(lit.,[22] b.p. 95.7 at 53 mm.) and *trans*-alcohol, b.p. 72.4–72.9° at 25 mm. (lit.,[22] b.p. 86.8° at 52 mm.).

1,2-Dimethylcyclohexene was prepared by dehydration of the mixed alcohols by heating the mixture with iodine. The distilled olefin, b.p. 136.0–136.1° at 735 mm. (lit.,[17] b.p. 135.4–135.9°) was shown to contain 85% 1,2-dimethylcyclohexene and 15% 2,3-dimethylcyclohexene by gas chromatographic analysis on a 6-foot column using Apiezon L grease as the liquid phase. The olefin peaks were distinct and well separated. Calculation was by triangulation,[23] and the results are reproducible to ±2%. The infrared spectrum of this sample was identical with that obtained by the previous workers.[17]

Procedure. For the hydration experiments, 15 ml. of aqueous nitric acid (1.0 or $0.1M$) was placed in a small flask and 1 g. of 1,2-dimethylcyclohexene added. The flask was fitted with a condenser and magnetic stirring bar and placed in a constant temperature bath (28° or 50°) where the solution was stirred for periods varying from 1 to 30 days. At the end of these intervals, the sample was extracted with pentane. The pentane solution was washed with water and sodium bicarbonate solution and dried briefly over anhydrous calcium sulfate. The pentane was then removed by distillation, and the products were analyzed by gas chromatography at 150° on a 6-foot column with Apiezon L grease as the liquid phase. The *cis*- and *trans*-alcohol peaks showed some overlapping but calculation (by triangulation)[22] of the amounts present was possible. However, because of this overlapping, the results are probably accurate only to ±3–4%.

For the equilibration experiments, 1 g. of an alcohol mixture of known composition was placed in 15 ml. of $0.1M$ nitric acid solution. Further treatment was identical with that of the hydration experiments.

Acknowledgment. We gratefully acknowledge support of this reasearch by the United States Army Office of Basic Ordinance Research. We are also indebted to Dr. Paul Schleyer for prepublication material and to Professor Robert Taft for many enlightening discussions of this subject.

AMES, IOWA

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(23) A. I. M. Keulemans, *Gas Chromatography*, Reinhold Publishing Corp., New York, N. Y. (1957), p. 32.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MONTANA STATE UNIVERSITY]

Addition of Nucleophilic Reagents to *o*- and *p*-Cyanostyrene

JOHN M. STEWART, IRWIN KLUNDT, AND KENNETH PEACOCK

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A new improved synthesis of *o*-cyanostyrene was developed. Reactions of a variety of amines and thiols with both *o*- and *p*-cyanostyrene were carried out and the yields were compared to those of similar reactions previously performed with α-cyanostyrene[3] and 2,4-pentadienenitrile.[2] Results indicate a considerable diminishing of the electron-withdrawing effect of the cyano group when passed through the benzene ring conjugation.

o-Cyanostyrene and *p*-cyanostyrene may be considered to be vinylogs of acrylonitrile. Vinylogs are related compounds of the type formula $A(CH{=}CH)_nB$, in which the groups A and B are linked through one or more conjugated vinylene groups. An empirical rule developed by Angeli[1] has been useful in correlating the relations observed in reactions of certain vinylogs. It states that substituent groups situated *ortho* or *para* to each other on a benzene nucleus behave qualitatively as though they were joined directly. Accordingly, it would be predicted that *o*-cyanostyrene might correspond closely to the open chain vinylog, 2, 4-pentadienenitrile ($CH_2{=}CH{-}CH{=}CH{-}CN$), of acrylonitrile—one conjugated vinylene group being part of the benzene ring.

