Metal Hydride Reduction of α -Phenylcinnamates

Sicher, Collect. Czech. Chem. Commun., 30, 413, 421 (1965); (d) G. Nagendrappa, R. K. Srivastava, and D. Devaprabhakara, J. Org. Chem., 35, 347 (1970). (15) (a) For examples of the reaction of THF with organometallic and

- (a) For examples of the reaction of THF with organometanic and anion radical intermediates, see R. B. Bates, L. M. Kroposki, and D. E. Potter, J. Org. Chem., **37**, 560 (1972); M. H. Hnoosh and R. A. Zingaro, J. Amer. Chem. Soc., **92**, 4388 (1970). (b) The reac-tion of MeLi with HMP to form methane⁹ and the base-catalyzed exchange of H for D in HMP [H. Normant, T. Cuvigny, and G. J. Martin, Bull. Soc. Chim. Fr., 1605 (1969)] both indicate that HMP can donate a proton to strong bases can donate a proton to strong bases. (16) As the first antibonding π orbital of acetylene is populated, the ge-
- trans-bent geometry. See B. M. Gimarc, J. Amer. Chem. Soc., 92, 266 (1970); G. W. Schnuelle and R. G. Parr, *ibid.*, 95, 8974 (1973).
- (a) For a recent review see L. A. Singer, Selec. Org. Transform., 2, 239 (1972);
 (b) G. D. Sargent and M. W. Browne, J. Amer. Chem. Soc., 89, 2788 (1967);
 (c) A. J. Fry and M. A. Mitnick, *ibid.*, 91, 6207 (1969);
 (d) M. C. Hoff, K. W Greenlee, and C. E. Boord, *ibid.*, 73, 3329 (1961).
 (e) The rate of inversion of vinyl radicals (17)has also been studied by examining the stereochemistry of the re-duction of the isomeric 2-bromo-2-butenes to the 2-butenes with n-Bu₃SnH in a reaction involving an intermediate 2-buten-2-yl radi-cal. H. G. Kuivila [Accounts Chem. Res., 1, 299 (1968)] found that at -75° , 2-bromo-cis-2-butene gave an olefin mixture containing 57% of cis-2-butene where the trans bromo olefin gave a mixture containing 15% of cis-2-butene G. M. Whiteoidee and C. B. Capov [L containing 15% c/s-2-butene. G. M. Whitesides and C. P. Casey [J. Amer. Chem. Soc., 88, 4541 (1966)] studied the same reaction at 25° and found that each isomeric bromo olefin gave the same mixture of 2-butenes containing 65% of the trans isomer and 35% of the cis isomer.
- (18) All melting points are corrected and all boiling points are uncorrect-ed. Unless otherwise stated MgSO₄ was employed as a drying agent. The ir spectra were determined with a Perkin-Elmer Model 237 or Model 257 infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202 recording spectrophotometer. The nmr spectra were determined at 60 MHz with Varian Model A-60 or Model T-60 nmr spectrometer. The chemical shifts are expressed in Sectors of the spectrometer were determined with a cary backware and the spectrometer. δ values (parts per million) relative to a Me₄Si internal standard. The mass spectra were obtained with an Hitachi Perkin-Elmer mass spectrometer, Model RMU-7, or a Varian Model M-66 mass spec-

trometer. All reactions involving strong bases or organometallic intermediates were performed under a nitrogen atmosphere. (19) P. D. Bartlett and L. J. Rosen, J. Amer. Chem. Soc., 64, 543

- (1942).
- (1942).
 (20) The procedure of W. H. Puterbaugh and M. S. Newman [*J. Amer. Chem. Soc.*, **81**, 1611 (1959)] was modified as described by H. O. House and M. J. Umen, *J. Org. Chem.*, **38**, 3893 (1973).
 (21) P. Pomerantz, A. Fookson, T. W. Mears, S. Rothberg, and F. L. Howard, *J. Res. Nat. Bur. Stand.*, No. 2, **52**, 51 (1954).
 (22) G. F. Hennion and T. F. Banigan, Jr., *J. Amer. Chem. Soc.*, **68**, 1202 (1946).
- 1202 (1946).
- This experiment was done in our laboratories by Dr. Norton P. Peet. (a) K. N. Campbell and B. K. Campbell, "Organic Syntheses," Col-lect. Vol. IV, Wiley, New York, N. Y., 1963, p 117; (b) K. N. Campbell and L. T. Eby, *J. Amer. Chem. Soc.*, **63**, 216 (1941); (c) R. A. Benkeser, G. Schroll, and D. M. Sauve, *ibid.*, **77**, 3378 (24)(1955)
- (1935).
 (25) F. D. Rossini, K. S. Pitzer, R. L. Arnett, R. M. Braun, and G. C. Pimentel, "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," API Research Project 44, Carnegie Press, Pittsburgh, Pa., 1953, p 66. (26) H. I. Waterman, P. Van't Spijker, and H. A. Van Wester, *Recl.*
- Trav. Chim. Pays-Bas, 48, 1097 (1929).
- (27) R. Mechoulam and F. Sondheimer, J. Amer. Chem. Soc., 80, 4386 (1958)
- (28) K. Ziegler, E Eimers, W. Hechelhammer, and H. Wilms, *Justus Liebigs Ann. Chem.*, **567**, 43 (1950).
 (29) Purchased from Columbia Organic Chemicals Co., Inc.
- Purchased from Chemical Samples Co. (30)
- Purchased from Aldrich Chemical Co., Inc. V. Prelog, K. Schenker, and W. King, Heiv. Chim. Acta, 36, 471 (32)(1953). (33) A. T. Blomquist, L. H. Liu, and J. C. Bohrer, J. Amer. Chem. Soc.,
- 74, 3643 (1952)
- (34) H. O. House, D. Koepsell, and W. Jaeger, J. Org. Chem., 38, 1167 (1973). (35) C. E.
- (1964)] have found that solutions of $CrSO_4$ will reduce both $HC \equiv CH$ and certain substituted acetylenes.
- (36) For a discussion of this reagent with leading references, see H. O. House and E. F. Kinloch, J. Org. Chem., in press.
 (37) R. C. Fahey and D.-J. Lee, J. Amer. Chem. Soc., 90, 2124 (1968).

