preparation of the 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline with the exception that a higher temperature (150–180°) was necessary for the reaction to occur. The oxazoline was a colorless, viscous liquid with an odor characteristic of all of the oxazolines. The yield was 82% based on unchanged ketone, b.p. 93–94° (2.5 mm.), $n^{20}D$ 1.4593, d_4^{20} 0.955.

Anal. Calcd. for $C_{12}H_{23}O_2N$: C, 67.56; H, 10.87; N, 6.6; MR, 61.60. Found: C, 67.48; H, 10.76; N, 6.7; MR, 61.54.

2-(1,3-Dimethyl-1-hydroxybutyl)-5-isobutyl-2,4,5-trimethyl-3-oxazoline.[17]—This oxazoline was prepared using the conditions that were employed for 5-ethyl-2-(1-hydroxy-1-methylpropyl)-2,4,5-trimethyl-3-oxazoline. A reaction period for 9 hr. gave a quantitative yield,[18] b.p. 90–91° (0.37 mm.), $n^{20}D$ 1.4626, d_4^{20} 0.917.

Anal. Calcd. for $C_{16}H_{31}O_2N$: C, 71.33; H, 11.60; N, 5.2; MR, 80.85. Found: C, 71.12; H, 11.45; N, 5.0; MR, 80.08.

2,3,4,5-Tetramethyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol.—The pressure reaction apparatus[19] was charged with 50 g. of an 85% aqueous solution of 3-hydroxy-2-butanone and 180 ml. of absolute alcohol. Anhydrous ammonia was introduced until a pressure of 100 p.s.i.g. was obtained. During the addition of ammonia the temperature rose from 22° to 50° (probably due to the heat of solution), then slowly dropped to room temperature. The pressure was maintained at 80–100 p.s.i.g. for 2.5 hr. by an occasional addition of ammonia. Following the removal of ammonia, ethanol and water, the residue was fractionated at reduced pressure,[20] yielding 34.2 g. (90.2%) of a light amber-colored, viscous liquid, b.p. 78–80° (6 mm.), $n^{20}D$ 1.4574, d_4^{20} 0.997.

Anal. Calcd. for $C_8H_{15}O_2N$: C, 61.13; H, 9.62; N, 8.9; MR, 43.12. Found: C, 60.63; H, 9.72; N, 9.0; MR, 42.87.

2,4-Dimethyl-3,5-dipropyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol.—The pressure reaction apparatus was charged with 50.6 g. of 3-hydroxy-2-hexanone and 100 ml. of 95% ethanol. The stirrer was started and anhydrous ammonia was introduced until a pressure of 100 p.s.i.g. was obtained. The pressure was maintained between 75 and 100 p.s.i.g. for approximately 9 hr. Fractionation of the reaction product yielded 42.3 g. of the pyrrolenine (91%), b.p. 94–95° (1.0 mm.), $n^{20}D$ 1.4646, d_4^{20} 0.957.

Anal. Calcd. for $C_{12}H_{23}O_2N$: C, 67.56; H, 10.87; N, 6.6; MR, 61.60. Found: C, 67.67; H, 10.72; N, 6.6; MR, 61.20.

Acid hydrolysis of 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline.—A 50.0-g. sample of 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline was dissolved in 182 g. of 10% hydrochloric acid, and the solution was refluxed for 23 hr. The reaction mixture was steam distilled, and the distillate was salted with ammonium sulfate. The upper layer from the salting was azeotropically distilled with benzene to remove the water, and the benzene solution was fractionated to yield 50.6 g. (92%) of 3-hydroxy-3-methyl-2-butanone. The residue from the steam distillation was filtered, decolorized with Norite and evaporated to yield 12.2 g. (82%) of ammonium chloride.

(17) The authors are indebted to Mr. Gary R. Hansen for the work on this reaction and most of the micro carbon and hydrogen analyses.

(18) The yield of oxazoline was found to be dependent on the reaction time. An 8–10-hr. period gave rise to essentially quantitative yields in all three cases.

(19) Pressures above atmospheric pressure were not necessary for the formation of the pyrrolenines; however, the reactions were extremely slow.

(20) If the pot temperature during distillation was allowed to rise above 100° (approximately), complete polymerization occurred.

The Preparation of and Equilibrium between Substituted α-Phenyl-*cis*- and *trans*-cinnamic Acids

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The amine-catalyzed Perkin condensations of a series of *p*-substituted phenylacetic acids and benzaldehydes are described. In every case, both *cis* and *trans* isomeric products have been characterized. Substitution of pyridine for triethylamine in condensations with *p*-nitrophenylacetic acids has resulted in increased yields. The equilibrium constant for each pair of isomers has been determined.

