375, 3555 cm^{-1}; ν_{NO_2} 1520, 1345 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 240 mμ (log ε 4.03), 255 (3.97); nmr peaks ($CDCl_3$) at 2.27 (1 H, s), 4.54 (2 H, d), 7.02 (1 H, s), 6.8–8.0 (9 H, multiplet).

Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.60; H, 5.14; N, 5.50. Found: C, 70.88; H, 5.31; N, 5.77.

A similar reduction run at −10° gave a 40% yield of 2,2′-azo-α-phenylcinnamyl alcohol: mp 172–174°; ν_{OH} 3420 cm^{-1}; nmr peaks (DMSO-d_6) at δ 4.38 (4 H, d), 5.27 (2 H, t), 7.0 (2 H, s) and 7.1–7.8 (18 H, multiplet).

Anal. Calcd for $C_{30}H_{26}N_2O_2$: C, 80.70; H, 5.88; N, 6.32. Found: C, 80.53; H, 6.09; N, 6.12.

***trans*-*o*-Nitro-α-phenylcinnamyl Bromide (8).**—A solution of the alcohol **6** (3.0 g, 0.012 mol) in ether (10 ml) was cooled to −10° and a solution of phosphorus tribromide (1.2 g, 0.0045 mol) in ether (20 ml) was slowly added. The reaction mixture was allowed to warm to room temperature and stirred for 5 hr.

The reaction mixture was poured onto ice and extracted with ether (100 ml). The ether layer was washed with dilute sodium carbonate, dried over sodium sulfate, and concentrated giving crystalline **8** (3.4 g, 0.011 mol, 92%): mp 87–88° after recrystallization from 8:2 hexane–benzene; ν_{NO_2} 1510, 1355 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 239 mμ (log ε 4.09), 263 (4.03); nmr peaks ($CDCl_3$) at δ 4.43 (2 H, d) and 6.75–8.1 (10 H, multiplet).

Anal. Calcd for $C_{15}H_{12}NO_2Br$: C, 56.50; H, 3.80; N, 4.40. Found: C, 56.36; H, 3.68; N, 4.27.

***trans*-*o*-Nitro-α-phenylcinnamyl Iodide (9).**—The bromide **8** (1.5 g, 0.0047 mol) was stirred with sodium iodide (0.71 g, 0.0047 mol) in acetone (25 ml) at 50° for 45 min. After filtration, the reaction mixture was diluted with benzene and washed with sodium thiosulfate. Concentration of the dried benzene solution gave **9** which was recrystallized from 8:2 hexane–benzene (1.1 g, 0.003 mol, 64%): mp 104–105°; ν_{NO_2} 1520, 1340 cm^{-1}; nmr peaks ($CDCl_3$) at 4.36 (2 H, s) and 6.7–8.0 (10 H, multiplet).

Anal. Calcd for $C_{15}H_{12}NO_2I$: C, 49.4; H, 3.32; N, 3.84. Found: C, 49.58; H, 3.10; N, 3.72.

***cis*-α-Methyl-2′-nitrostilbene (2).**—A solution of the bromide **8** (5.0 g, 0.016 mol) in ether (100 ml) was added dropwise over 20 min to a suspension of lithium aluminum hydride (0.372 g, 0.0098 mol) in dry ether (90 ml). After addition was complete, the solution was refluxed for 2.5 hr. After cooling, excess lithium aluminum hydride was destroyed by addition of moist ether and then water. The reaction mixture was hydrolyzed with 10% sulfuric acid and extracted with ether. The crude product was purified by chromatography on silicic acid (150 g). Hexane–benzene (8:2) eluted **2** as a yellow oil (1.5 g, 0.0063 mol, 52%): ν_{NO_2} 1520, 1340 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 240 mμ (log ε 4.03), 256 (4.00); nmr peaks ($CDCl_3$) at δ 2.24 (3 H, d), 6.7 (1 H, d), and 6.8–8.0 (9 H, multiplet).

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.49; N, 5.86. Found: C, 75.18; H, 5.30; N, 5.69.

Unreacted bromide (1.3 g, 0.0041 mol) was eluted with 6:4 hexane–benzene.

***trans*-α-Methyl-*o*-nitrocinnamaldehyde (10).**—*o*-Nitrobenzaldehyde (7.5 g, 0.050 mol) and propionaldehyde (8.7 g, 0.15 mol) were dissolved in ether (40 ml). There was added 60 ml of a solution prepared by diluting 8 ml of 25% aqueous sodium hydroxide with 200 ml of ethanol. The reaction mixture was stirred for 18 hr and then extracted with water. The ether layer was dried over magnesium sulfate and evaporated, leaving a yellow oil with spectral properties in accord with those expected for the intermediate aldol condensation product. The oil was dissolved in benzene (300 ml), *p*-toluenesulfonic acid (2.1 g) was added, and the solution was refluxed for 75 min. The benzene solution was washed with water and dilute sodium bicarbonate and then concentrated leaving a black oil. Vacuum distillation gave *o*-nitrobenzaldehyde (1.9 g, 0.013 mol) and **10** (4.5 g, 0.023 mol, 64%): bp 130–131° (0.25 mm); $\nu_{C=O}$ 1685 cm^{-1}; ν_{NO_2} 1520, 1340 cm^{-1}; nmr peaks ($CDCl_3$) at δ 1.9 (3 H, d), 7.5–8.5 (5 H, multiplet) and 9.8 (1 H, s).