Complex Metal Hydride Reduction of Carbon-Carbon Unsaturation. I. Sodium Borohydride Reduction of α -Phenylcinnamates and Related Systems^{1a}

J. Herman Schauble,* Gerald J. Walter, ^{1b,c} and J. Guy Morin^{1d}

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

Received August 10, 1973

The substituted methyl cinnamates 4 and 5 have provided a unique system for the study of various mechanistic aspects of the nucleophilic 1,4 addition of sodium borohydride to α,β -unsaturated esters. Competitive rates of reduction for two sets of methyl α -phenyl-trans-cinnamates (4), para-substituted in the α and β rings, respectively, correlate linearly with Hammett σ_p values. The similarity in ρ_{α} (1.74) and ρ_{β} (1.44) indicates that the transition state for hydride transfer occurs before significant change in geometry of the α,β -unsaturated carbonyl system occurs. Competitive rate studies for methyl α -(para substituted phenyl)acrylates (2) and methyl α -phenyl-cis- and -trans-crotonates (14 and 15) are corroborated by the data obtained for the cinnamates.

Carbon-carbon double bonds conjugated with strong anion-stabilizing groups (e.g., COR, CO₂R, CN, SO₂R, NO_2) have occasionally been observed to undergo reduction with sodium borohydride.²⁻¹¹ Although it is recognized that sodium borohydride exhibits nucleophilic behavior,^{3,4} little is known concerning the mechanism or even the general structural requirements for the occurrence of such reactions.

This paper presents preliminary studies on the scope and mechanism of the borohydride reductions of carboncarbon double bonds in α,β -unsaturated esters. Although esters are less prone to undergo this type of reduction than are more electrophilic systems such as ketones or nitro compounds, reduction of the carbon-carbon unsaturation was not complicated (in the cases studied) by significant reduction of the ester function or by other side reactions.

 α,β -Unsaturated esters having an additional electronwith drawing substituent at the α position (e.g., 1a-f) are known to undergo facile carbon-carbon double bond re-







^a Similar results were obtained with the α -(*p*-chlorophenyl)cinnamate (40). ^b Shifts (parts per million) were obtained in DMSO- d_6 solution, relative to TMS.



a, $X = NO_2$; **b**, X = Cl; **c**, X = F; **d**, X = H; **e**, $X = OCH_3$



duction with sodium borohydride in solvents such as alcohols, dimethoxyethane, or diglyme.¹²⁻¹⁵

We have examined a number of α,β -unsaturated esters in order to find systems of lower electrophilicity than the alkylidene cyanoacetates and malonates, but which would still be susceptible to borohydride reduction. As expected, simple α - or β -alkyl acrylates such as methyl methacrylate, methyl crotonate, or methyl cyclopentene-1-carboxylate and β -aryl acrylates such as methyl cinnamate and methyl p-nitrocinnamate were not reduced by sodium borohydride in methanol at room temperature.^{16,17} However, under similar conditions, the series of methyl α -(para substituted phenyl)acrylates (2a-c) were reduced cleanly to the dihydro esters $3a-e^{.18}$ Methyl α -(p-nitrophenyl)acrylate (2a) was completely reduced in 1 min at -5° . This rate was gualitatively 100 times that observed for reduction of the *p*-methoxy ester 2e. The α -(para substituted phenyl)-trans-cinnamates (41-p) were also prepared and all were found to undergo reduction with sodium borohydride in dimethoxyethane at room temperature. The time required for complete reduction ranged from 10 min for 4m to more than 1 week for 4p. The stoichiometry of the reductions were shown to be 4:1 (ester:borohydride).

These reductions in aprotic solvent apparently occur by 1,4 addition of borohydride to provide intermediates of type 8^{19} which undergo successive 1,4 additions to give the enol boronates (9) in which all four hydride hydrogens have been utilized.



The nmr spectrum for the product obtained by reaction of a 4:1 molar ratio of methyl α -phenyl-trans-cinnamate (41) to sodium borohydride in anhydrous DMSO- d_6 solution is consistent with the enol boronate structure 10. A comparison of the proton nmr data for this intermediate with that for the cinnamate 41 is presented in Table I. The methylene protons (b, b') in structure 10 might be expected to exhibit magnetic nonequivalence owing to the conformational restraint placed on the benzyl group as a result of phenyl c to boronate and phenyl c to phenyl d interactions. The 14-Hz coupling observed for the pair of doublets at 3.00 and 3.33 ppm is within expectation for a geminally coupled methylene group adjacent to a π bond.²⁰ The alternate E geometry for 10 was excluded from consideration owing to the steric strain which would be imposed by a phenyl group cis to the alkoxyboronate function.