The amine-catalyzed Perkin condensation of phenylacetic acids with benzaldehydes[1,2] and the Oglialoro modification[3,4] in which the amine and the acid are replaced by a salt of the acid, both afford α-phenyl-*trans*-cinnamic acids. A minor product is often the isomeric *cis* acid[1-4] but in about half of the condensations reported none of the *cis* acid has been obtained.

Although we were primarily interested in the *trans* acids as intermediates for the synthesis of *cis*-stilbenes, there are several reasons for wanting samples of the *cis* isomers. First, the isolation and spectroscopic study of both isomers provides more direct evidence for the stereochemistry of the products. Second, the system offers interesting possibilities for studying the effect that substituents on the two different rings have on the relative rates of formation of the acids, on the equilibrium between the *cis* and *trans* isomers and upon their acidities. Finally, in view of the known antibacterial and antifungal activity of cinnamic acids,[5] it was of interest to have these properties evaluated in the *cis*- as well as the α-phenyl-*trans*-cinnamic acids.

The condensation of benzaldehyde, anisaldehyde and *p*-nitrobenzaldehyde with each of three similarly *p*-substituted phenylacetic acids has been studied. The data on the preparation of these nine pairs of *cis* and *trans* isomers are summarized in Table I. It was found that the *trans* isomer in each pair was as expected the

(1) (a) L. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., p. 182; (b) J. R. Johnson, *Org. Reactions*, **1**, 225 (1942). Reference 1a names these as *cis*- or *trans*-α-phenylcinnamic acids where the prefixes *cis* and *trans* refer to the relationship between the two phenyl groups, whereas ref. 6 names them as α-phenyl-*cis*- or *trans*-cinnamic acids in which the prefixes refer to the relationship between the carboxylic acid function and the β-phenyl group—*i.e.*, the cinnamic acid moiety. The latter nomenclature is used throughout this report.

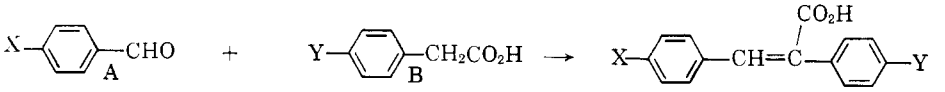
(2) (a) R. E. Buckles, M. P. Bellis, and W. D. Coder, Jr., *J. Am. Chem. Soc.*, **73**, 4972 (1951); (b) R. E. Buckles and E. A. Hausman, *ibid.*, **70**, 415 (1948); (c) R. E. Buckles, E. A. Hausman, and N. G. Wheeler, *ibid.*, **72**, 2494; (1950); (d) R. Stoermer and L. Prigge, *Ann.*, **409**, 20 (1915).

(3) (a) H. Lettré and O. Linsert, German Patent 840,091 (May 26, 1952); (b) D. Papa, E. Klingsberg, and E. Schwenk, U. S. Patent 2,606,922 (December 3, 1949); (c) O. Linsert and H. Lettré, U. S. Patent 2,691,039 (April 11, 1951); (d) British Patent 559,024 (August 31, 1942).

(4) (a) M. Bakunin, *Gazz. chim. ital.*, **25**, 137 (1895); (b) D. Papa, H. Breiger, E. Schwenk, and V. Peterson, *J. Am. Chem. Soc.*, **72**, 4906 (1950); (c) B. B. Dey and U. Ramanathan, *Proc. Natl. Inst. Sci., India*, **9**, 193 (1943); (d) V. M. Fedosova and O. Yu. Magidson, *J. Gen. Chem., USSR*, **24**, 701 (1954); (e) M. Crawford and G. W. Moore, *J. Chem. Soc.*, 3445 (1955); (f) T. R. Lewis, M. G. Pratt, E. D. Homiller, B. F. Tullar, and S. Archer, *J. Am. Chem. Soc.*, **71**, 3749 (1949); (g) E. Schwenk, D. Papa, B. Whitman, and H. F. Ginsberg, *J. Org. Chem.*, **9**, 175 (1944).

(5) I. A. Pearl and D. L. Beyer, *ibid.*, **16**, 216 (1951).