Compounds which contain an alkene linkage directly connected to a highly electron-withdrawing group, or conjugated with it through other vinylene linkages, react by addition across the alkene linkage with nucleophilic reagents which contain labile hydrogen atoms—for example, with primary and secondary amines, thiols, and phenols. Thus, reactions of this type have been carried out with 2,4-pentadienenitrile[2] and atroponitrile[3] (α-cyanostyrene), and the results have been compared with the familiar cyanoethylation reactions of acrylonitrile. It was of interest, therefore, to study the addition of nucleophilic reagents to *o*-cyanostyrene and *p*-cyanostyrene and to determine whether the electron-withdrawing effect of the cyano group upon the alkene linkage is diminished when passed through the benzene ring conjugation.

o-Cyanostyrene has been prepared by Marvel and Hein[4] by the decarboxylation of *o*-cyanocinnamic acid following a sequence of reactions starting with *o*-tolunitrile. The compound has also been reported as prepared in a British patent to the Wingfoot Corporation[5] by direct chlorination of *o*-ethylbenzonitrile, followed by pyrolysis of the chloroethyl derivative to give *o*-cyanostyrene. It was impossible to duplicate the latter procedure in this investigation. The over-all yield in method

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(1) A. Angeli, *Atti. accad. Linei* [v] *32i*, 443 (1923), *Chem. Abstr.*, **18**, 1118 (1924); R. C. Fuson, *Chem. Revs.* **16**, 1 (1933).

(2) J. M. Stewart, *J. Am. Chem. Soc.* **76**, 3228 (1954).

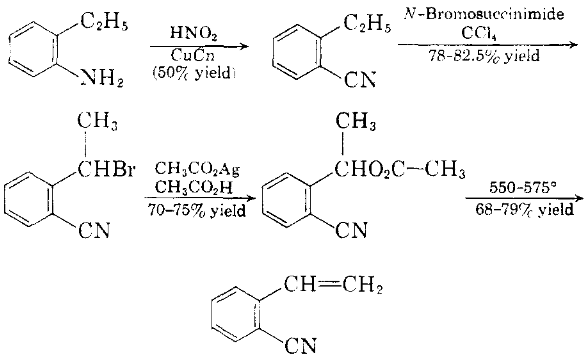
(3) J. M. Stewart and C. H. Chang, *J. Org. Chem.* **21**, 635 (1956).

(4) C. S. Marvel and D. W. Hein, *J. Am. Chem. Soc.* **70**, 1895 (1948).

(5) Wingfoot Corporation, Brit. Pat. **571**, 829 *Chem. Abstr.* **41**, 3322 (1947).

by Marvel and Hein was extremely low (5%). Therefore, the first step in this investigation was the development of a better synthesis of *o*-cyanostyrene.

Numerous routes to a new synthesis of *o*-cyanostyrene were investigated before a satisfactory method was developed. The method finally used involved the following sequence of reactions:



This route gave an overall yield of 18.5–24.4% of *o*-cyanostyrene, which represents a substantial improvement over the method of Marvel and Hein.[4] In the final pyrolysis step an inhibitor was necessary to prevent polymerization of the styrene as it formed. Hydroquinone proved to be a poor inhibitor, *N*-phenyl 2-naphthyl amine was only fair, and picric acid appeared to prevent polymerization almost completely.

By use of several modifications in the method of Marvel and Hein, the principal one being the preparation of *o*-cyanobenzaldehyde by alcoholic silver nitrate hydrolysis of *o*-cyanobenzal bromide, the over-all yield by this route was raised to 12–16%.

Several other methods which were tried but which proved unsatisfactory were: (1) pyrolysis of *o*-(α-bromoethyl)benzonitrile; (2) dehydrohalogenation of *o*-(α-bromoethyl)benzonitrile, or the chlorination product of *o*-ethylbenzonitrile, with quinoline, pyridine, or sodium amide; (3) pyrolysis of the trimethyl quaternary ammonium hydroxide prepared from *o*-(α-bromoethyl)benzonitrile; (4) selective reaction of methyl magnesium iodide with the aldehyde group in *o*-cyanobenzaldehyde to be followed by dehydration of the carbinol; (5) the sequence,

$$\text{phthalyl chloride} \xrightarrow[\text{H}_2\text{O}]{\text{NH}_3} o\text{-cyanobenzoic acid} \xrightarrow[0^\circ]{\text{PCl}_5} o\text{-cyanobenzoyl chloride} \xrightarrow{(\text{CH}_3)_2\text{Cd}} o\text{-cyanoacetophenone} \longrightarrow o\text{-cyanophenylmethylcarbinol} \longrightarrow o\text{-cyanostyrene.}$$

The last method (5) failed to give good results in the preparation of *o*-cyanoacetophenone from the acid chloride.