Compd ^{<i>a</i>}	Chemical s	shift, ^{b, c} ppm	Coupling constant, Hz
PhCH ₂ CHAr CO ₂ CH ₃ 6m	$egin{array}{c} H_a \ H_b \ H_o \end{array}$	3.02 3.38 3.97	$J_{ab} = 15$ $J_{ac} = 8$ $J_{bc} = 6-7$
PhCH ₂ CDAr CO ₂ CH ₃ 11	$\mathbf{H}_{\mathtt{a}}$ $\mathbf{H}_{\mathtt{b}}$	2.98 3.45	$J_{\rm ab} = 14$
PhCHDCHAr ^d CO ₂ CH ₃	$\mathbf{H}_{\mathbf{a}}$ $\mathbf{H}_{\mathbf{b}}$ $\mathbf{H}_{\mathbf{c}}$	3.03 3.42 4.00	$J_{ac}{}^{e} = 8$ $J_{bc}{}^{e} = 8$

 Table II

 Nmr Data for Methyl 2-(p-Nitrophenyl)-3-phenylpropionates

^{*a*} Ar = *p*-nitrophenyl. ^{*b*} Shifts were determined in CCl₄ solutions relative to TMS. ^{*c*} The methoxyl singlet appeared at 3.62 ppm. ^{*d*} Diastereomers. ^{*e*} Peaks were broadened owing to geminal deuterium coupling.

 Table III

 Relative Rate Data for Sodium Borohydride Reductions

Compd^a	Relative rate ^b	Reduction time, min	ρ
	Methyl α -(Para substituted phenyl)-tran	as-cinnamates (41–p)	
NO_2/Cl	12.77	3	
$CO_{9}CH_{3}/Cl$	2.63	15	
Cl/H	5.40°	42, 50	$+1.74^{d}$
OCH ₃ /H	0.49	70, 100	
•,	Methyl α -Phenyl(para substituted phenyl)-tr	cans-cinnamates $(4l, 4q-t)$	
NO_2/H	14,05°	25	
CO_2CH_3/H	4.05°	60	
NO_2/Cl	4.77°	60	
$CO_{2}CH_{3}/Cl$	1.63	60	+1.44'
Cl/H	3,08	95,60	
OCH₃/H	0.38	90	
•,	Methyl α -(Para substituted phenyl)	acrylates (2b-e)	
Cl/H	4.31	20	
\mathbf{Cl}/\mathbf{F}	2.39	20	+2.33
OCH_{3}/H	$0.25^{e,g}$	45	

^a Pairs were selected on the basis of relative rates of reduction and separability of reactants and products by glpc. ^b Average for two runs. The relative rate for each run was determined from an average of five glpc injections. Response factors were very close to 1:1. Deviations between runs were <3% of lower value. ^c The difference between runs was 6.8%. ^d The standard error was 0.148; the correlation coefficient was 0.978. ^c Results for a single run. ^f The standard error was 0.116, with a correlation coefficient of 0.978. ^g Relative rate was determined by nmr.

It is evident that enol boronates derived from α -aryl cinnamates might exhibit color due to the auxochromic effect of the divalent oxygen functions attached to the styrene type chromophore. However, it is also possible that these compounds would be colored due to the enolate ions which would be present due to some dissociation of the boronates. Johnson and Rickborn³ have provided evidence for dissociation of similar proposed intermediates obtained by reduction of α,β -unsaturated aldehydes and ketones with sodium borohydride in isopropyl alcohol. A deep burgundy-colored intermediate was formed when sodium borohydride was added to a solution of methyl α -(p-nitrophenyl)-trans-cinnamate (4m) in anhydrous dimethoxyethane or dimethyl sulfoxide solution. Colored intermediates were also observed for 4n (orange) and 2a (red) in dimethoxyethane. The intermediates from other α -aryl cinnamates were colorless to pale yellow, except for that from 4q which was pale orange. These intermediates were stable for weeks in sealed tubes; however, the colors faded quickly in moist air or when water was added. Such intermediates were not observed for reductions carried out in methanol owing to rapid solvolysis to the dihydro esters.

Chemical shifts and coupling constants for the aliphatic proton absorptions in the nmr spectrum of methyl 2-(*p*nitrophenyl)-3-phenylpropionate (6m) (obtained by the sodium borohydride reduction of 4m in dimethoxyethane solution with subsequent hydrochloric acid work-up) are listed in Table II. Referring to the pertinent Newman projections (6m), it is apparent that H_a and H_b are diastereo-



6 m

topic; however, as a consequence of rapid rotamer interconversion, they give rise to simple geminal AB coupling and vicinal coupling with H_c .²¹

Reduction of 4m with sodium borohydride in anhydrous dimethoxyethane, followed by deuterolysis with 2 N deuterium chloride in deuterium oxide and a parallel reaction employing sodium borodeuteride, followed by hydrochloric acid work-up, afforded the propionates 11 and 12 (Table II) deuterated in the α and β positions, respectively. The α -deuteriopropionate (11) exhibited the expected simple geminal AB coupling. The β -deuterio compound (12) showed the expected H_c doublet, but the β -proton resonance appeared as two AB doublets, indicating the presence of diastereomers 12a and 12b (only one conformer of each is shown) in equal amounts. The same mixture of diastereomers was obtained from borodeuteride reduction of methyl α -(*p*-nitrophenyl)-*cis*-cinnamate (5m). Similarly, identical mixtures were obtained from borodeuteride reduction of methyl α -phenyl-*p*-nitro-*cis*- and -*trans*-cinnamates (5q and 4q). Diastereomers are, of course, expected to result from hydrolysis of the proposed enol boronate intermediates.