The analytical sample was prepared by chromatography using a silicic acid column and benzene as the eluent.

Anal. Calcd for $C_{10}H_9NO_3$; C, 62.90; H, 4.74; N, 7.33. Found: C, 62.87; H, 4.75; N, 7.06.

***trans*-α-Methyl-*o*-nitrocinnamyl Alcohol-d_1 (11).**—A solution of **10** (5 g, 0.026 mol) in methanol (25 ml) which had been adjusted to pH 8 was added dropwise to sodium borodeuteride (0.30 g, 0.0079 mol) in methanol (30 ml) which had been adjusted to pH 8 with aqueous sodium hydroxide. The solution was stirred for 1.5 hr and diluted with water. The reaction mixture was extracted with ether and the extract was dried over magnesium sulfate, leaving **11** as a yellow oil (3.7 g, 0.019 mol, 72%): ν_{OH} 3325; ν_{NO_2} 1520, 1350 cm^{-1}. The compound showed tlc behavior identical with an undeuterated sample.

Undeuterated **11** was prepared in 77% yield using sodium borohydride: nmr peaks ($CDCl_3$) at δ 1.71 (3 H, d), 2.92 (1 H, broad singlet), 4.25 (2 H, broad singlet), 6.8 (1 H, s, broad), and

(9) D. F. DeTar and Y. W. Chu, *J. Amer. Chem. Soc.*, **76**, 1686 (1954).

(10) F. K. Beilstein, "Handbuch der organischen Chemie," Vol. 9, 1918, p 694.

7.25–8.11 (4 H, multiplet). The analytical sample was purified by chromatography on silicic acid using 8:2 benzene–ether as the eluent.

Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.20; H, 5.74; N, 7.24. Found: C, 62.42; H, 5.87; N, 6.88.

trans-α-**Methyl**-*o*-**nitrocinnamyl Bromide**-d_1 (**12**).—Phosphorus tribromide (1.98 g, 0.0073 mol) in dry ether (25 ml) was added dropwise to deuterated **11** (3.7 g, 0.019 mol) in dry ether (42 ml) at −10°. After addition of phosphorus tribromide was complete, the solution was stirred at room temperature for 7 hr. The reaction mixture was poured onto ice and extracted with ether. The ether was washed with aqueous sodium carbonate, dried over magnesium sulfate, and concentrated. The residual oil was distilled, giving a yellow oil (4.3 g, 0.017 mol, 87%): bp 111–113° (0.1 mm); ν_{NO_2} 1520, 1340 cm^{-1}.

An undeuterated sample was prepared by an identical procedure from unlabeled **11**: nmr peaks ($CDCl_3$) at δ 1.87 (3 H, d), 4.17 (2 H, d), 6.96 (1 H, broad singlet) and 7.30–8.20 (4 H, multiplet).

Anal. Calcd for $C_{10}H_{10}NO_2Br$: C, 46.90; H, 4.21; N, 5.46. Found: C, 47.00; H, 3.97; N, 5.50.

trans-**2-Methyl-1-**(*o*-**nitrophenyl**)-**1-propene-3**-d_2.—A solution of deuterated **11** (5.0 g, 0.019 mol) in dry ether (70 ml) was added dropwise to lithium aluminum deuteride (0.412 g, 0.0098 mol) in dry ether (75 ml). After addition was complete, the reaction mixture was refluxed for 2.5 hr. Excess lithium aluminum deuteride was destroyed with moist ether and water and the reaction mixture was hydrolyzed with 10% sulfuric acid. The ether layer was washed with water, dried, and evaporated. Chromatography of the residual oil on silicic acid gave **3** (1.07 g, 0.0060 mol, 30%): ν_{NO_2} 1520, 1340 cm^{-1}; nmr peaks ($CDCl_3$) at δ 1.69 (3 H, d), 1.91 (1 H, d), 6.48 (1 H, broad singlet), and 7.1–8.0 (4 H, multiplet). Except for the diminished intensity of the signal at δ 1.91, the nmr spectrum is identical with an unlabeled sample of **3** from unlabeled **12** and with a sample previously prepared by an independent procedure.[3]

Standard Deoxygenation Procedure.—The nitrostyrene was refluxed with a 6 *M* ratio of triethyl phosphite under a nitrogen atmosphere for 6 hr. The solution was cooled and triethyl phosphite [bp ~25° (0.1 mm)] and triethyl phosphite [bp 43–46° (0.2 mm)] were removed by vacuum distillation. The residue was dissolved in ether, washed with water, dried, and concentrated. The residue was chromatographed on silicic acid (60–70 g, packed as a slurry in hexane). The solvent sequence was hexane, 9:1 hexane–benzene, 4:1 hexane–benzene, 1:1 hexane–benzene, and 9:1 benzene–ether. The course of the chromatography was followed by tlc.

