It is obvious that aromatic substitution suffers steric hindrance, for as the size of the substituent increases, the amount of *ortho* substitution decreases. In addition, the so-called law of invariable *ortho–para* substitution is not adhered to. When *ortho* substitution (in the cumene run) is substantially prevented, *meta* and *para* substitution are statistical in quantity.

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[CONTRIBUTION FROM THE WM. H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

The Effect of Ring Formation on Optical Rotatory Power. A Comparison of the Optical Rotations of 2-Phenylcyclopentanone and of Some Acyclic α-Phenyl Ketones

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2-Phenylcyclopentanone has been resolved *via* its tartramazone. The extraordinarily high value of the specific rotation of this ketone, $[\alpha]^{28}\text{D}$ +4190° (cyclohexane), is five to ten times larger than that of any of ten acyclic analogs, whose maximum rotations have been established in this work. A convincing demonstration has thus been provided that ring formation results in an enhancement of optical activity.

While the problem of optical rotatory power may be regarded, in principle, as solved,[1,2] very few simple empirical generalizations are known which make possible predictions of rotatory power from an *a priori* inspection of over-all structural features. One of the most consistently successful such rules had already been noted by van't Hoff,[3] who remarked that "the interaction of the several groups, r_1, r_2, r_3 and r_4 attached to the asymmetric carbon atom which may be accompanied by ring formation, appears to have quite an extraordinary influence on the magnitude of the sign of the rotation." This effect on rotatory power of ring formation has been noted in miscellaneous instances, such as in comparisons of hydroxy acids with their lactones,[4] of diesters with cyclic ketoesters derived therefrom,[5] of acyclic with cyclic amino acids,[6] of alkylsuccinic and alkylglutaric acids with their anhydrides,[7] of polyols with (cyclic) aldohexoses and aldopentoses[2] and of 3-methylpentanal with 3-methylcyclopentanone.[2] Unfortunately, in none of the cited cases are comparisons entirely satisfactory: either new asymmetric atoms are introduced, or the functional groups are considerably different in the compared systems. Nevertheless the trend is unescapable, and it is a generally accepted dictum, based on firm theoretical grounds, that ring formation enhances the rotatory power approximately tenfold.[2]

The present investigation was initiated with a view toward subjecting this generalization to a somewhat more systematic experimental scrutiny. The choice of the system to be studied, the α-phenyl ketones, was motivated by the convenience entailed in determining the maximum rotations of the acyclic members of the series (*vide infra*), while the selection of a five-membered ring for the cyclic ketone was principally governed by the consideration that an observed effect might be more pronounced in the cyclopentane than in the cyclohexane system: the rotation of 3-methylcyclopentanone[8] considerably exceeds that of 3-methylcyclohexanone.[9]

Ten unbranched acyclic α-phenyl ketones (I), containing a total of four to seven atoms in the straight-chain portion of the molecule, were studied for purposes of comparison of optical rotatory power with 2-phenylcyclopentanone. These ketones, prepared by the reaction of partially resolved acids II and alkyllithium III frequently were contaminated with tertiary carbinols, formed by further reaction of I and III.[10] Purification of the ketones involving negligible racemization could be effected through hydrolysis of the recrystallized semicarbazones in a refluxing ligroin–dilute hydrochloric acid mixture. The physical and optical properties of the ten ketones thus prepared are listed in Table I.

$$\underset{\text{II}}{\mathrm{RCH(C_6H_5)COOH}} + \underset{\text{III}}{\mathrm{R'Li}} \longrightarrow \underset{\text{I}}{\mathrm{RCH(C_6H_5)COR'}}$$

Since partial racemization accompanies the preparation of I,[11] the optical purity of I was judged by comparison with that of V, obtained by the stereospecific[11] perbenzoic acid oxidation of I to ester IV, followed by hydrolysis to V. Results of the oxidation–hydrolysis are reported in Table II, while cal-

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[1] *E.g.*, J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937); E. U. Condon, *Rev. Modern Phys.*, **9**, 432 (1937); E. Hückel, *Z. Elektrochem.*, **50**, 13 (1944); W. Kuhn, *ibid.*, **56**, 506 (1952); G. W. van Vloten, *Chem. Weekblad*, **48**, 977 (1952); T. R. Thomson, THIS JOURNAL, **75**, 6070 (1953).

[2] W. J. Kauzman, J. E. Walter and H. Eyring, *Chem. Revs.*, **26**, 339 (1940); *cf.* especially p. 376 ff.

[3] J. H. van't Hoff, "The Arrangement of Atoms in Space," 2nd ed. (translated by A. Eiloart), Longmans, Green and Co., London, 1898, p. 146.

[4] I. I. Kutyukov, *Bull. Siberian Inst. Tech.*, **50**, no. 2 (1929); *C. A.*, **24**, 2978 (1930); D. M. Bovey and E. E. Turner, *J. Chem. Soc.*, 3223 (1951); J. A. Reid and E. E. Turner, *ibid.*, 3219 (1951).

[5] A. Haller and M. Desfontaines, *Compt. rend.*, **140**, 1205 (1905).

[6] L. F. Fieser, *Rec. trav. chim.*, **69**, 410 (1950).

[7] E. Berner and R. Leonardsen, *Ann.*, **538**, 1 (1939).

