

CCXXXV.—*The Properties of Nicotine and its Derivatives. Part II. Optical Rotatory Power and Rotatory Dispersion.*

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THE experiments described in this paper were begun mainly because the optical rotatory power of nicotine can be measured with an accuracy that is roughly 10 times greater than in the case of other

organic compounds, and only 10 times less than in the case of quartz, since the observed rotation of a 6-dcm. column of the base ranges from  $757^\circ$  at 6708 to  $2266^\circ$  at 4358 Å.U. Moreover, unlike most compounds of high optical rotatory power, it contains only a single asymmetric carbon atom, and might therefore be expected to exhibit very simple optical properties. In particular, it gives rise to a single well-defined absorption band (see Part I, this vol., p. 1376), and its rotatory dispersion can be expressed, at least approximately, by a single term of Drude's equation. The first objects of the present investigation were therefore (1) to establish a definite value for the specific rotatory power of the pure base, regenerated from the crystalline zinc chloride compound according to Ratz's method of purification (*Monatsh.*, 1905, **26**, 1241), (2) to make measurements of maximum accuracy of its rotatory dispersion over a wide range of wave-lengths, (3) to make a rigid test of the applicability of the one-term Drude equation to these data, and (4) to correlate the characteristic frequency deduced from the rotatory dispersion with that of the observed maximum of selective absorption. The observations were, however, also extended to cover the salts and the methiodides, most of which are characterised by a reversal of sign of their optical rotatory power.

### 1. Negative Rotations.

(a) *Pure Nicotine*.—The most trustworthy values recorded by earlier workers for the density and specific rotatory power of nicotine are collected in Table I. This table also shows the observed, specific, and molecular rotations for two wave-lengths of a series of fresh samples of purified nicotine, together with their densities. The lævo-rotations observed in nicotine and its derivatives, which are set out in full in Tables II—VII, are also summarised in Table I.

Sample 1 was a specimen which Lowry and Singh (*Compt. rend.*, 1925, **181**, 909) had prepared by fractional distillation; before use it was redistilled in a current of hydrogen at 2 mm. pressure. Sample 2 was Jephcott's nicotine (*J.*, 1919, **115**, 104) purified in the same way before use. Sample 3 was the same as 1 after purification through the zinc chloride compound. Samples 5 and 6 were also purified through the zinc chloride compound, but were preserved from oxidation by an atmosphere of hydrogen during measurements of dispersion extending over several hours.

The best values for the specific rotation of nicotine seem to be  $[\alpha]_D = 169.3^\circ$ ,  $[\alpha]_{5461} = 204.1^\circ$ . The consistently lower value given by Jephcott may perhaps be attributed to some subsidiary factor such as a difference in the mean wave-length of the sodium light; on the other hand, his densities are definitely more trustworthy than ours.

TABLE I.

*Observed, Specific, and Molecular Rotations of Nicotine at 20°.*(i) *Earlier measurements.*

	$d_4^{20}$ .	$[\alpha]_D^{20}$ .
Ratz (1905)	—	-166.77° *
Jephcott (1919)	1.00925	-169.54 †
	1.00920	-168.52 ‡
	1.00925	-168.61 †
	1.00925	-168.40 †
	1.00925	-168.66 †
Patterson and Fulton (1925) ( <i>J.</i> , <b>127</b> , 2435)	1.0095	-168.02 †
	1.0100	-167.78 †
Lowry and Singh (1925)	1.00931	-168.2° *
		-169.5° *

\* By fractional distillation.

† Through the ZnCl<sub>2</sub> compound.

‡ Through the nitroso-compound.

(ii) *New samples.*

Sam- ple.	$d_4^{20}$ .	$\alpha_D$ ( $l = 6$ ).	$\alpha_{5461}$ ( $l = 6$ ).	$[\alpha]_D$ .	$[\alpha]_{5461}$ .	$[M]_D$ .	$[M]_{5461}$ .
1	1.00984	-1023.0°	-1234.68°	-168.84°	-203.76°	-273.82°	-330.46°
2	1.01002	-1024.55	-1234.78	-169.06	-203.76	-274.19	-330.46
3	1.01122	-1026.42	-1236.68	-169.17	-203.83	-274.36	-330.56
4	1.01022	-1025.71	-1237.38	-169.23	-204.14	-274.45	-331.08
5	1.01010	-1026.29	-1237.06	-169.35	-204.12	-274.66	-331.04