TABLE I



No.	X	Y	T°,[a]	t[b]	A:B[c]	% Yield[d] and m.p.,[e] °C. *trans*	% Yield[d] and m.p.,[e] °C. *cis*	Purified m.p., °C. *trans*	Purified m.p., °C. *cis*	Solvents[g] pH[f]	I[h]	II[i]	III[j]
I	H	H	170	45	1.61	68 162–166	11 136–137	172–173[k]	138–139[k]	6	E	E-P	E-P
II	OCH_3	H	170	60	1.61	57 174–181	6.6 118–121	189–190[l]	120–122[m]	6	M	C-P	C-P
III	H	OCH_3	170	60	1.61	72 146–148	19 115–128	150–152[n]	116–118 or 129–130	6	E	E-P	E-P
IV	OCH_3	OCH_3	170	90	1.61	64 197–208	9.3 125–128	216–217[o]	131–132	6.2	M	A	B-H
V	NO_2	H	140	25	1.10	69 195–205	29 138–140	208–210[p]	141–143[p]	4.5	M	A	B
VI	H	NO_2	130	45	1.61	38 214–219	23 142–146	221–224[q]	149–151[q]	4.5	M	A	B
VI[r]	H	NO_2	150	90	1.61	56 214–220	11 143–147						
VII	NO_2	NO_2	130	45	1.10	52 180–250	10 180–200	269–271[s]	215–217	4.0	M	A	A
VII[r]	NO_2	NO_2	150	60	1.10	77 255–265	10 204–207						
VIII	OCH_3	NO_2	150	45	1.61	8.2 216–232	5.5 180–182	235–237[t]	184–185	5.5	M	A	Et
VIII[r]	OCH_3	NO_2	150	120	1.61	40 215–230	5 181–184						
IX	NO_2	OCH_3	120	20	1.10	82 170–185	10 143–146	191–192	145–147	5.5	M	A	B

[a] Bath temperature. [b] Reaction time in minutes. [c] Ratio of reactants (A + B). [d] Based on B. [e] Crude. [f] pH used to precipitate the *trans* acid. [g] E—ether, P—petroleum ether (30–60°), A—acetic acid, B—benzene, H—hexane, M—methylene chloride, Et—ethanol. [h] Extraction solvent. [i] Solvent used to recrystallize the *trans* acid. [j] Solvent used to crystallize the *cis* acid. [k] Ref. 1 gives 173 and 130°. [l] Ref. 2a gives 188–189°. [m] Ref. 2d gives 123°. [n] Ref. 4g gives 152°. [o] Ref. 3b gives 217–218°. *Cf.* also Ref. 7. [p] Ref. 4a gives 123–124° and 138–143°. [q] Ref. 4f gives 219–221° and 150–152°. [r] Pyridine substituted for triethylamine. [s] Ref. 2a gives 266–268°. [t] Ref. 2a gives 235–236°.

main product and that it had a lower solubility and was the weaker acid. The assignment of *cis* and *trans* structures to these pairs of isomers was confirmed by reference to their ultraviolet and infrared spectra. The *cis* isomers, which contain the strong *trans* stilbene chromophore, absorb at longer wave lengths in the ultraviolet than the isomeric acids which contain the weaker *cis*-stilbene and *trans*-cinnamic acid chromophores. The infrared carbonyl absorptions of the conjugated carboxyl groups of the *trans* acids appear at lower wave numbers than those of the unconjugated, perpendicular[6] carboxyl groups of the *cis* acids. These data are in Table II.

In the reactions with *p*-nitrophenylacetic acid and either benzaldehyde or anisaldehyde the high reactivity of the acid and the relatively low reactivity of the aldehydes caused a large amount of self condensation of the acid to give polymeric and enolic substances, the nature of which have not been further investigated. The low yields obtained in these condensations of *p*-nitrophenylacetic acid contrast with the favorable yields obtained in the Oglialoro modification where the base is acetate or *p*-nitrophenylacetate. Since these bases are weaker than triethylamine by several powers of ten, it was reasoned that better yields might be achieved if a less basic amine such as pyridine were used as the catalyst. This change resulted in a four-fold increase in the yield of α-*p*-nitrophenyl-*trans*-*p*-methoxycinnamic acid. Substantial increases were also obtained in the other condensations with *p*-nitrophenylacetic acid.