[8] M. Godchot, G. Cauquil and R. Calas, *Bull. soc. chim.*, [5] **6**, 1353 (1939).

[9] H. S. French and M. Naps, THIS JOURNAL, **58**, 2303 (1936).

[10] C. Tegnér, *Acta Chem. Scand.*, **6**, 782 (1952).

[11] K. Mislow and J. Brenner, THIS JOURNAL, **75**, 2318 (1953).

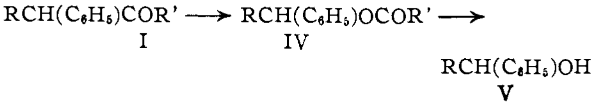
TABLE I

PHYSICAL AND OPTICAL PROPERTIES OF STARTING KETONES, $RCH(C_6H_5)COR'$

R	R'	B.p. °C.	B.p. Mm.	$n^{25}D$	d^{25}_4	MD Calcd.	MD Found	$[\alpha]^{28}$ Toluene 546.1 mμ	Toluene 589.3 mμ	Toluene c, g./100 ml.	Cyclohexane 546.1 mμ	Cyclohexane 589.3 mμ	Cyclohexane c, g./100 ml.
CH_3	CH_3[a]	60–61	1.7	1.5073	0.975	44.79	45.27	354°	279°	5.61	328°	263°	4.89
CH_3	C_2H_5[b]	94–95	4.8	1.5049	.957	49.41	50.21	117	96.4	4.98	111	87.7	6.30
CH_3	C_3H_7[c]	84–86	2	1.4988	.941	54.03	54.89	99.2	79.8	7.22	98.6	76.9	6.45
CH_3	C_4H_9[d]	96–97	1.8	1.4964	.938	58.65	59.21	148	116	4.63	124	99.5	4.22
C_2H_5	CH_3[e]	82–84	4	1.5041	.958	49.41	50.07	186	150	6.70	172	139	5.10
C_2H_5	C_2H_5[f]	75–77	2	1.5011	.949	54.03	54.64	263	213	5.66	238	193	6.40
C_2H_5	C_3H_7[g]	87	2	1.4961	.937	58.65	59.23	220	174	5.55	206	162	5.40
C_3H_7	CH_3[h]	83–84	2	1.5023	.951	54.03	54.65	80.7	63.8	5.42	70.2	55.8	5.27
C_3H_7	C_2H_5[i]	82	1.9	1.5006	.945	58.65	59.37	80.5	62.9	5.72	73.1	57.4	5.47
C_4H_9	CH_3[j]	92–94	1.8	1.4997	.942	58.65	59.28	98.2	79.3	5.40	84.9	69.1	6.08

[a] Ref. 11. [b] J. Levy and A. Tabart, *Bull. soc. chim.*, **49**, 1776 (1931), reported b.p. 225–228° (760 mm.). [c] J. Levy and A. Tabart, ref. *b*, gave b.p. 235° (760 mm.), d^0_4 0.970. [d] J. Levy and P. Jullien, *Bull. soc. chim.*, **45**, 941 (1929), reported b.p. 256–257° (760 mm.). [e] E. M. Schultz, *et al.*, THIS JOURNAL, **75**, 1072 (1953), gave b.p. 116–123° (23 mm.), $n^{20}D$ 1.5048. [f] J. Levy and A. Tabart, ref. *b*, gave b.p. 114–116° (13 mm.). [g] I. N. Nazarov and I. L. Kothyarevskii, *Zhur. Obschei Khim.*, **18**, 911 (1948), reported b.p. 85–88° (1.5 mm.), $n^{20}D$ 1.4970, d^{20}_4 0.943. [h] E. M. Schultz, *et al.*, ref. *e*, noted b.p. 120–124° (18 mm.), $n^{20}D$ 1.5022. [i] J. Levy and P. Jullien, ref. *d*, cited b.p. 240–245° (760 mm.). [j] E. M. Schultz, *et al.*, ref. *e*, reported b.p. 131–135° (16 mm.), $n^{20}D$ 1.4995.

culated maximum rotations of I are reported in Table III.[12]



$$\underset{\text{I}}{RCH(C_6H_5)COR'} \longrightarrow \underset{\text{IV}}{RCH(C_6H_5)OCOR'} \longrightarrow \underset{\text{V}}{RCH(C_6H_5)OH}$$

TABLE II

PHYSICAL AND OPTICAL PROPERTIES OF DERIVED CARBINOLS, $RCH(C_6H_5)OH$

Starting ketone $RCH(C_6H_5)$-COR' R	R'	Derived carbinol B.p. °C.	Mm.	$n^{25}D$	$[\alpha]^{26}D$ (homog.)	Optical purity, %
CH_3	CH_3[a]					
CH_3	C_2H_5	80	3	1.5255	−5.50°	12.7[b]
CH_3	C_3H_7	79	2.6	1.5259	−4.91	11.3[b]
CH_3	C_4H_9	81	2.7	1.5256	−7.70	17.8[b]
C_2H_5	CH_3	75	3.5	1.5173	−6.08	20.9[c]
C_2H_5	C_2H_5	78	3.9	1.5177	−9.46	32.5[c]
C_2H_5	C_3H_7	78	4.0	1.5177	−8.37	28.8[c]
C_3H_7	CH_3	116–118 M.p. 46	20		−4.38[d]	9.5[d]
C_3H_7	C_2H_5	116–118 M.p. 46	20		−5.07[d]	11.0[d]
C_4H_9	CH_3	103	3.8	1.5078	−2.44	14.2[e]

[a] See ref. 11. [b] $[\alpha]D$ (max.) 43.4° (ref. 35, text). [c] $[\alpha]^{28}D$ (max.) 29.1° (R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, 45 (1911); 1115 (1914)). [d] Rotations in benzene, *c* 5.8, compared with $[\alpha]D$ (max.) 45.9° (Experimental). [e] $[\alpha]^{28}D$ (max.) 17.2° (P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **97**, 379(1932)).