The *o*-cyanostyrene produced by new methods as well as that produced by the method of Marvel and Hein in this work had the same boiling point as that reported by those investigators but a widely different refractive index, n_D^{20} 1.5650, as compared to their value of n_D^{20} 1.5756. It reacted with bromine to give the same dibromo derivative. It appears that in the work of the previous investigators two small samples of *o*-cyanostyrene were prepared and that the one actually analyzed had a value of n_D^{20} 1.5705 and not n_D^{20} 1.5756 as reported. (Private communication from Prof. C. S. Marvel.)

p-Cyanostyrene was made by the method of Overberger and Allen[6] by pyrolysis of *p*-cyanophenyl methyl carbinol acetate following the sequence of reactions:

bromobenzene ⟶ *p*-bromoacetophenone ⟶
p-cyanoacetophenone ⟶ *p*-cyanophenylmethylcarbinol
⟶ *p*-cyanophenylmethylcarbinol acetate.

The over-all five-step yield was 26.4%.

A number of secondary amines, primary amines, and thiols were tried as nucleophilic addition reactants with *o*-cyanostyrene. A 40% water solution of Triton B was first used as catalyst since it had proved extremely successful in similar addition reactions of arylonitrile, 2,4-pentadienenitrile and atroponitrile (α-cyanostyrene). In the amine reactions, high yields were obtained only with dimethylamine (75%). Fair yields were obtained with piperidine (23%) and low yields with ethylamine, *n*-butylamine, and morpholine (8–14%). Others which apparently failed to react included diethylamine, di-*n*-butylamine, benzylamine, cyclohexylamine, and 40% aqueous methylamine. Use of other basic catalysts, including sodium methoxide, sodium, and anhydrous tetramethylguanidine did not give improved yields. Use of anhydrous cupric acetate as catalyst resulted in little, if any, addition reaction.

In the addition reactions of thiols with *o*-cyanostyrene, using 40% Triton B as catalyst, the more reactive thiols added quite readily—thiophenol, β-mercaptoethanol, and thioglycolic acid giving fair yields (30–60%) of addition products and butanethiol-1 giving a low yield (9%).

p-Cyanostyrene gave very similar results in its addition reactions with amines and thiols. As seen in Tables I and II, yields were significantly different only in the case of the *n*-butanethiol reaction, and the same amines again failed to give any addition product under the conditions used.

Upon comparison of these addition reactions of amines and thiols to *o*-cyanostyrene and to *p*-cyanostyrene with addition of the same reagents to α-cyanostyrene[3] or 2,4-pentadienenitrile,[2] it appears that the electron-withdrawing effect of the cyano group upon the alkene group is considerably diminished when passed through the benzene ring conjugation. Except in the case of dimethylamine, yields from the same amines were much smaller or

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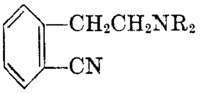
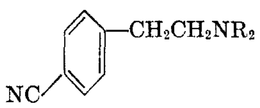
[6] C. G. Overberger and R. E. Allen, *J. Am. Chem. Soc.* 68, 722 (1946).