(iii) *Lævorotatory solutions.*

Table.	Compound.	Solvent.	Spec. rotn. of base, $[\alpha]_{5461}$ .	Mol. rotn. $[M]_{5461}$ .	$\frac{\alpha_{4358}}{\alpha_{5461}}$ .	$\lambda_0^2$ .	$\lambda_0$ Å.U.
II.	Nicotine	None	-204.13°	-331.06°	1.831	0.0600	2450
III.	Nicotine	Acetone (28.77%)	-209.0	-339.0	1.817	0.0575	2400
IV.	Nicotine	Water (25.5%)	-97.64	-158.35	1.876	0.0664	2575
V.	Butyrate	Acetone	-99.2	-160.9	1.877	0.0627	2500
VI.	Crotonate	Acetone	-125.9	-204.1	1.819	0.0575	2400
VII.	isoMeth- iodide	Water (6.88%)	-128.7	-208.7	1.866	0.0652	2550

The rotatory dispersion of two of the purest samples are set out in Table II, which also shows the values of the dispersion ratio  $\alpha/\alpha_{5461}$  as calculated (i) from the two-constant formula

$$\alpha/\alpha_{5461} = 0.2383/(\lambda^2 - 0.060),$$

and (ii) from the three-constant formula

$$\alpha/\alpha_{5461} = 0.21415/(\lambda^2 - 0.06376) + 0.0257/\lambda^2.$$

The two-constant formula shows an average error of only 0.001 in the dispersion ratio for a series of 18 wave-lengths in the visible region from 6708 to 4358 Å.U., and this could have been reduced to still smaller proportions by readjusting the constants; but the photographic readings would then have risen somewhat steeply above the calculated values in the early ultra-violet region. The

TABLE II.

*Rotatory Dispersion of Nicotine at 20°.*Densities : I,  $d_4^{20} = 1.01022$ ; II,  $d_4^{20} = 1.01010$ .Specific rotations : I,  $[\alpha]_{5461} = -204.14^\circ$ ; II,  $[\alpha]_{5461} = -204.12^\circ$ .Molecular rotations : I,  $[M]_{5461} = -331.08^\circ$ ; II,  $[M]_{5461} = -331.04^\circ$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 6$ ).		$\alpha/\alpha_{5461}$ .			Diff. = 1000 $\times$ (Obs.—Calc.).	
	I.	II.	I.	II.	Mean.	(i).	(ii).
<i>Visible series.</i>							
Li 6707.8	— 756.89°	— 756.79°	0.61168	0.61176	0.61172	+0.6	—0.1
Cd 6438.5	— 832.25	— 831.78	0.67258	0.67230	0.67244	+0.3	$\pm 0$
Zn 6362.3	— 855.35	— 855.46	0.69125	0.69153	0.69139	+0.3	$\pm 0$
Li 6103.7	— 943.75	— 943.66	0.76269	0.76283	0.76276	+0.4	+0.3
Na 5892.9	— 1025.71	— 1026.29	0.82893	0.82962	0.82827	—0.7	$\pm 0$
Cu 5782.1	— 1074.81	— 1074.64	0.86861	0.86870	0.86866	$\pm 0$	+0.4
Hg 5780.1	— 1076.14	— 1076.00	0.86969	0.86980	0.86975	+0.4	+0.7
Cu 5700.2	— 1112.92	— 1111.56	0.89941	0.89855	0.89898	—0.5	$\pm 0$
Hg 5460.7	— 1237.38	— 1237.06	1.00000	1.00000	1.00000	—0.4	+0.3
Cu 5218.2	— 1387.58	— 1386.91	1.12138	1.12113	1.12125	—1.2	$\pm 0$
Ag 5209.0	— 1394.17	—	1.12670	1.12681	1.12675	—0.7	+0.5
Cu 5153.3	— 1432.91	— 1432.61	1.15801	1.15808	1.15804	—1.3	$\pm 0$
Cu 5105.5	— 1467.84	— 1481.83	1.18624	1.18645	1.18634	—1.2	+0.2
Cd 5085.8	— 1482.41	— 1481.83	1.19801	1.19786	1.19793	—1.7	—0.2
Zn 4810.5	— 1717.49	— 1717.33	1.38800	1.38824	1.38812	—2.1	—0.2
Cd 4799.9	— 1727.78	— 1726.70	1.39631	1.39581	1.39606	—2.4	—0.6
Zn 4722.2	— 1806.25	— 1805.62	1.45973	1.45961	1.45967	—2.4	—0.5
Hg 4358.3	— 2266.31	— 2265.65	1.83152	1.83147	1.83149	—2.3	—0.8