The rotation of phenylpropylcarbinol being in doubt, we repeated the resolution of this compound and obtained results in agreement with those of Kenyon and Partidge,[13] and in conflict with those reported by Levene and co-workers.[14,15]

Optically active 2-phenylcyclopentanone was obtained by direct resolution; the resolving agent selected was tartramidic acid hydrazide (tartramazide).[16] One of the diastereomeric 2-phenylcyclopentanone tartramazones was obtained in pure form after ten recrystallizations from methanol–chloroform; hydrolysis in ligroin–hydrochloric acid yielded the resolved ketone. Rotational data are presented in Table IV.

Discussion

The present investigation has convincingly demonstrated the exaltation of optical rotatory power ascribed to ring formation: the rotation of 2-phenylcyclopentanone (Table IV) is five to ten times that of any comparable acyclic α-phenyl ketone (Table III). Although the theoretical foundations for this effect have been discussed carefully,[2] certain interesting aspects, peculiar to the system studied in this work, deserve mention.

In the case of all of the α-phenyl ketones studied, rotations of toluene solutions exceed those of cyclohexane solutions.[17] Rotivity corrections[18] reduce but do not eliminate the divergence between rotations in the two solvents. The magnitudes of the rotations themselves are remarkably high; indeed, the value of the *specific* rotation of 2-phenylcyclopentanone (Table IV) appears to exceed any heretofore reported for an organic compound,[19] excluding metal chelates,[20] a fact the more astonishing

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(12) The oxidation of (+)-I resulted in (−)-V in every case; the configurational relationship between 3-phenyl-2-butanone and phenylmethylcarbinol[11] therefore can be generalized to one between (+)-I and (−)-V, since phenylalkylcarbinols of the same sign of rotation are configurationally related (P. A. Levene and A. Rothen, *J. Org. Chem.*, **1**, 76 (1936)).

(13) J. Kenyon and S. M. Partridge, *J. Chem. Soc.*, 128 (1936).

(14) P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **97**, 386 (1932).

(15) P. A. Levene and A. Rothen, *ibid.*, **127**, 237 (1939).

(16) F. Nerdel and E. Henkel, *Chem. Ber.*, **85**, 1138 (1952).

(17) A. McLean (*J. Chem. Soc.*, 351 (1934)) has shown that polar substances, such as menthyl *p*-nitrobenzoate, have lower rotations in cyclohexane solution than in solutions in aromatic solvents, including toluene.

(18) C. O. Beckmann and K. Cohen, *J. Chem. Phys.*, **4**, 784 (1936).

(19) Some abnormally high specific rotations, chosen at random from the recent literature, are: (a) 1-bromocodeinone dinitrophenylhydrazone, $[\alpha]^{27}D$ −1940° (chloroform) (*cf.* M. Gates and G. Tschudi, THIS JOURNAL, **74**, 1109 (1952)); (b) 9,10-dihydrodibenzo[a,f]phenanthrene, $[\alpha]^{22}_{5461}$ + 1496° (benzene) (D. M. Hall and E. E. Turner, *Chem. and Ind.*, 1177 (1953); *cf.* also M. K. Hargreaves, *J. Chem. Soc.*, 1781 (1954)); (c) condensation product of 2,2'-diamino-4,4-diphenic acid and benzil, $[\alpha]D$ −955° (0.5 *N* sodium hydroxide) (F. Bell, *ibid.*, 1527 (1952)).

(20) The specific rotations of many metal chelate complex compounds exceed that of 2-phenylcyclopentanone, *cf.*, *e.g.*, F. P. Dwyer, *et al.*, THIS JOURNAL, **74**, 4188 (1952).

TABLE III

CALCULATED MAXIMUM SPECIFIC AND MOLECULAR ROTATIONS OF KETONES $RCH(C_6H_5)COR'$

		Toluene					Cyclohexane				
		546.1 mμ (Hg)		589.3 mμ (D)			546.1mμ (Hg)		589.3 mμ (D)		
R	R'	[α]	[M]	[α]	[M]	αHg/αD	[α]	[M]	[α]	[M]	αHg/αD
CH_3	CH_3[a]	1170°	1730°	918°	1360°	1.27	1080°	1600°	866°	1280°	1.25
CH_3	C_2H_5	916	1480	753	1220	1.21	871	1410	691	1120	1.26
CH_3	C_3H_7	874	1540	704	1240	1.24	869	1530	678	1190	1.28
CH_3	C_4H_9	831	1580	651	1240	1.27	696	1320	559	1060	1.24
C_2H_5	CH_3	886	1440	714	1160	1.24	819	1330	662	1070	1.24
C_2H_5	C_2H_5	813	1430	656	1160	1.24	733	1290	595	1050	1.23
C_2H_5	C_3H_7	767	1460	605	1150	1.27	716	1360	564	1070	1.27
C_3H_7	CH_3	843	1480	669	1180	1.26	736	1300	586	1030	1.26
C_3H_7	C_2H_5	731	1390	572	1090	1.28	664	1260	522	990	1.27
C_4H_9	CH_3	692	1320	559	1060	1.24	598	1140	485	920	1.23

[a] See Experimental part for calculation.