TABLE I

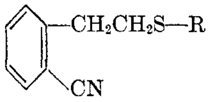
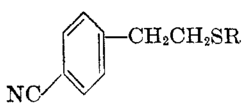
ADDITION PRODUCTS OF AMINES AND *o*- OR *p*-CYANOSTYRENE

	Adduct			Hydrochloride Prepared Direct from Crude Adduct			
Amine	Yield, %	B.P.°	n_D^{20}	Yield, %	M.P.°	Chlorine Analysis, % Calcd.	Chlorine Analysis, % Found
A. With *o*-Cyanostyrene (*N*-substituted-β-(*o*-cyanophenethyl)amines							
Dimethyl	75	98–101(2)	1.5266	46	153–155	16.83	16.66
Piperidine	23	130(2)	1.5425	34	209–212	14.14	14.19
Morpholine	14[a]			3	237–240	13.98	14.23
Ethyl	8.5[a]			6	174–176	16.83	16.71
n-Butyl	10–11[a]			8	188–190	14.78	14.55
Diethyl, Dibutyl, Methyl (40% soln.) *tert*-Butyl, Cyclohexyl, Benzyl	0			0			
B. With *p*-Cyanostyrene (*N*-substituted-β-(*p*-cyanophenethyl)amines,							
Dimethyl	90	118–121(3)	1.5274		176–178	16.83	16.50
Piperidine	60[b]	168–169(1)	1.5413	21	199–201	14.14	14.03
n-Butyl	15[a]			11	211–212	14.85	15.12
Ethyl	22[a]			14	212–214	16.83	17.05
Diethyl, Di-*n*-butyl and Benzyl	0			0			

[a] This is yield of undistilled product which was then converted directly to the hydrochloride. [b] This run was heated at 70–75° for 24 hr., and let stand a further 48 hr.

TABLE II

ADDITION PRODUCTS OF THIOLS AND *o*- OR *p*-CYANOSTYRENE

Thiol	B.P.°	Refractive Index	Yield, %	Analysis, % Calcd.	Analysis, % Found
A. With *o*-Cyanostyrene [Alkyl (or Aryl)-β-(*o*-cyanophenethyl) sulfides],					
n-Butyl	151–153(2)	n_D^{20} 1.5450	9	C, 71.18; H, 7.81	C, 71.97; H, 7.50
Thiophenol	165–170(2)	n_D^{31} 1.6072	30.4	S, 13.40	S, 13.18
β-Mercaptoethanol	185–190(2)	n_D^{20} 1.5756	52.4	*Anal.* of 3,5-dinitrobenzoate derivative (m.p. 86.5–88)	
				C, 53.85; H, 3.76	C, 53.90; H, 3.75
Benzyl			0		
B. With *p*-Cyanostyrene [Alkyl (or Aryl)-β-(*p*-cyanophenethyl) sulfides],					
n-Butyl	165–168(2)	n_D^{20} 1.5497	54.8	C, 71.18; H, 7.81	C, 71.01; H, 7.71
Thiophenol			27.7[a]	*Anal.* of sulfone	(m.p. 137–140°)
				C, 66.40; H, 4.83	C, 66.68; H, 4.81
Thioglycolic acid			91 (crude)	*Anal.* of benzylisothiouronium salt (m.p. 165–166°)	
				C, 58.89; H, 5.46	C, 58.35; H, 4.78

[a] Crude yield. Decomposed on attempted distillation.

no reaction at all took place. Some amines which gave 30–50% yields of addition products with α-cyanostyrene or 2,4-pentadienenitrile failed to react under comparable conditions or even more drastic conditions with both *o*-cyanostyrene and *p*-cyanostyrene.

EXPERIMENTAL[7]

o-Ethylbenzonitrile. A Sandmeyer reaction was used, following the general procedure of H. T. Clarke and R. R. Reed.[8] *o*-Ethylaniline (Eastman) was converted to *o*-ethylbenzonitrile in a yield of 50%, b.p. 91–93°/12 mm.; n_D^{24} 1.5218; lit.,[9] b.p. 103°/19 mm.; n_D^{20} 1.5232.

o-(α-Bromoethyl)benzonitrile. In a 1-l. flask fitted with a reflux condenser (protected by a calcium chloride drying tube) was placed 60 g. (0.46 mole) of *o*-ethylbenzonitrile, 82 g. (0.46 mole) of *N*-bromosuccinimide, 5.5 g. (5 mole % based on *N*-bromosuccinimide) of benzoyl peroxide, and 350 ml. of carbon tetrachloride. The reaction was illuminated with a 235 watt sun lamp and heated under reflux for 2.5 hr., cooled, and filtered to remove the succinimide. The solvent was then removed under reduced pressure and the residual material was fractionally distilled to yield 79.4 g. (82.5%) of a pale yellow liquid, b.p. 99° (2–3 mm.), n_D^{20} 1.5759.