The α -aryl cinnamates provided an ideal system for mechanistic studies, since the electron availability at the α and β positions could be varied by use of substituents on either the α or β phenyl group. Hammett σ_p correlations were obtained on two series of methyl α -phenyltrans-cinnamates. In one series, the α phenyl group was unsubstituted while the para substituents on the β ring were varied (41, 4q-t). In the second series, the β phenyl group was held constant while the α ring was altered (41**p**). Competitive reductions of these cinnamates with sodium borohydride were carried out in anhydrous dimethoxyethane and the reaction mixtures were quenched with dilute hydrochloric acid to provide the corresponding propionates (6). Since quenching occurred instantly, the yields of propionates indicated the rates of formation of the boronate intermediates.

Table III lists relative rate data for the competitive reductions of the methyl α -(para substituted phenyl)-transcinnamates (41-p). A Hammett plot of this data vs. σ_p^{22} was linear; ρ was +1.74. The data obtained from competitive reduction of the methyl α -phenyl-trans-cinnamates (41, 4q-t) are also given in Table III. The ρ value for this series was +1.44. Although it has not been determined whether the first hydride transfer in the reduction of cinnamates is rate determining, as has been observed in the borohydride reduction of ketones,²³ it appears likely that this is the case. In any event, the linear Hammett correlations obtained are indicative of a constancy of mechanism for the range of substituents employed in both cases.²⁴ This was further demonstrated by competitive reduction of methyl α -(p-nitrophenyl)-trans-p-methoxycinnamate (4u) vs. methyl α -(p-nitrophenyl)-trans-cinnamate (4m), which showed a linear σ_{α} + σ_{β} contribution.²⁵ The rate factor (CH_3O/H) was 0.381, comparing favorably to the predicted value of 0.357 (Table III).

Correlation of both sets of relative rate data with $\sigma_{\rm p}$ are consistent with a rate-determining step involving hydride transfer to the carbon-carbon double bond in the cinnamate. The magnitudes of ρ are indicative of substantial negative charge stabilization during this step.^{25,26} The remarkable similarity in magnitudes of the ρ values suggests that the transition state for hydride transfer is attained before a considerable change in geometry of the cinnamate occurs.

Competitive rate studies on the methyl α -(para substituted phenyl)acrylates (2a-e) were quite problematic owing to difficulty in obtaining a sufficient number of compounds in this series and their tendencies to polymerize. On the basis of three reactions carried out in methanol solution at -5° (Table III), a linear Hammett plot was obtained, $\rho = +2.3$. This value was in line with that anticipated from the ρ value of 1.74 obtained for the α -(para substituted phenyl)-trans-cinnamates. The decreased ρ values observed for the cinnamates are explained by a *cis*-

stilbene type interaction of the aryl groups²⁷ which prevents them from achieving maximum resonance interaction with the developing anion.

In the α -phenyl-trans-cinnamates, steric hindrance forces the α and β phenyl groups out of plane with the carbon-carbon π bond, but has little effect on the carbomethoxyl group, which can still achieve maximum conjugative overlap. In the *cis*-cinnamate system, however, interaction between the carbomethoxyl and β -phenyl groups forces the ester function out of conjugation.27 The decreased ability of the carbomethoxyl group to achieve coplanarity and thus stabilize incipient anion formation appears to be the prime factor governing the differences in rates of reduction of cis- vs. trans- α -phenyl cinnamates. Reduction of methyl α -phenyl-trans-cinnamate (41) was slow (5.5% in 90 min); however, the cis isomer was not detectably (less than 0.1%) reduced under similar conditions. The methyl α -(p-nitrophenyl)cinnamates exhibited similar behavior. The trans isomer (4m) was completely reduced in less than 10 min, while the cis isomer required about 8 hr for complete reduction. Analogously, Truce and coworkers9 report that trans-1-mesityl-2-(mesitylsulfonyl)ethylene was reduced to the dihydrosulfone by sodium borohydride in diglyme. The cis isomer was inert to these conditions. In view of these results, the reported failure of diethyl diphenylmethylidenemalonate (1g) to undergo borohydride reduction appears to be as much a consequence of steric hindrance to anion development as the proposed decreased electrophilicity of the β carbon atom due to conjugation of the double bond with the β phenyl group.13

In contrast to the failure of methyl α -phenyl-*cis*-cinnamate to undergo reduction, α -phenyl-*cis*-cinnamonitrile was easily reduced (40% in 90 min) by sodium borohydride in dimethoxyethane. Likewise, Knabe and coworkers⁷ have reported that the substituted α -phenylcinnamonitriles 13a-c undergo double-bond reduction in good



yield upon heating with sodium borohydride in tetrahydrofuran solution. In the cinnamonitrile cases, the symmetrical nitrile function is not conformationally restricted to overlap.²⁷ The nitrile function is, however, a somewhat better anion-stabilizing moiety than the ester function.²⁸

Steric restraint of coplanarity of the carbomethoxyl function by a cis β -methyl group is expected to be much less dramatic than that observed with a cis β -phenyl group. Thus both the cis (14) and trans (15) isomers of methyl α -phenylcrotonate were found to undergo slow reduction with sodium borohydride in methanol to yield methyl α -phenylbutyrate. Competitive rate studies in methanol showed the trans crotonate to be 2.6 times more reactive than the cis isomer.