TABLE IV

ROTATIONS OF 2-PHENYLCYCLOPENTANONE AT 28°

Solvent	Wave length, mμ	α	l, dm.	c, g./100 ml.	[α]	[M]
Toluene	546.1	109.95°	2	1.042	5280°	8450°
		54.92	1	1.042		
		27.50	0.5	1.042		
	589.3	23.15	.5	1.042	4440	7110
Cyclohexane	546.1	25.87	.5	1.058	4890	7820
	589.3	22.14	.5	1.058	4190	6700

in view of the simple architecture of the ketone.[21] Apparently the high rotations are specifically associated with the presence of the $-CH(C_6H_5)CO-$ system, since the molecular rotation of a branched analog, 3-methyl-3-phenyl-2-pentanone,[22] has a value, 137°, very much smaller than that of any unbranched α-phenyl ketone,[23] although its dispersion ratio, $\alpha_{546.1}/\alpha_{589.3}$ 1.26, is the same as that of the unbranched analogs, 1.252 ± 0.017. This deduction finds further confirmation in the related fact that the molecular rotations in benzene solution of hydratropic acid ($R'CH(C_6H_5)COOH$) have the values[24] +139.0° (589.3 mμ) and +166.0° (546.1 mμ), while the corresponding values for 2-methyl-2-phenylhexanoic acid ($R'R''C(C_6H_5)COOH$) are +46.1 and +55.7°, respectively[25]; yet both compounds have the same dispersion ratio, $\alpha_{546.1}/\alpha_{589.3}$ 1.20 ± 0.01.

It is worthy of note that the rotation of the cyclic ketone is relatively less affected by a change in temperature than are the rotations of some acyclic analogs (Table V). This observation accords with the belief that a rigid ring structure is less susceptible to conformational alternations than is a nonrigid acyclic structure. Consequently the populations of conformational isomers of a ring compound, and their rotations, will be less influenced by thermal changes.[26]

TABLE V

TEMPERATURE VARIATION OF ROTATION OF SOME α-PHENYL KETONES

Ketone	$[M]_D$ (toluene) 28°	$[M]_D$ (toluene) 60°	$\Delta[M]_D/\Delta t$	Per cent. change in $[M]_D$ obsd.
3-Phenylcyclopentanone	7110°	7060°	−1.6	−0.7
4-Phenyl-3-hexanone	1160	1100	−1.9	−5.2
3-Phenyl-2-heptanone	1060	990	−2.2	−6.6

A final point of interest is revealed by the spectral properties of 2-phenylcyclopentanone, whose infrared spectrum shows a carbonyl band at 1740 cm.$^{-1}$, as compared with 1718 cm.$^{-1}$ for 3-phenyl-2-butanone,[11,27] and whose ultraviolet spectrum exhibits broad absorption and shifts to longer wave lengths as contrasted with 3-phenyl-2-butanone and 2-phenylcyclohexanone; the change in the spectrum is accompanied by a rotatory dispersion term, $\alpha_{546.1}/\alpha_{589.3}$ 1.18 ± 0.01, considerably different from that of the acyclic analogs, 1.25.[28] More detailed comment must await an extensive investigation of the rotatory dispersion.

Experimental

(+)-2-Phenylpropanoic Acid (Hydratropic Acid).—The acid was prepared[29] by the oxidation of hydratropaldehyde (Matheson, Coleman and Bell) and resolved[24] *via* the strychnine salt. The product, b.p. 158° (20 mm.), had $[\alpha]^{28}_D$ 94.4° (homogeneous) (lit.[24] α^{16}_D 51.8° (l 0.5, homogeneous)).

(+)-2-Phenylbutanoic Acid.—The racemic acid (Matheson, Coleman and Bell), resolved[30] *via* the cinchonidine salt, had the following properties: b.p. 138° (4 mm.), $[\alpha]^{28}_D$ 90.8° (homogeneous) (lit.[30] b.p. 155–156° (16 mm.), $[\alpha]_D$ 89.9°).

(+)-2-Phenylpentanoic Acid.—Alkylation of benzyl cyanide (1.0 mole) with propyl bromide (1.5 moles) in the

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[21] It can be surmised that even higher rotations may obtain in certain suitably substituted 2-arylcyclopentanones; the important role played by mesomeric effects in the rotatory power of a variety of substances has been demonstrated by M. Betti (*Trans. Faraday Soc.*, **26**, 337 (1930)) and more recently by F. Nerdel and co-workers (*Z. Elektrochem.*, **56**, 234 (1952); *Ann.*, **580**, 35 (1953); *Chem. Ber.*, **87**, 217 (1954)).