TABLE II

INFRARED AND ULTRAVIOLET SPECTRAL DATA

No.	Infrared cm.$^{-1}$ *trans*	Infrared cm.$^{-1}$ *cis*	Ultraviolet *trans* mμ (ε × 10^{-4})	Ultraviolet *cis* mμ (ε × 10^{-4})
I	1678	1712	282 (1.53)	288 (2.21)
II	1670	1715	302 (2.30)	309 (2.04)
III	1670	1691	274 (1.45)	298 (2.32)
IV	1665	1695	300 (1.88)	302 (2.12)
V	1682	1710	314 (1.41)	333 (1.85)
VI	1670	1695	269 (2.05)	332 (1.90)
VII	1695	1700	300 (1.84)	340 (2.56)
VIII	1672	1723	288 (2.30)	357 (2.32)
IX	1690	1728	286 (1.47)	358 (2.18)

All but one of the *trans* acids have been previously described,[1–4,6,7] whereas five of the *cis* isomers have not been described.[1,2d,4a,f] The analyses of these compounds are given in Table III.

The separation of *cis* and *trans* isomers was accomplished by first precipitating the weaker *trans* acid with acetic acid at the appropriate pH.[1a] For instance, in the case of the *p*,*p*′-dimethoxy acid this is 6.2; and for the *p*,*p*′-dinitro acid, 4.0. The pH adjustment required to precipitate the various *trans* acids is included in Table I. The *cis* acid was then precipitated with hydrochloric acid.

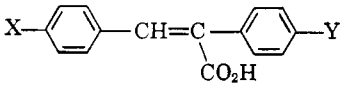
Milder reaction conditions[2a–c,6] have been shown in some cases to afford almost exclusively the *trans* acid,

(6) H. E. Zimmerman and L. Ahramjian, *J. Am. Chem. Soc.*, **81**, 2086 (1959).

(7) F. D. Greene, W. Adam, and J. E. Cantrill, *ibid.*, **83**, 3461 (1961).

TABLE III

ANALYTICAL DATA ON



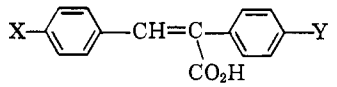
				Calcd.			Found		
X	Y	*cis* or *trans*	Formula	C	H	N	C	H	N
H	OCH_3	*cis*	$C_{16}H_{14}O_3$	75.52	5.55	..	75.50	5.51	..
OCH_3	OCH_3	*cis*	$C_{17}H_{16}O_4$	71.82	5.67	..	71.71	5.62	..
NO_2	OCH_3	*trans*	$C_{16}H_{13}NO_5$	64.21	4.38	4.68	64.07	4.49	4.39
NO_2	OCH_3	*cis*	$C_{16}H_{13}NO_5$	64.21	4.38	4.68	63.50	4.25	4.82
OCH_3	NO_2	*cis*	$C_{16}H_{13}NO_5$	64.21	4.38	4.68	64.51	4.39	4.75
NO_2	NO_2	*cis*	$C_{15}H_{10}N_2O_6$	57.34	3.21	8.92	57.13	2.96	9.30

presumably at the expense of the *cis* isomer. More vigorous reaction conditions were employed here in order to obtain larger amounts of the *cis* isomers.

Since the *cis* isomers often constituted only about 10% of the reaction products, a better method for their preparation was sought. In the unsubstituted α-phenylcinnamic acids, Zimmerman has shown[6] that at equilibrium there is present 19% of the *cis* isomer, so that one could expect to effect partial conversion of *trans* to *cis* by equilibration of the *trans* isomer.[8] In addition we had reason to hope that in the case of some of the substituted α-phenylcinnamic acids, the equilibrium mixture would contain even more of the *cis* isomer as a result of increased resonance stabilization of the substituted *trans*-stilbene moiety. We therefore undertook equilibration of the *trans* acids with acetic anhydride and triethylamine. Zimmerman had started with the *cis* acid in his determination of the equilibrium constant.[6] We have confirmed this constant for the α-phenylcinnamic acids by achieving the same equilibrium mixture starting with the *trans* isomer. In those few cases where it seemed possible that we might not have attained equilibrium, the correctness of the determination was checked by starting from the *cis* isomer. In all cases the same value for the equilibrium constant was obtained in the same time span irrespective of the direction from which it was attained. These values for the variously substituted α-phenylcinnamic acids are given in Table IV.

TABLE IV

cis–trans- RATIO AT EQUILIBRIUM FOR



No.	X	Y	% *trans*[a]	% *cis*[a]	% Total recovery
I	H	H	80[b]	20[b]	95
II	OCH_3	H	82	18	97
III	H	OCH_3	73	27	98
IV	OCH_3	OCH_3	90	10	98
V	NO_2	H	37	63	90
VI	H	NO_2	70	40	92
VII	NO_2	NO_2	88[c]	12[c]	92
VIII	OCH_3	NO_2	74	26	92
IX	NO_2	OCH_3	52	48	96

[a] Percent of *cis* or *trans* in recovered material, ±3%. [b] Ref. 6 gives 81% *trans* and 19% *cis*. [c] Four-hour reflux using pyridine instead of triethylamine.