Experimental Section²⁹

Reagents. Sodium borohydride (SBH) and sodium borodeuteride were obtained from Matheson Coleman and Bell and from Stohler Isotopes, Inc., respectively. α -Phenyl-trans-cinnamic acid was purchased from Aldrich Chemical Co. Dimethoxyethane (DME) was refluxed over freshly cut sodium for several days and distilled from calcium hydride under nitrogen just prior to use. Solutions of SBH in anhydrous DME were standardized by titration with hydrochloric acid to a Methyl Orange endpoint.³⁰

Preparation of Methyl α -(Para substituted phenyl)acrylates (2a-e). Preparation of 2a was reported previously;³¹ 2b-e were prepared by the procedure of Dutta and Biswas³² for the preparation of ethyl α -(p-methoxyphenyl)acrylate, except that the appropriate methyl para-substituted phenyl acetates, sodium methoxide in methanol, and dimethyl oxalate were employed instead of the corresponding ethyl compounds. Nmr and glpc analysis of the crude products after short-path distillation indicated 25-40% yields of acrylates 2b-e contaminated with 15-20% of the methyl para-substituted phenyl acetates. Small samples of pure 2b-e were obtained by distillation of the crude products through a 60-cm platinum spinning band column. The boiling points follow: 2b, 78° (0.10 mm); 2c, 57° (0.11 mm); 2d, 69° (0.76 mm); 2e, 89° (0.10 mm). The nmr spectra were conclusive for the assigned structures.³³

Reduction of Acrylates 2a-e. SBH (1 mmol) was dissolved in 5 ml of methanol at -65° under nitrogen. A solution of 1 mmol of the acrylate in 5 ml of methanol at -65° was added and the solution was allowed to warm to room temperature and was stirred for 2 hr longer. Cold 0.4 N HCl (25 ml) was added and the mixture was extracted four times with 25-ml portions of ether. The combined ether extract was washed with NaHCO₃ solution and twice with 25-ml portions of water, then dried (MgSO₄), filtered, and evaporated through a Vigreux column. The propionates 3a-e were purified by evaporative distillation (bath temperature, pressure): 3a, 116° (0.15 mm); 3b, 82-86° (1.2 mm); 3c, 57-65° (0.2 mm); 3d, 65° (0.25 mm); 3e, 100-120° (2.1 mm). Small amounts (5-10%) of residues were obtained in each case. Nmr and glpc analysis indicated 95-100% carbon-carbon double bond reduction and the absence of other products. Preparative glpc was employed to obtain analytical samples of $3a-e.^{33}$

Competitive Reductions of the Acrylates 2b-e. Three reactions were conducted with the pairs of acrylates indicated in Table III. Methyl α -(p-nitrophenyl)acrylate was omitted since its rate of reduction was too fast to permit quantitative comparison with the other acrylates available.

A solution of 0.35 mmol of each of the indicated pair of acrylates in 27.5 ml of methanol was prepared under nitrogen. The solution was cooled to -5° . SBH solution (prepared by stirring 0.80 mmol of SBH in 2.5 ml of methanol at -5° for 2 min) was added in one portion to the stirred acrylate solution. After stirring at -5° for the time indicated in Table III, the reaction was quenched with 30 ml of cold 1 N HCl. Work-up was carried out as described above for reduction of the individual acrylates. The relative rates for Cl/H and Cl/F were determined by glpc analysis. The CH₃O/H ratio could not be determined in this manner owing to unsatisfactory resolution of all four peaks. Since the vinyl proton peaks in the nmr spectrum of a mixture of 2d and 2e were completely separated, the relative rate was determined from the rate of disappearance of these peaks. Mesitylene was employed as an internal concentration standard to determine the amounts of 2d and 2e remaining after partial reduction.

 α - and β -(Para substituted)- α -phenyl-cis- or -trans-cinnamic Acids. The trans-cinnamic acids 4b,³⁴ 4c, 4d,³⁵ 4e,³⁴ 4f,³⁴ 4g, 4h,³⁶ 4i,³⁴ 4j,³⁴ and 4k³⁴ were prepared by triethylamine-catalyzed condensation of the appropriate para-substituted benzaldehyde and phenylacetic acid in acetic anhydride solution according to the procedure of Buckles and coworkers (recrystallized from methanol).^{37,38} Compounds 4c, mp 191-192°, and 4g, mp 304° (both obtained in ~80 yield), apparently have not been reported previously. The assigned structures were confirmed by microanalyses on the corresponding methyl esters³³ and by nmr and ir spectroscopy.

The cis-cinnamic acids **5a**, **5b**, and **5f** were isolated from the equilibrium mixtures obtained by refluxing the corresponding trans acids in triethylamine-acetic anhydride solution for 3 hr.³⁴

Preparation of the Methyl Esters of the *cis-* or *trans-*Cinnamic Acids (4a-j, 5a, 5b, and 5f). An ice-cold solution of diazomethane in ether³⁹ was added slowly to a cold suspension or solution of the appropriate α - or β -(para-substituted)- α -phenylcinnamic acid in 25 ml of anhydrous ether until evolution of nitrogen ceased and excess diazomethane was visibly present. After stirring for 0.5 hr (ice bath), the ether solution was allowed to warm to room temperature and excess diazomethane was destroyed by addition of a little acetic acid. The ether solution was extracted with 50 ml of 10% Na_2CO_3 solution, dried (MgSO₄), and evaporated.