[22] D. J. Cram and J. D. Knight, THIS JOURNAL, **74**, 5835 (1952).

[23] It is noteworthy that this difference is not reflected in the near-ultraviolet spectrum: the spectra of 3-phenyl-2-butanone and of 3-methyl-3-phenyl-2-butanone are virtually superimposable (W. D. Kumler, L. A. Strait and E. L. Alpen, *ibid.*, **72**, 1463 (1950)).

[24] C. L. Arcus and J. Kenyon, *J. Chem. Soc.*, 916 (1939).

[25] J. F. Lane and E. S. Wallis, THIS JOURNAL, **63**, 1674 (1941).

[26] M. P. Balfe, *J. Chem. Soc.*, 1871 (1950).

[27] This shift is diagnostic: the carbonyl band of cyclopentanone lies at 1744 cm.$^{-1}$, as compared to butanone (1721 cm.$^{-1}$) and cyclohexanone (1714 cm.$^{-1}$); *cf.* E. J. Hartwell, R. E. Richards and H. W. Thompson, *ibid.*, 1436 (1948).

[28] In this connection it should be noted that the rotatory powers and absorption spectra of 3-methylhexanal (P. A. Levene and A. Rothen, *J. Chem. Phys.*, **4**, 48 (1936)) and of 3-methylcyclohexanone[9] are very similar, while the rotatory power of 3-methylcyclopentanone is very much greater[9]; at the same time the ultraviolet spectra of cyclohexanone and cyclopentanone differ significantly (G. Förster, R. Skrabal and J. Wagner, *Z. Elektrochem.*, **43**, 290 (1937); H. Mohler and H. Lohr, *Helv. Chim. Acta*, **20**, 1183 (1937).

[29] E. L. Eliel and J. P. Freeman, THIS JOURNAL, **74**, 923 (1952).

[30] P. A. Levene, L. A. Mikeska and K. Passoth, *J. Biol. Chem.*, **88**, 27 (1930).

presence of sodium amide (1.1 moles) under the usual conditions[31] gave a 67% yield of α-phenylvaleronitrile, b.p. 127–128° (13 mm.), $n^{25}\mathrm{D}$ 1.5033 (lit.[32] b.p. 120–123° (7 mm.), $n^{25}\mathrm{D}$ 1.5039). A mixture of the nitrile (106 g.), water (90 ml.), glacial acetic acid (115 ml.) and concentrated sulfuric acid (125 ml.) was refluxed for four hours and the resulting upper layer separated, washed with water and dissolved in 2 *N* sodium hydroxide. The alkaline solution was extracted with ether, acidified, and the separated acid washed with water, dried and distilled to yield 60 g. (52%). b.p. 147–149° (3 mm.) (lit.[30] b.p. 161–163° (10 mm.)). Partial resolution[30] *via* the cinchonidine salt gave the acid with $[\alpha]^{25}\mathrm{D}$ +16.7° (ether) (lit.[30] $[\alpha]\mathrm{D}$ 33.1°).

(+)-2-Phenylhexanoic Acid.—Alkylation of benzyl cyanide (1.0 mole) with butyl bromide (1.75 moles) in the presence of sodium amide (1.1 moles) under the usual conditions[31] gave a 61% yield of α-phenylcapronitrile, b.p. 135–136° (10 mm.), $n^{25}\mathrm{D}$ 1.5003 (lit.[32] b.p. 152–155° (20 mm.), $n^{25}\mathrm{D}$ 1.5007). The nitrile was hydrolyzed as described for the homolog in the preceding section, and the resulting (57%) acid, which had b.p. 155–157° (7 mm.) (lit.[33] b.p. 182° (20 mm.)), was partially resolved by crystallization of the strychnine salt from 1:1 ethanol–water. The resulting product had $[\alpha]^{25}\mathrm{D}$ +43.78° (homogeneous).

(−)-Phenylpropylcarbinol.—Butyraldehyde (72 g.) was added to an ethereal solution of phenylmagnesium bromide (from 172 g. of bromobenzene and 24.3 g. of magnesium). The Grignard adduct was hydrolyzed with ice-cold dilute hydrochloric acid and the product worked up in the usual manner to yield 115 g. (76%) of phenylpropylcarbinol, b.p. 116–118° (20 mm.) (lit.[14] b.p. 120° (15 mm.)). The acid phthalate, prepared[13] in 57% yield by heating a mixture of 115 g. of phenylpropylcarbinol, 171 g. of phthalic anhydride and 60 g. of anhydrous pyridine for four hours on the steam-bath, was recrystallized from a mixture of petroleum ether and carbon disulfide; it melted at 88° (lit.[13] m.p. 90–91°). Strychnine (187 g.) was added to 173 g. of the acid phthalate in 650 ml. of 1:3 water–methanol. After three days in the refrigerator, 175 g. of an oil was obtained. The oil was dissolved in 1:2 water–methanol and induced to crystallize by scratching and cooling. The crop of crystals thus obtained (150 g.) was recrystallized five times more from the same solvent to yield 56 g. of crystals. The salt was then treated with excess aqueous ammonia and the precipitated strychnine filtered. The filtrate was acidified and extracted with ether. The organic layer was dried, the solvent stripped, and the residual acid phthalate, m.p. 53°, $[\alpha]\mathrm{D}$ −10.2° (*c* 5.38, ether) (lit.[13] m.p. 52–53°, $[\alpha]\mathrm{D}$ −10.0°, lit.[14] $[\alpha]\mathrm{D}$ −7.0°), hydrolyzed in hot 10% sodium hydroxide. The resulting carbinol was distilled: b.p. 116–117° (16 mm.), m.p. 49–50°, $[\alpha]^{27}\mathrm{D}$ −45.93° (*c* 6.1, benzene) (lit.[13] b.p. 115° (14 mm.), m.p. 49°, $[\alpha]\mathrm{D}$ −45.9°, lit.[14] $[\alpha]\mathrm{D}$ −35.8°).