*Photographic series.*

	$\alpha$ ( $l = 1$ ).		$\alpha/\alpha_{5461}$ .	1000 $\times$ Calc. (i). Calc. (ii).		(Obs.—Calc.).	
	$\alpha_{5461}$ .						
Fe 4272	— 399.5°	— 205.47°	1.944	1.946	1.945	—2	—1
Fe 4251	— 405.8	— 205.58	1.974	1.974	1.975	$\pm 0$	—1
Fe 4202	— 419.8	— 205.38	2.044	2.044	2.044	$\pm 0$	$\pm 0$
Fe 4199	— 2531.9*	— 1236.90	2.047	2.049	2.048	—2	—1
Fe 4176	— 428.0	— 205.38	2.084	2.084	2.084	$\pm 0$	$\pm 0$
Fe 4145	— 438.5	— 205.62	2.133	2.132	2.132	+1	+1
Fe 4132	— 442.9	— 205.58	2.154	2.153	2.153	+1	+1
Fe 4072	— 462.8	— 205.61	2.251	2.252	2.253	—1	—2
Fe 4062	— 2804.4*	— 1237.17	2.268	2.269	2.271	—1	—3
Fe 4046	— 472.7	— 205.58	2.299	2.298	2.300	+1	—1
Fe 4005	— 488.7	— 205.58	2.377	2.373	2.376	+4	+1
Fe 3967	— 504.0	— 205.58	2.452	2.447	2.451	+5	+1
Fe 3953	— 510.5	— 205.58	2.483	2.476	2.480	+7	+3
Fe 3903	— 531.3	— 205.58	2.584	2.581	2.587	+3	—3
Fe 3887	— 539.4	— 205.72	2.622	2.616	2.622	+6	$\pm 0$

\*  $l = 6$ .

deviations, although so small as to be almost negligible in the visible region, are therefore too systematic to be ignored, and show that, as in the well-established cases of sodium tartrate, octyl oxalate, and (partially dissociated) borotartaric acid, the two-constant equation gives only an approximation to the true form of the dispersion curve. The deviations are, however, so small that it is not possible to deduce from them the values of *two* more arbitrary constants. We have

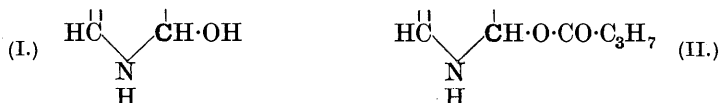
therefore tabulated under (ii) the deviations from a three-constant equation, in which the second dispersion-constant is ignored, so that  $\lambda_2^2 = 0$ . This equation gives an average error of 0.00027 for 18 values of the dispersion ratio in the visual region, and 0.0012 for 15 values in the photographic region, and these errors are distributed so irregularly as to leave no systematic error for correction with the help of a fourth arbitrary constant.

The wave-length of the predominant absorption is given by the two-constant equation as 2450 Å.U., and by the three-constant equation as 2525 Å.U. In accordance with previous experience (J., 1924, **125**, 2521; 1925, **127**, 611, 1266, 1507), these values are all less than the wave-length of the observed maximum of selective absorption at 2650 Å.U., and the explanation already given of this discrepancy is probably valid also in this additional case. It is, however, of interest that the high-frequency partial rotation, which may be attributed to the fixed or inherent asymmetry of the asymmetric carbon atom in the pyrrolidine ring, is nearly 10 times smaller than the low-frequency partial rotation, which we attribute to the induced asymmetry of the unsaturated pyridyl radical; as usual, it is of opposite sign. It may also be remarked that, whenever a low-frequency partial rotation can be attributed to the *induced* asymmetry of an unsaturated radical, we may expect it to be accompanied by the high-frequency partial rotation of a saturated centre of *fixed* asymmetry, although the latter may easily be disguised, as in the case of camphorquinone (J., 1925, **127**, 604; compare Lifschitz, *Z. physikal. Chem.*, 1923, **105**, 49), by the predominating influence of the nearer absorption band, thus giving rise to a dispersion which can be expressed within the limits of experimental error by a single term of Drude's equation.

(b) *Nicotine in Acetone*.—A solution of nicotine in acetone (Table III) gave practically the same constants as pure nicotine, the specific rotation being  $[\alpha]_{5461} = -209^\circ$ , as compared with  $-204^\circ$  for the pure base, whilst the dispersion ratio  $\alpha_{4358}/\alpha_{5461}$  was 1.817 as compared with 1.831. The visual readings can be expressed by a two-constant equation  $\alpha/\alpha_{5461} = 0.24074/(\lambda^2 - 0.0575)$ , with a limiting wave-length  $\lambda_0 = 2400$ , but one may suspect that ultra-violet readings would again reveal the presence of a small high-frequency partial rotation of opposite sign.