Anal. Calcd. for C_9H_8BrN: Br, 38.04. Found: Br, 38.04.

o-Cyano-α-phenethyl acetate. In a 1-l. flask fitted with a reflux condenser (protected with a calcium chloride drying tube), stirrer, and dropping funnel was placed 83 g. (0.50 mole) of silver acetate and 400 ml. of glacial acetic acid. To this was added dropwise over 2 hr. 79 g. (0.38 mole) of *o*-(α-bromoethyl)benzonitrile. The addition was carried out with the acetic acid just starting to reflux and with rapid stirring. After the addition was complete, the reaction mixture was stirred for an additional 9 hr., cooled, and the silver bromide filtered off. The solution was then diluted with 4 l. of water and extracted with ether six times. The ether was stripped and the crude product was distilled at reduced pressure to yield 53 g. (75%) of colorless liquid, b.p. 95–97° (0.5 mm.), n_D^{20} 1.5120.

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.84; H, 5.82; N, 7.43. Found: C, 68.94; H, 5.88; N, 8.15.

o-Cyanostyrene. A Vicor pyrolysis tube filled with pieces of Vicor tubing was heated to a temperature of 550–575° in a vertical electrical heater and 26 g. (0.14 mole) of *o*-cyano-α-phenethyl acetate containing a small amount of picric acid was dropped through it over a period of 35 min. The receiver contained some picric acid and was cooled in an ice bath. Distillation of the pyrolysis mixture in an Argon atmosphere gave 14.28 g. (78%) of a colorless liquid, b.p. 70–72° (3 mm.), n_D^{20} 1.5650; lit.,[4] b.p. 53°/0.15 mm.; n_D^{20} 1.5756. (see Discussion).

o-(α,β-Dibromoethyl)benzonitrile. A sample of *o*-cyanostyrene was dissolved in glacial acetic acid and an excess of bromine was added. The reaction mixture was allowed to stand for 15 min., diluted with water, cooled, and extracted with ether. The ether was dried over anhydrous magnesium sulfate. The ether was removed under reduced pressure and the crude material was recrystallized from an ethanol-water mixture to yield a white solid, m.p. 85–86°; lit.,[4] m.p. 86–86.5°.

Anal. Calcd. for $C_9H_7Br_2N$: Br, 55.30. Found: Br, 55.09.

o-Cyanobenzal bromide. The procedure of Fuson[10] was followed. From 117 g. (1 mole) of *o*-tolunitrile there was obtained 265 g. of crude black crystalline product which was used without purification.

o-Cyanobenzaldehyde. The procedure of Blicke and Patelski[11] for hydrolysis of *o*-cyanobenzal bromide was used with some modifications. A solution of 340 g. (2 moles) of silver nitrate in 2200 ml. of 95% ethanol was added fairly rapidly with stirring to a solution of 263 g. crude *o*-cyanobenzal bromide in 1500 ml. of ethanol maintained at about 60°. After the addition was completed, stirring was continued at 60° for 1 hr. A solution of sodium chloride was then added to remove excess silver nitrate, and the mixture was filtered. The silver halide residue was washed several times with ether and the washings were added to the filtrate. The filtrate was then added to an equal volume of concd. sodium chloride solution, and the mixture was extracted four times with ether. The ether solution was dried over anhydrous magnesium sulfate and the ether was removed under partial vacuum, leaving 110 g. of crude solid product. A sample recrystallized from cyclohexane melted at 104–106°, lit.,[11] m.p. 107–108°.

o-Cyanocinnamic acid. The method used by Rapoport[12] for preparation of *p*-cyanocinnamic acid was followed. Yields of crude product ranged from 60 to 70%. Recrystallization from 95% ethanol gave crystals, m.p. 255–257°; lit.,[4] m.p. 253–254°.

o-Cyanostyrene (by decarboxylation of o-cyanocinnamic acid). The general procedure of Walling and Wolfstirn[13] was modified considerably.