Preparation and Oxidation of Ketones $\mathrm{RCH(C_6H_5)COR'}$ (I).—Alkyl halide (bromides in all cases except methyl iodide, 0.33 mole) was added to lithium metal (ribbon, 0.7 mole) suspended in 200 ml. of anhydrous ether, and the mixture was stirred for one hour under a nitrogen atmosphere. The suspension was filtered rapidly through a glass wool plug and an aliquot of the solution was titrated with standard acid solution to determine the alkyllithium content. An amount of acid, $\mathrm{RCH(C_6H_5)COOH}$ (II), in 30 ml. of anhydrous ether, equal in moles to one-third the number of moles of available alkyllithium, LiR' (III), was added dropwise to the ethereal solution of alkyllithium. The mixture was stirred for 20 minutes and poured into water containing a quantity of ammonium chloride sufficient to neutralize the lithium hydroxide produced. The solution was extracted with ether and the organic layer washed with a saturated aqueous solution of sodium chloride until the washings were neutral to Hydrion paper. The ether layer was dried, the solvent stripped, and the residue distilled. The distillate was added to a solution of semicarbazide acetate (1 g. of distillate to a filtered methanolic solution of 2 g. of semicarbazide and 3 g. of sodium acetate); the mixture was warmed, placed in the refrigerator overnight, and the resulting crystalline semicarbazone washed with small quantities of methanol; yields varied from 80 to 95%.

The semicarbazone was added to a mixture of equal volumes of redistilled 60–90° ligroin and dilute hydrochloric acid. The mixture was stirred at the interface and warmed under reflux on a steam-bath for 15 minutes. The organic layer was separated, washed with water until the washings were neutral, dried, and distilled; the yields of recovered ketones were 60 to 80%. Physical and optical properties of the purified ketones are listed in Table I. This process evidently involved very little racemization: for example, a slightly impure sample of 2-phenyl-3-pentanone, $n^{25}\mathrm{D}$ 1.5019, $\alpha^{29}\mathrm{D}$ −40.85° (*l* 0.5, homogeneous), after purification had $n^{25}\mathrm{D}$ 1.5049, $\alpha^{27}\mathrm{D}$ −39.9° (*l* 0.5, homogeneous).

The ketone I was oxidized with perbenzoic acid, and the product worked up, precisely following the directions earlier given[11] for the oxidation of 3-phenyl-2-butanone. The ester IV[34] was saponified by refluxing in a 50% aqueous ethanol solution of potassium hydroxide (3 moles of potassium hydroxide per mole of ester). The hydrolysis mixture was stripped of ethanol, extracted with ether and the extract washed with water until the washings were neutral. The ethereal solution was dried and distilled, affording carbinol in yields from 30 to 40% of the theoretical. The physical and optical properties of the carbinols are listed in Table II.

Calculation of Maximum Rotations of Ketones (I).—Calculations in all cases, with the exception of 3-phenyl-2-butanone, followed a pattern analogous to the one here illustrated for 2-phenyl-3-pentanone: observed $\alpha^{28}\mathrm{D}$ +2.76° (*l* 0.5, *c* 6.30, cyclohexane), therefore $[\alpha]^{28}\mathrm{D}$ +87.7° (cyclohexane). Perbenzoic acid oxidation of this sample gave phenylmethylcarbinol, $\alpha\mathrm{D}$ −2.79° (*l* 0.5, homogeneous), or $[\alpha]\mathrm{D}$ −5.50° (homogeneous), that is, 12.7% optically pure, compared with $[\alpha]\mathrm{D}$ 43.4° (homogeneous), the maximum rotation of the carbinol.[35] If 12.7% is also taken as the optical purity of precursor ketone, it follows that the $[\alpha]\mathrm{D}$ of the optically pure ketone has the value 87.7°/0.127 = 691°, whence $[\mathrm{M}]\mathrm{D}$ 691° (162/100) or 1120° (cyclohexane).

In the case of 3-phenyl-2-butanone the material on hand had $\alpha\mathrm{D}$ +49.85° (*l* 0.5, homogeneous), or 30.3% optically pure by comparison with the reported[11] maximum rotation, $\alpha\mathrm{D}$ 164.5° (*l* 0.5, homogeneous). The same sample had $\alpha^{28}\mathrm{D}$ +6.42° (*l* 0.5, *c* 4.89, cyclohexane), and therefore $[\alpha]^{28}\mathrm{D}$ +263° (cyclohexane). The $[\alpha]\mathrm{D}$ of the optically pure ketone should therefore have the value 263°/0.303 = 866°, whence $[M]\mathrm{D}$ 866° (148/100) or 1280° (cyclohexane).