The crude cinnamates were recrystallized from hexane or methanol. The yields ranged from 89 to 96%. The melting points follow: 41, 72-73°; 51, liquid; 4m, 102-103° (lit.⁴⁰ 104°); 4n, 126°; 4o, 87-88°; 4p, 82.5-83°; 5m, 101-103°; 4q, 139-140°; 5q, 149-150°; 4r, 104-105°; 4s, 105-106°; 4t, 73-74°; 4u, 113-114°; 4v, 96-97°. The assigned structures were confirmed by elemental analysis³³ and by mr and ir spectroscopy.

Sodium Borohydride Reduction of the Cinnamates 41-v. 51. 5m, and 5q. A mixture of 1.0 mmol of the particular methyl α phenylcinnamate, 1.0 mmol (37.8 mg) of SBH, and 10 ml of anhydrous DME was stirred at room temperature. After sufficient time for complete reduction (ranging from about 10 min for 4m to more than 1 week for 4p or 4t) the mixture was neutralized with 1 N HCl and the solvent was removed in vacuo. Saturated aqueous NH₄Cl solution (5 ml) was added and the mixture was extracted three times with a total of 20 ml of chloroform. The combined extract was dried over MgSO₄, concentrated, and sublimed or evaporatively distilled at 100-110° (0.1 mm). These dihydroesters were all liquids except **6m**, mp 60-61°; **6q**, mp 78-80°; **6r**, mp 63-64°; **6t**, mp 60-61°; **6u**, mp 73-78°. Reduction of **4v** was extremely slow-gc analysis indicated that 6v was formed in only 1% yield after 2 weeks reduction time. The dihydrocinnamate structures were verified by microanalysis³³ and nmr (data in Table II are typical) spectroscopy. Glpc indicated that these compounds were the only reaction products in all cases. This was confirmed by tlc.

Competitive Reductions of Methyl α - or β -(Para-substituted)- α -phenyl-trans-cinnamates. Five milliliters of a standardized solution containing 5.67 mg (0.15 mmol) of SBH in anhydrous DME was added to a stirred solution of 0.33 mmol each of the two cinnamates (Table III) in 2 ml of dry DME at 25°. After the reaction time indicated, the reaction was guenched with a few drops of 2 N HCl. The solvent was removed in vacuo, 5 ml of saturated NH₄Cl solution was added, and the mixture was extracted three times with a total of 25 ml of ether; the combined extract was dried (MgSO₄) and evaporated before glpc analysis.

Preparation of Intermediates for Nmr Analysis (Table I). Samples were prepared in a glove box under nitrogen. A solution of 4.33 mmol of methyl α -phenyl-trans-cinnamate (41) or the pchlorophenyl ester (40) in 2 ml of anhydrous DMSO-d₆ (1% TMS) was prepared in a dry 4-ml septum-capped vial. Sodium borohydride (1.08 mmol) was added and the sample was sealed and stirred magnetically to effect solution. Samples were then transferred to oven-dried nmr tubes fitted with conventional polyethylene caps.

Preparation of Methyl 2-Deuterio-2-(p-nitrophenyl)-3-phenylpropionate (11). One millimole (283 mg) of 4m was dissolved in 20 ml of dry DME under nitrogen and 1 mmol of SBH was added. The mixture was stirred for 10 min, then quenched with a few drops of 2 N DCl in D₂O solution. The solvent was evaporated *in* vacuo at room temperature. The residue was extracted twice with 5-ml portions of ether, and the combined extract was dried over MgSO₄ and evaporated *in* vacuo. The crude product was recrystallized from hexane to yield 206 mg (76% yield) of 11, mp 58-59°. Nmr data for 11 are given in Table II.

Preparation of Methyl 2-(p-Nitrophenyl)-3-deuterio-3-phenylpropionate (12). A solution of 0.5 mmol of methyl α -(p-nitrophenyl)-cis- or -trans-cinnamate (4m or 5m) was dissolved in 10 ml of dry DME under nitrogen. An equimolar amount of sodium borodeuteride was added and the mixture was stirred at room temperature (10 min for 4m, overnight for 5m). A few drops of water was then added and the solvent was evaporated in vacuo at room temperature. Work-up was carried out as described for the preparation of the 2-deuterio compound (11). Nmr on the crude product (Table II) indicates that both reactions gave 1:1 mixtures of the diastereomers of 12.

Borohydride Reduction of α -Phenyl-cis-cinnamonitrile. Reduction of α -phenyl-cis-cinnamonitrile (K and K Laboratories) was carried out for 1.5 hr at room temperature, using the amounts and procedure described for the cinnamates. The crude product was examined by glpc and by nmr and found to contain \sim 40% 2,3-diphenylpropionitrile.