A mixture of 120 ml. freshly distilled quinoline, 3 g. of copper powder (freshly prepared by hydrogen reduction of cupric oxide), and 0.5 g. of cuprous cyanide was heated to about 200° in a 500-ml. 3-necked round-bottomed flask, fitted with thermometer, mechanical stirrer and a short take-off head. A 10-g. portion of *o*-cyanocinnamic acid was added, stirring was begun, and the temperature was raised until distillation occurred. The distillation temperature rose slowly from 220° to 228° (680 mm.) at which time the reaction temperature was lowered to 200° and a second 10-g. portion of *o*-cyanocinnamic acid was added. This process was repeated a third time and finally all the liquid present was allowed to distill. The distillate was added to excess $3N$ hydrochloric acid, and the mixture was extracted three times with ether. The combined ether extracts were washed with $3N$, hydrochloric acid, $3N$ sodium hydroxide, and saturated sodium chloride solution and dried over calcium chloride. Distillation gave yields varying from 35–45% of *o*-cyanostyrene, b.p. 68–71° (3 mm.); n_D^{20} 1.5648, lit.,[4] b.p. 53°/0.15 mm.; n_D^{20} 1.5756. (See discussion and other method of preparation of *o*-cyanostyrene.)

Reactions of o- and p-cyanostyrene with primary and secondary amines. The cyanostyrene (0.02 mole) was mixed with 0.04 mole of the amine and 3 drops of 40% Triton B solution in a pressure bottle. The bottle was sealed and heated at 60–70° for 24 hr. The mixture was taken up in ether and washed four times with water to remove unchanged amine. The ether solution was then extracted with $3N$ hydrochloric acid and the combined acid extracts were extracted once with ether. The acid solution was made basic with $3N$ sodium hydroxide and the crude product was extracted with ether. The ether solution was dried over anhydrous magnesium sulfate. In most cases the products could not be distilled without some decomposition and were isolated as the hydrochloride salts by bubbling dry hydrogen chloride through the ether solutions.

The hydrochloride salts of the addition products were analyzed for chloride by the Volhard method.

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[7] Carbon, hydrogen, nitrogen, and bromine analyses were done by Geller Microanalytical Laboratories, Bardonia, N. Y. Chlorine analyses were done by the authors.

[8] H. T. Clarke and R. R. Read, *Org. Syn.*, **Coll. Vol. I**, p. 514 (1932).

[9] H. R. Snyder and G. I. Poos, *J. Am. Chem. Soc.* **71**, 1057 (1949).

[10] R. C. Fuson, *J. Am. Chem. Soc.*, **48**, 1093 (1926).

[11] F. F. Blicke and R. A. Patelski, *J. Am. Chem. Soc.*, **58**, 559 (1936).

[12] H. Rapoport, *J. Am. Chem. Soc.*, **75**, 1125 (1953).

[13] C. Walling and K. B. Wolfstirn, *J. Am. Chem. Soc.*, **69**, 852 (1947).

Reactions of o- and p-cyanostyrene with thiols. These reactions were carried out as with the amines. Except in the case of the addition product of thioglycolic acid, ether solutions of the product mixtures were washed first with 5% sodium hydroxide to remove unchanged thiol, dried over calcium chloride and either distilled directly to give the addition product or stripped of ether and converted to a derivative for analysis. The ether solution of the thioglycolic acid adduct was washed repeatedly with water to remove unchanged thioglycolic acid. The crude product was then isolated by extraction from the ether by 10% sodium hydroxide solution, followed by reacidification, ether extraction, drying, and stripping of the ether. A part of this crude product was converted to a benzylisothiouronium salt derivative (see Table II).