(+)-3-Methyl-3-phenyl-2-pentanone.—A sample of this ketone[36] having $\alpha^{25}\mathrm{D}$ +68.4° (homogeneous), *i.e.*, virtually optically pure, had $[\alpha]^{28}\mathrm{D}$ +77.9°, $[\mathrm{M}]\mathrm{D}$ 137° (*c* 5.51, cyclohexane) and $[\alpha]^{28}_{545\cdot1}$ +98.3°, $[\mathrm{M}]_{546\cdot1}$ 173° (*c* 5.51, cyclohexane), whence $\alpha_{546\cdot1}/\alpha\mathrm{D}$ 1.26.

2-Phenylcyclopentanone.—Chlorine, 71 g., was passed into a well-stirred, ice-cold solution of 84 g. of cyclopentanone in 400 ml. of water. The solution was extracted with ether and the organic layer dried and distilled. The product, 2-chlorocyclopentanone, 35 g. (30%), distilled at 81–83° (10 mm.) (lit.[37] b.p. 80° (10 mm.)).

A solution of 35 g. of 2-chlorocyclopentanone in 400 ml. of dry ether was added to a well-stirred, ice-cold solution of phenylmagnesium bromide (from 8.5 g. of magnesium and 55 g. of bromobenzene in 700 ml. of ether). The ether was removed by distillation, 150 ml. of xylene was added and the solution was heated briefly under reflux. The cooled solution was poured onto ice and dilute hydrochloric acid. The product was extracted with benzene, and the organic layer was washed with dilute sodium hydroxide and water, and dried. Distillation afforded 26 g. (55%) of the desired product, b.p. 140–142° (10 mm.) (lit.[38] b.p. 135–140° (9 mm.)), m.p. 36–37° after two recrystallizations from ligroin (lit.[38] m.p. 36–37°). For the determination of the ultra-

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[31] As described for the preparation of α-phenylpropionitrile (A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946)).

[32] L. H. Baldinger and J. A. Nieuwland, THIS JOURNAL, **55**, 2851 (1933).

[33] R. Dolique, *Ann. chim.*, [10] **15**, 425 (1931).

[34] While a mixture of esters, $\mathrm{RCH(C_6H_5)OCOR'}$ and $\mathrm{RCH(C_6H_5)COOR}$,' conceivably could have been obtained, the migratory aptitude of the phenylalkylcarbinyl group, to judge from related results (ref. 11; also D. J. Cram and J. Allinger, THIS JOURNAL, **76**, 4516 (1954)), seems vastly to exceed that of alkyl groups, making a mixture relatively improbable.

[35] E. Downer and J. Kenyon, *J. Chem. Soc.*, 1156 (1939); A. J. H. Houssa and J. Kenyon, *ibid.*, 2260 (1930).

[36] The sample was kindly furnished by Dr. D. J. Cram.

[37] M. Godchot and F. Taboury, *Compt. rend.*, **156**, 332 (1913).

[38] R. T. Arnold, J. S. Buckley, Jr., and R. M. Dodson, THIS JOURNAL, **72**, 3153 (1950).

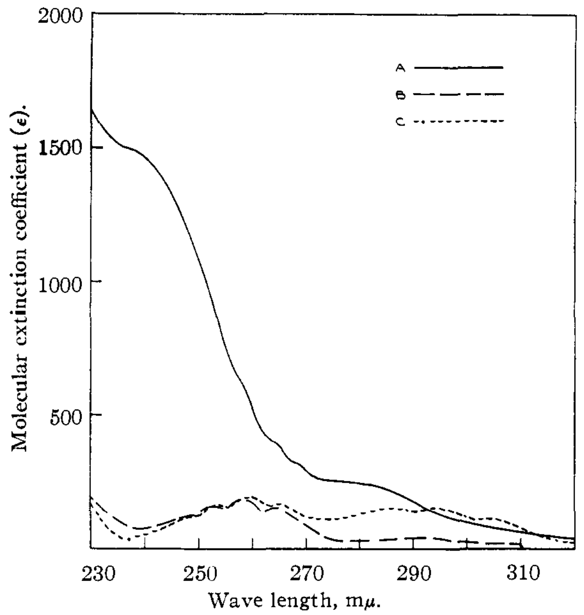

Fig. 1.—Ultraviolet spectra of: A, 2-phenylcyclopentanone; B, 2-phenylcyclohexanone (adapted from W. C. Wildman and R. B. Wildman, *J. Org. Chem.*, **17**, 581 (1952)); C, 3-phenyl-2-butanone (adapted from W. D. Kumler, *et al.*[23]); solvent 95% ethanol.

violet and infrared spectra,[39] the ketone was freshly purified *via* the semicarbazone.[40] The ultraviolet spectrum (0.02 wt. % solution) is reproduced in Fig. 1; it is characterized by a shelf near 280 mμ, three shoulders in the 250–270 mμ region and a broad absorption band below 250 mμ. The infrared spectrum features a strong carbonyl band at 5.75 μ.