Preparation of Methyl α -**Phenyl**-cis- and -trans-crotonates (14, 15). A 15-g sample of α -phenylcrotonic acid⁴¹ was esterified by refluxing for 22 hr with 100 ml of a 10% solution of concentrated H₂SO₄ in methanol. The crude product was poured into ice

water and extracted into ether. The ether extract was washed with water, dried (MgSO₄), evaporated, and distilled at 70-73° (0.3 mm) to give 6.8 g (42% yield) of a 9:91 mixture of methyl α phenyl-cis- and -trans-crotonates (14 and 15, respectively). These isomers were separated by preparative glpc. The nmr spectrum of the trans-crotonate 15 had peaks at 1.68 (d, J = 7 Hz, CH₃), 3.58 (s, OCH₃), 7.08 ppm (q, J = 7 Hz, =CH), partly obscured by the phenyl absorptions (7.05–7.40, m). Peaks for the *cis*-crotonate 14 were at 1.96 (d, J = 7 Hz, CH₃), 3.65 (s, OCH₃), 6.14 (q, J = 7Hz, ==CH), 7.05-7.40 ppm (m, phenyl).

Borohydride Reduction of the Crotonates 14 and 15. A solution of 189 mg (5 mmol) of SBH in 20 ml of methanol was prepared under nitrogen at -78° . A solution of 881 mg (5 mmol) of methyl phenyl-cis- and -trans-crotonates (9:91) in 5 ml of methanol was added, the cooling bath was removed, and the mixture was stirred for 2 hr at room temperature (29°). Work-up with dilute HCl, etc., as described for the acrylate reductions, followed by glpc analysis, indicated that $\sim 20\%$ reduction had occurred. The crude product was redissolved in methanol at 0° under nitrogen, 0.5 g of SBH was added, and the mixture was allowed to warm to 25° over 1.25 hr. The solution was again cooled to 0° and another 0.5-g portion of SBH was added. The mixture was allowed to warm to 25° over 1.5 hr. Work-up with dilute HCl, etc., as before, gave 775 mg of colorless liquid. Glpc indicated that 15-20% unreacted crotonates (cis:trans ratio ca. 2:3) remained as well as a major and minor (<5%) product. Samples of these products were collected by glpc. The major product was methyl α phenylbutyrate (16), confirmed by ir, uv, and microanalysis.33 The minor product was 2-phenylbutanol (nmr).

Competitive Reduction of the Crotonates. A solution of 21 mg (0.12 mmol) of a mixture of methyl α -phenyl-cis- and -trans-crotonate (41.7% cis, 58.3% trans) in 1 ml of methanol at 28° was treated with a total of 28.7 mg (0.75 mmol) of SBH, added in three portions at 1.25-hr intervals. After addition of a few drops of cold dilute HCl, work-up was carried out as described for the acrylate reductions. Glpc analysis on the crude product indicated that the trans-crotonate (15) was reduced 2.6 times faster than the cis isomer. Only a trace of 2-phenylbutanol was observed. Reduction of a sample of cis-crotonate under similar conditions ruled out the possibility of cis-trans isomerization of starting material.

Registry No.-2a, 28042-27-5; 2b, 50415-59-3; 2c, 50415-66-2; 2d, 1865-29-8; 2e, 50415-68-4; 3a, 50415-69-5; 3b, 50415-70-8; 3c, 50415,71-9; 3d, 31508-44-8; 3e, 50415-73-1; 4c, 50415-74-2; 4g, 50415-75-3; 41, 36854-27-0; 4m, 23848-96-6; 4n, 50415-78-6; 4o, 50415-79-7; 4p, 42443-25-4; 4q, 42443-21-0; 4r, 50415-82-2; 4s, 42307-43-7; 4t, 36854-29-2; 4u, 50415-61-7; 4v, 50415-62-8; 5l, 41366-87-4; 5m, 42443-20-9; 5q, 31499-32-8; 6m, 50415-50-4; 6q, 50415-51-5; 6r, 50415-52-6; 6t, 5448-41-9; 6u, 50415-54-8; 10, 50404-58-5; 11, 50415-55-9; 12a, 50415-56-0; 12b, 50415-83-3; 14, 50415-84-4; 15, 50415-85-5; 16, 2294-71-5; sodium borohydride, 16940-66-2.

References and Notes

- (1) (a) Presented at the Middle Atlantic Regional Meeting of the American Chemical Society, Dover, Del., April 1970. (b) Abstracted in part from the Ph.D. Thesis of G. J. W., Villanova University, May 1970. (c) NASA Fellow, 1966-1969. (d) M.A. degree recipient, Vil-Ianova University, August 1973. (2) A survey of the literature on these reductions is presented in the
- Ph.D. Thesis of G. J. W. (ref 1b); representative studies are cited in ref 3-11.
- M. R. Johnson and B. Rickborn, J. Org. Chem., 35, 1041 (1970).

- M. R. Johnson and B. Rickborn, J. Org. Chem. 33, 1041 (1970).
 W. R. Jackson and A. Zurqiyah, J. Chem. Soc., 5280 (1965).
 K. Iqbal and W. R. Jackson, J. Chem. Soc., 616 (1968).
 M. S. Brown and H. Rapoport, J. Org. Chem., 28, 3261 (1963).
 J. Knabe, P. Herbort, and N. Ruppenthal, Arch. Pharm. (Weinheim), 299, 534 (1966).
 D. C. Dittmer and M. E. Christy, J. Amer. Chem. Soc., 84, 399 (1962). (1962).