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MISSOULA, MONT.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF STANFORD UNIVERSITY AND WAYNE STATE UNIVERSITY]

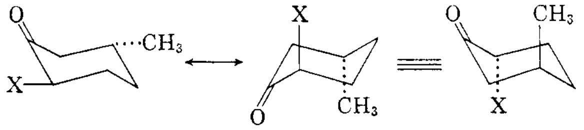
Optical Rotatory Dispersion Studies. XXXIII.[1] α-Haloketones (Part 6).[2] *trans*-2-Bromo-5-*t*-butylcyclohexanone[3]

CARL DJERASSI, E. J. WARAWA, ROBERT E. WOLFF,[4] AND E. J. EISENBRAUN

Received November 30, 1959

Resolution of *cis*-3-*t*-butylcyclohexanol was accomplished through the brucine salt of its acid phthalate, while *trans*-3-*t*-butylcyclohexanol (prepared by catalytic hydrogenation of *m*-*t*-butylphenol) was resolved *via* its 3β-acetoxy-Δ^5-etienate. Oxidation of either resolved alcohol provided optically active 3-*t*-butylcyclohexanone, which was transformed into *trans*-2-bromo-5-*t*-butylcyclohexanone. Rotatory dispersion and ultraviolet and infrared measurements in different solvents indicated the complete absence of conformational mobility (due to the anchoring effect of the equatorial *t*-butyl group) in this system, in marked contrast to the behavior observed (ref. 5) with *trans*-2-halo-5-methylcyclohexanones.

In an earlier investigation,[5] we have demonstrated by the remarkable changes in the rotatory dispersion Cotton effect curves in solvents of different polarity that there exists a mobile equilibrium in the *trans*-2-halo-5-methylcyclohexanone system (I) between the two chair forms I, t,e and I t,a.[6] This was confirmed by dipole moment, infrared and ultraviolet measurements,[7] and quantitative calculations (in the case of I. X=Br) of the conformer composition (I, t,e *vs.* I t,a) in different solvents.



I t,e X = Cl or Br I t,a

A second, independent verification of these conclusions would involve the synthesis of a relative of *trans*-2-bromo-5-methylcyclohexanone (I, X=Br), where conformational mobility is inhibited on steric grounds, and to subject such a substance to the same physical measurements. In spite of recent comments,[8] the most straightforward approach appeared to be to replace the methyl group in I by a *t*-butyl function. Winstein and Holness[9] pointed out that such a bulky substituent would invariably anchor the cyclohexane ring in that conformation in which the *t*-butyl group occupies the equatorial orientation.[10]

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(1) Paper XXXII, C. Djerassi, *Rec. Chem. Progress*, **20**, 101 (1959).

(2) Part 5, C. Djerassi, N. Finch, and R. Mauli, *J. Am. Chem. Soc.*, **81**, 4997 (1959).

(3) Grateful acknowledgment is made to the National Cancer Institute of the National Institutes of Health for financial support (grant No. CY-2919 at Wayne State University and grant No. CY-4818 at Stanford University). The major portion of the experimental work was carried out in the Department of Chemistry of Wayne State University.

(4) Present address: Institut de Biologie Physicochimique, Paris V.

(5) C. Djerassi and L. E. Geller, *Tetrahedron*, **3**, 319 (1958); C. Djerassi, L. E. Geller, and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

(6) As proposed to us by Dr. W. Klyne, we are employing two suffixes, the first denoting the relationship between the halogen atom and the alkyl group (c = *cis*, t = *trans*) and the second the orientation of the halogen atom (e = equatorial, a = axial).

(7) N. L. Allinger, J. Allinger, L. E. Geller, and C. Djerassi, *J. Org. Chem.*, **25**, 6 (1960).

(8) W. Hückel and M. Hanack, *Ann.*, **616**, 18 (1958).

(9) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(10) For other examples where a *t*-butyl group was employed to fix the conformation of a cyclohexane ring see: H. L. Goering, R. L. Reeves, and H. H. Espy, *J. Am. Chem. Soc.*, **78**, 4926 (1956); E. L. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957); R. A. Pickering and C. C. Price, *J. Am. Chem. Soc.*, **80**, 4931 (1958); N. L. Allinger and J. Allinger, *J. Am. Chem. Soc.*, **80**, 5476 (1958).