Resolution of 2-Phenylcyclopentanone.—The resolving agent was prepared[15] by conversion of methyl (+)-tartrate into methyl (+)-tartramide, m.p. 132–135°, $[\alpha]_D$ +57.8° (water) (lit.[15] m.p. 136–140°, $[\alpha]_D$ 62.9°), followed by conversion into the (+)-tartramazide, m.p. 147–148°, $[\alpha]^{25}_D$ +122° (water) (lit.[15] m.p. 146–148°, $[\alpha]_D$ 124°).

A solution of 43 g. (0.26 mole) of (+)-tartramazide and of 36 g. (0.225 mole) of 2-phenylcyclopentanone in 100 ml. of methanol was refluxed for three hours. The oil which separated on standing could not be induced to crystallize. A solution of the oil in 3:1 methanol–chloroform, on standing in the refrigerator, deposited a crop of crystals. This material was recrystallized from the same solvent mixture ten times, until melting point and rotation had reached a constant value. There was thus obtained 0.75 g. of (+)-2-phenylcyclopentanone (+)-tartramazone, m.p. 151°, $[\alpha]^{27}_D$ +183.1° (*c* 4.98, methanol).

Anal. Calcd. for $C_{16}H_{19}O_4N_3$: N, 13.76. Found: N, 13.64.

The above tartramazone was added to a well-stirred refluxing mixture of ligroin and dilute hydrochloric acid. The ligroin layer yielded 0.2 g. of (+)-2-phenylcyclopentanone, m.p. 25–27°. Rotations[41] are recorded in Table IV.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.5; H, 7.55. Found: C, 82.4; H, 7.42.

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[39] In this connection, the assistance afforded by correspondence with Dr. Ralph Nusbaum and his staff, Spectroscopy Section, Atomic Energy Project, U.C.L.A., Los Angeles, Calif., is gratefully acknowledged.

[40] On prolonged standing, both 2-phenylcyclopentanone (W. Baker and P. G. Jones, *J. Chem. Soc.*, 787 (1951)) and 2-phenylcyclohexanone (W. E. Bachmann, G. I. Fujimoto and L. B. Wick, This Journal, **72**, 1995 (1950)) are known to deteriorate.

[41] No claim for optical purity can be made, but it seems reasonable to suppose that the method employed in the hydrolysis of the tartramazone should be conducive to as negligible a degree of racemization as was observed in the hydrolysis of 2-phenyl-3-pentanone semicarbazone, under the same conditions.

[Contribution from the Department of Chemistry of the University of Michigan]

Addition of Hydrogen Halides to α,β-Unsaturated Acids[1]

By Wyman R. Vaughan, Robert L. Craven,[2] Randel Q. Little, Jr.,[3] and A. Charles Schoenthaler

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Evidence for the *trans* addition of hydrogen halides to α,β-unsaturated acids is reviewed and new evidence is presented to show that in general the addition occurs by a *trans* mechanism, which cannot involve formation of a simple enolic intermediate or a classical carbonium ion.

It has been assumed generally that hydrogen halides add to olefinic and acetylenic linkages in a *trans* sense. It is our purpose to establish the generality of this assumption as factual for olefinic acids in which the double bond is conjugated with the carboxyl group.

Fittig has reported that tiglic and angelic acids both afford the same hydrobromide,[4] but the hydroiodides of these acids differ, and upon dehalogenative decarboxylation, respectively, yield *trans*- and *cis*-butene[5] as would be expected from *trans* hydrohalogenation followed by *trans* dehalogenative decarboxylation.[6–9] In the same sense α-ethylcrotonic acid adds hydrogen iodide[10] and hydrogen bromide[11] to give hydrohalides both of which afford *trans*-2-pentene on treatment with base. Likewise *cis*-2-methyl-3-ethyl- and *trans*-2-methyl-3-ethylacrylic acids afford, respectively, *trans*- and *cis*-2-pentene by way of their hydroiodides.[12]

The formation of pure *meso*-2,3-dibromosuccinic acid by hydrobromination of bromomaleic acid would be convincing evidence for *trans* hydrobromination

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[1] Abstracted in the main from portions of the Ph.D. Dissertations of Robert L. Craven (1954) and Randel Q. Little, Jr. (1953), University of Michigan.

[2] American Brake Shoe Company Fellow 1951–1952, Albert B. Prescott Fellow in Organic Chemistry 1953.

[3] American Brake Shoe Company Fellow 1952–1953.

[4] R. Fittig and A. Pugenstrecker, *Ann.*, **195**, 108 (1879).

[5] W. G. Young, R. T. Dillon and H. J. Lucas, This Journal, **51**, 2528 (1929).

[6] W. R. Vaughan and K. M. Milton, *ibid.*, **74**, 5623 (1952).

[7] S. J. Cristol and W. P. Norris, *ibid.*, **75**, 632, 2645 (1953).

[8] E. Grovenstein and D. E. Lee, *ibid.*, **75**, 2639 (1953).

[9] R. L. Craven, Ph.D. Dissertation, University of Michigan, 1954.

[10] M. L. Sherrill and E. S. Matlack, This Journal, **59**, 2134 (1937).

[11] W. M. Lauer and F. H. Stodola, *ibid.*, **56**, 1216 (1934).

[12] H. J. Lucas and A. N. Prater, *ibid.*, **59**, 1682 (1937).