The effect that various substituents have on the equilibrium between the *cis* and *trans* isomers can be explained by the effectiveness of their resonance interactions with the *trans*-stilbene or the *trans*-cinnamic acid structures.

Substitution of either a methoxy or a nitro group in the *para* position of the α-phenyl ring produces an increase in the amount of *cis* isomer present at equilibrium. The increased resonance stabilization afforded the *cis* isomers by these substituents apparently helps to overcome the steric hindrance engendered by the carboxyl group to the coplanarity of the α-phenyl group with the remainder of the *trans*-stilbene structure.[6]

Substitution of a *p*-methoxy group on the β-phenyl ring would be expected to extend the conjugation of either the *trans*-stilbene or the *trans*-cinnamic acid system. However, since the carboxyl group is more electron-withdrawing than the phenyl group the electron-donating methoxy group would be expected to interact more favorably with the carboxylic acid function and stabilize the *trans* relative to the *cis* isomer. The slight increase in the percentage of *trans* isomer caused by this substitution is explicable on these grounds. The introduction of *p*-methoxy groups on both rings would further favor the *trans* isomer since the carboxyl group is even more electron-withdrawing compared to the methoxy-substituted α-phenyl group. Thus the minimum of 10% *cis* is reached in the dimethoxy acid.

A *p*-nitro substituent on the β-phenyl ring should have an effect opposite to that of methoxy, since the electron withdrawing nitro group would not effectively conjugate with the electronically similar carboxyl group. The 63% of *cis* isomer observed is far larger than any other case and certainly more than predicted.

The unsymmetrically disubstituted compounds should both be expected to give an increased amount of the *cis* isomer, but in the case of the α-(*p*-methoxyphenyl)-*p*-nitrocinnamic acids the 42% *cis* is less than predicted on the basis of the two related monosubstituted compounds.

In the case of the dinitro acids the 22-hour equilibration time caused extensive decomposition. It was found that either the *cis*- or the *trans*-dinitro acid was equilibrated in a four-hour reflux period in pyridine–acetic anhydride to a mixture of 88% *trans* and 12% *cis*. This is the expected effect of having two nitro groups working against each other, thereby decreasing

(8) H. E. Zimmerman (ref. 6) stated that "the rate of equilibration of the more stable isomer must be slower." This seems to imply that the time required to attain equilibrium must be longer in the case of the more stable isomer. This cannot be the case. The rate constant for the conversion of the more stable to the less stable isomer must be smaller but the time required to reach equilibrium must be the same irrespective of the isomer with which one starts.

the stability of the *cis* isomer relative to the situation in the unsubstituted α-phenylcinnamic acids.

Experimental[9]

α-Phenylcinnamic Acids.—The preparation of the acids was carried out according to Fieser's directions.[1a] The only modifications were those made necessary by the relatively low solubility of many of the *trans* acids in ether. The pH adjustment required for precipitation of the *cis* isomer was checked with a Leeds and Northrup pH meter. The immiscible solvent used in the extraction, the recrystallization solvents, and the pH adjustment made to precipitate the *trans* acids are given in Table I.

The details are illustrated by the preparation of α-*p*-nitrophenyl-*cis*- and *trans*-*p*-nitrocinnamic acid from *p*-nitrophenylacetic acid and *p*-nitrobenzaldehyde (the low solubility of this *trans* acid and its salts requires the most extensive changes in conditions). A solution of 6.11 g. (0.040 mole) of *p*-nitrobenzaldehyde and 6.66 g. (0.037 mole) of *p*-nitrophenylacetic acid in 4 ml. of pyridine and 4 ml. of acetic anhydride was heated under reflux in an oil bath maintained at 150° for 30 min. A precipitate often forms during this heating period. The reaction mixture was acidified with 8 ml. of concentrated hydrochloric acid, the solid broken up and the whole mass transferred to a separatory funnel and dissolved in 1200 ml. of methylene chloride. This solution was washed with several 200-ml. portions of water and then extracted with three 200-ml. portions of 0.2% sodium hydroxide. The combined extracts were then acidified to a pH of 4.0 with about 10 ml. of acetic acid. The *trans* acid was filtered from the solution containing the salt of the *cis* acid and washed with water. The yield was 8.95 g., m.p. 255–265°. Recrystallization from 200 ml. of acetic acid gave 7.5 g., m.p. 265–270°. The *cis* isomer was precipitated by the addition of 10 ml. of concentrated hydrochloric acid to the above solution to give 1.2 g., m.p. 204–207°.