Deoxygenation of *trans*-α-**Methyl-2′-nitrostilbene** (**1**).—Deoxygenation of **1** (3.1 g, 0.013 mol) gave an oil (0.016 g) eluted by hexane and tentatively identified as **16** on the basis of an nmr spectrum: nmr peaks at δ 1.2 (t), 2.3 (s), 4.2 (q) 7.0–7.8 (multiplet). Hexane–benzene (9:1) eluted **14** as an oil (0.28 g, 0.0012 mol, 9%) which was identified by spectral comparison with an authentic sample.[3] Hexane–benzene (1:1) eluted **13** (1.43 g, 0.0069 mol, 53%) containing **15** as a contaminant as shown by tlc comparison with authentic **15**. The methyl signal of **15** at δ 2.34 was not discernible in the nmr spectrum (<2% yield). The infrared and nmr spectrum of the product were identical with an authentic sample of **13**.[11]

Deoxygenation of *cis*-α-**Methyl-2′-nitrostilbene** (**2**).—Deoxygenation of **2** (2.5 g, 0.010 mol) gave **14** (0.39 g, 0.0012 mol, 12%), **13** (1.13 g, 0.0055 mol, 54%), and a 1:1 mixture of **14** and **15** (0.035 g, 0.8% yield of each) as identified by tlc and nmr spectral data.

Deoxygenation of β,β-**Dimethyl**-*o*-**nitrostyrene**-d_2 (**3**).—Deoxygenation of **3** (1.50 g, 0.0084 mol) gave **17** (0.28 g, 0.0019 mol, 22%) which was eluted with 1:1 hexane–benzene and identified by tlc and nmr comparison with unlabeled **17**. The integrated intensity of the peaks at δ 1.80 and 2.10 in benzene-d_6 were identical. Benzene–ether (9:1) eluted 2,2-dimethyl-3-indolinone (0.30 g, 0.0018 mol, 22%) which was identified by tlc and infrared data. A deoxygenation of unlabeled **3** gave similar product yields.

Control Experiment.—Partial deoxygenation of *cis*-α-methyl-2′-nitrostilbene (1 hr) permitted recovery of 10% of the nitrostilbene shown by nmr to be an 83:17 mixture of **2** and **1**, indicating that thermal isomerization of **2** to **1** is slow relative to deoxygenation.

Partial deoxygenation of **3** (1 hr) permitted recovery of 5.5% of unreacted **3**. The nmr spectrum of **3** showed a 1:3 integration ratio for the peaks at δ 1.9 and 1.7 indicating no interchange of the methyl and methyl-d_2 groups.

Registry No.—**2**, 20072-75-7; **3**, 20072-76-8; **6**, 20072-77-9; **7**, 20072-78-0; **8**, 20072-79-1; **9**, 20072-83-7; **10**, 20072-80-4; **11**, 20072-81-5; **12**, 20072-82-6; **11** (undeuterated), 20073-27-2; **12** (undeuterated, 20073-28-3; 2,2′-azo-α-phenylcinnamyl alcohol, 20072-84-8.

(11) E. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 612 (1953).

The Enol Acetylation of Alkylated Δ^4-3-Oxo Steroids. A Novel Enone–Phenol Transformation

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The perchloric acid catalyzed acetic anhydride acylation of a number of mono- and dialkylated steroids at the C-2 and C-6 positions has been investigated. In those cases where $\Delta^{2,4}$-dienol acetate formation is favored a novel hydride abstraction reaction is described which leads to intermediates which undergo dienone–phenol rearrangement. In contrast, the isopropenyl acetate enol acetylation of these compounds invariably led to the exclusive formation of $\Delta^{3,5}$-dienol acetate except in the one instance where the presence of a 6β substituent resulted in a 1:1 mixture of $\Delta^{2,4}$- and $\Delta^{3,5}$-dienol acetates.

As part of a program to examine the influence of remote substituents on the enolization properties of Δ^4-3-oxo steroids, we have been studying the perchloric acid catalyzed acetic anhydride enol acetylation of steroids. The enol acetylating conditions chosen are known to reflect the enolization properties of saturated keto steroids.[1] However, in a previous study[2] with conjugated ketones it was demonstrated that under these conditions the enol acetylation reaction leads to mixtures of O- and C-acylated products. The major products from the reaction of 17β-hydroxyandrost-4-en-3-one (**1a**) were 3,17β-diacetoxy-2-acetylandrosta-2,4-diene and 3,17β-diacetoxy-6-acetylandrosta-3,5-diene. The C-acylation reaction was shown to proceed *via* the intermediate $\Delta^{3,5}$- and $\Delta^{2,4}$-dienol diacetates. The subsequent acetylium ion[3] attack on the isomeric

(1) A. J. Liston, *J. Org. Chem.*, **31**, 2105 (1966).

(2) A. J. Liston and P. Toft, *ibid.*, **33**, 3109 (1968).

(3) The identity of the acetylating species in perchloric acid catalyzed enol acetylations has not been unequivocally established. However, there is increasing evidence that this ion must play a significant role [*cf.* D. P. N. Satchell, *Quart. Rev.* (London), **17**, 196 (1963)].