- (9) W. E. Truce, H. G. Klein, and R. B. Kruse, J. Amer. Chem. Soc., 83, 4636 (1961).
- H. Schechter, D. E. Ley, and E. B. Roberson, Jr., J. Amer. Chem. Soc., **78**, 4984 (1956). (10)

- (11) A. I. Meyers and J. S. Sircar, J. Org. Chem., 32, 4134 (1967).
 (12) J. A. Meschino and C. H. Bond, J. Org. Chem., 28, 3129 (1963).
 (13) S. B. Kadin, J. Org. Chem., 31, 620 (1966).
 (14) J. A. Marshall and R. D. Carroll, J. Org. Chem., 30, 2748 (1965).
 (15) D. Cabaret and Z. Welvart, C. R. Acad. Sci., Ser. C, 274, 1200 (1970). (1972).
- (16) Owing to solvolysis of sodium borohydride by methanol [H. C. Brown and K. Ichikawa, J. Amer. Chem. Soc., 83, 4372 (1961)], reductions which proceeded very slowly would not have been detected.
- (17) Brown and Rapoport (ref 6) have observed partial reduction of double bonds in certain $\dot{\beta}$ -aryl acrylates under forcing conditions (tenfold excess of sodium borohydride in refluxing methanol). (18) During the course of this work, Kadin (ref 13) reported the analo-
- gous reduction of ethyl α -phenylacrylate (1e) with sodium borohydride in ethanol.
- (19) Jackson and Rickborn and coworkers (ref 3-5) have proposed similar intermediates for borohydride reductions of α, β -unsaturated ketones.
- .. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic (20) Resonance Spectroscopy in Organic Chemistry, "Pergamon Press, Elmsford, N. Y., 1969, p 274. The proton nmr data are also com-patible with the alternate 1,2-addition product, [PhCH₂- $C(PhCO_2CH_3)]_4B^{-}Na^+$; however, this structure would ap-pear to be excluded on the basis of the severe steric hindrance which would result during the third and fourth hydride transfers required for its formation.
- Reference 20, p 372.
- Substituent constants were obtained from the tables of C. D. Ritch-ie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964). H. C. Brown, O. H. Wheeler, and K. Ichkawa, *Tetrahedron*, **1**, 214 (22)
- (23)(1957)
- (1957).
 (24) H. H. Jaffe, Chem. Rev., 53, 191 (1953).
 (25) Cf. T. I. Crowell, G. C. Heisley, R. E. Lutz, and W. L. Scott, J. Amer. Chem. Soc., 85, 443 (1963), who observed that base-catalyzed addition of methanol to a series of trans-p.p'-disubstituted dibenzoylethylenes gave a Hammett plot linear in $\sigma_{\rm p}$ + $\sigma_{\rm p'}$ (ρ = 1.00).
- (26) The ρ value for Michael addition of barbiturate ion to β -nitrostyrene is 0.74: M. J. Kamlet and D. J. Glover, J. Amer. Chem. Soc., **78**, 4556 (1956).
- H. E. Zimmerman and L. Ahramjian, J. Amer. Chem. Soc., 81, 2086 (1959). (27)
- (28) R. G. Pearson and R. L. Dillon, J. Amer. Chem. Soc., 75, 2439 (1953).
- Glpc was carried out on a Hewlett-Packard F & M Model 700 in-(29) Glpc was carried out on a Hewlett-Packard F & M Model /00 in-strument equipped with 12 ft \times 0.125 or 0.25 in. stainless steel col-umns packed with 15% SE-30 on acid- and base-washed, silanized Chromosorb W. Analytical glpc for the crotonate reduction was done on a Wilkins Instrument Co. Hi Fi chromatograph equipped with a 12 ft \times 0.125 in. TCEP column. Nmr spectra were obtained with a Varian A-60 spectrometer using TMS as the internal reference. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points are uncorrected. (30) W. D. Davis, L. S. Mason, and G. Stegeman, J. Amer. Chem. Soc..
- 71, 2775 (1949)
- (31) J. H. Schauble, E. H. Freed, and M. D. Swerdloff, J. Org. Chem., 36, 1302 (1971).
- (32) J. Dutta and R. N. Biswas, J. Indian Chem. Soc., 40, 629 (1963).
 (33) Microanalysis (C, H, N, or halogen) for 2b, 2d, 2e, 3a-e, 4I-v, 5I, 5m, 5q, 6I-v, and 16 were all within ±0.25% of the calculated values. Repetitive analyses for 2c were erratic, apparently owing to incomplete combustion.

- (34) R. Ketcham and D. Jambotkar, J. Org. Chem., 28, 1034 (1963).
 (35) J. F. Codington and E. Mosettig, J. Org. Chem., 17, 1027 (1952).
 (36) P. Schmid, U. S. At. Energy Comm., UCRL-8883 (1959); Chem. Abstr., 54, 7647 (1960).
 (37) R. E. Buckles, M. P. Bellis, and W. D. Coder, Jr., J. Amer. Chem. Soc., 73, 4972 (1951).
 (39) B. E. Buckles and K. Bremer in "Ornanic Syntheses" Collect. Vol.

- (38) R. E. Buckles and K. Bremer in "Organic Syntheses," Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 777.
 (39) T. J. DeBoer and H. J. Backer in "Organic Syntheses," Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 250.
 (40) G. Drefahl, G. Heublein, and G. Tetzlaff, J. Prakt. Chem. 23, 318
- u. Dre (1964) P. P
- Pfeiffer, I. Engelhardt, and W. Alfuss, Justus Liebigs Ann. (41) Chem., 467, 181 (1928)