Alternately the reaction mixture, after acidification with 8 ml. of concentrated hydrochloric acid, can be stirred with 100 ml. of water, the solid collected, and washed with water. This solid can be extracted by stirring with successive portions of 0.2% sodium hydroxide and the *trans* and *cis* acids precipitated with acetic and hydrochloric acid, respectively, as described above. The reaction proceeds at lower temperature (100° for 2 hr.) or in the presence of larger amounts of either acetic anhydride or pyridine or both. The yield is not affected by these changes.

The separation of the *trans* and *cis* isomers sometimes is not satisfactory. This is easily detected by either the melting point or the infrared spectrum. In these cases the incompletely separated fraction can be redissolved in alkali and reprecipitated as described above. These difficulties may stem from the fact that the optimum pH for precipitation of the *trans* isomer is a function of the ionic strength, temperature, and concentrations of acids as well as the nature of the acids being separated.

Conversion of the α-Phenyl-*trans*-cinnamic Acids to the Equilibrium Mixtures of *cis* and *trans* Isomers.—Equilibration was accomplished by the method of Zimmerman[6] by heating 2.2 mmoles of the purified *trans* acid under reflux in a mixture of 5 ml. of triethylamine and 5 ml. of acetic anhydride for 22 hr., except in the case of the dinitro acids where triethylamine was replaced with pyridine and the reaction time decreased to 4 hr.

The composition of the acidic fractions of the equilibrium mixtures was determined by analysis of the infrared spectra of the acids and reaction product mixtures in potassium bromide.[10] Synthetic mixtures of the experimentally determined composition gave spectra that were identical with those obtained from the reaction mixtures. The fact that a ratio of concentration rather than absolute concentrations were determined decreases many errors encountered in infrared analyses in potassium bromide.

In those cases where the infrared bands were not sufficiently resolved (III, IV, and VI) the mixtures were analyzed by carefully separating the isomers by the method described under the preparative experiments. When the equilibration reactions were carried out for preparative purposes the ratios for the *cis* and *trans* isomers were always within 3% of the analyses reported in Table III. The acidic fraction gave no evidence of decomposition. Any stilbene formed by decarboxylation would have been removed in the extraction process. The per cent recovery of the acids is given in Table III.

Infrared and Ultraviolet Spectra.—The ultraviolet spectra were measured in 95% ethanol with a Carey, Model 11, spectrophotometer. The infrared spectra in potassium bromide were recorded on a Perkin–Elmer, Model 21, spectrophotometer.

Acknowledgment.—The authors are indebted to Dr. L. A. Strait for many helpful discussions, to Mr. Michael Hrenoff for measurement of infrared and ultraviolet spectra, and to Messrs. William Herlocker, Richerd Pfarrer, Peter Wong, and Richard Cavestri for preparing some of the acids used in equilibration studies. This research was supported (in part) by Cancer Research Funds, University of California.

(9) Melting points are uncorrected. Microanalyses are by the Microanalytical Laboratory, Department of Chemistry, University of California, Berkeley, Calif.

(10) Many of the substituted α-phenyl-*trans*-cinnamic acids were not sufficiently soluble in carbon disulfide which was the solvent that Zimmerman (ref. 6) used for his infrared analyses. Our results, therefore, probably are not so accurate as his.

The Preparation of Radioactive D-Galactose from Radioactive D-Glucose[1]

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D-Galactose-U-C^{14},4-T was prepared from D-glucose-U-C^{14} by conversion to 2,3:5,6-di-*O*-isopropylidene D-glucose-U-C^{14} dimethyl acetal. This substance was oxidized to di-*O*-isopropylidene-4-keto D-glucose-U-C^{14} dimethyl acetal which was subsequently reduced with lithium aluminum tritide, yielding the corresponding galactose and glucose derivatives from which the free sugars were obtained after hydrolysis.

The mechanism whereby biological systems bring about an epimerization of the hydroxyl group on carbon 4 of D-galactose to form D-glucose has been the subject of numerous investigations[3–9] and a number of possible mechanisms have been postulated and investigated. Largely from experiments using isotopes, it has been

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