(c) *Nicotine in Water*.—A concentrated aqueous solution of nicotine (Table IV) gave specific rotations which were only about half as great,  $[\alpha]_{5461} = 97.64^\circ$ , but showed the same approximation to a two-constant dispersion equation  $\alpha/\alpha_{5461} = 0.23178/(\lambda^2 - 0.06642)$ , with a limiting wave-length  $\lambda_0 = 2575$  Å.U. This result is somewhat anomalous, since, if the water behaved merely as a weak acid, con-

verting the tertiary nitrogen atoms into ammonium ions, the rotation of the ionised hydrate should be positive like that of the salts (p. 1779). Actually, however, the rotation of the aqueous solution remains negative in sign like that of the free base, and shows no indication of becoming positive even at infinite dilution, since our readings tend to a limiting specific rotation  $[\alpha]_{5461} = 96^\circ$  (Table IV), whilst Jephcott's measurements show a minimum negative rotation at  $p = 10\%$ . We conclude that nicotine is not converted into a nicotinium ion by the action of water, but that it forms an un-ionised hydrate, with a similar dispersion to that of the free base but a much lower rotatory power. In accordance with the views already expressed in Part I, we regard this hydrate as a pseudo-base, and attribute to it a structure in which the pyridine ring has lost one of its double bonds, as in the formula (I).



(d) *Nicotine Butyrate and Crotonate in Acetone.*—The experiments which are set out in Section 2 below (Tables X and XI), on the rotatory dispersion of nicotine butyrate in butyric acid and of nicotine crotonate in water, were undertaken with the idea that the unsaturated acid might perhaps produce some effects which could not be explained by the mere transfer of a hydrogen ion from the acid to the base. Actually, both compounds showed the normal properties of nicotinium salts, giving rise to dextrorotatory solutions for which  $\lambda_0^2 = 0.03$  approximately. On the other hand, solutions in

TABLE III.

*Rotatory Dispersion of Nicotine in Acetone at 20°.*

28.7734 G. of nicotine in 100 g. of solution :  $d_4^{20} = 0.850$ ;  $[\alpha]_{5461} = -209.0^\circ$ ;  $[M]_{5461} = -339.0^\circ$ ;  $a/a_{5461} = 0.24074/(\lambda^2 - 0.0575)$ .

$\lambda$ , Å.U.	$a$ ( $l = 4$ ).	$a/a_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	-126.03°	0.616	0.613	+3
Zn 6363	-141.81	0.694	0.693	+1
Li 6104	-156.81	0.766	0.764	+2
Na 5893	-169.81	0.830	0.831	-1
Cu 5782	-177.87	0.870	0.870	$\pm 0$
Hg 5782	-178.06	0.871	0.870	+1
Cu 5700	-184.17	0.901	0.900	+1
Hg 5461	-204.48°	1.000	1.000	$\pm 0$
Cu 5218	-228.89	1.119	1.121	-2
Cu 5153	-236.61	1.157	1.157	$\pm 0$
Cu 5105	-242.28	1.185	1.185	$\pm 0$
Zn 4811	-283.11	1.385	1.384	+1
Zn 4722	-297.16	1.453	1.454	-1
Hg 4358	-371.56	1.817	1.817	$\pm 0$

TABLE IV.

*Rotatory Dispersion of Nicotine in Water at 20°.*

25·4983 G. in 100 g. of solution :  $d_4^{20} = 1.0172$ ;  $[\alpha]_{5461} = -97.64^\circ$ ;  
 $[M]_{5461} = -158.35^\circ$ ;  $\alpha/\alpha_{5461} = 0.23178/(\lambda^2 - 0.06642)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 6$ ).	$\alpha/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	- 91.83°	0.604	0.604	$\pm 0$
Cd 6438	-101.17	0.666	0.666	$\pm 0$
Zn 6363	-104.23	0.686	0.685	+1
Li 6104	-115.04	0.757	0.757	$\pm 0$
Na 5893	-125.37	0.825	0.825	$\pm 0$
Cu 5782	-131.35	0.864	0.865	+1
Hg 5780	-131.53	0.866	0.866	$\pm 0$
Cu 5700	-136.20	0.896	0.897	-1
Hg 5461	-151.95	1.000	1.000	$\pm 0$
Cu 5218	-171.03	1.126	1.128	-2
Cu 5153	-176.86	1.164	1.164	$\pm 0$
Cu 5106	-181.36	1.193	1.193	$\pm 0$
Cd 5086	-183.21	1.206	1.206	$\pm 0$
Zn 4810	-213.65	1.406	1.405	+1
Cd 4800	-214.83	1.414	1.413	+1
Zn 4722	-225.02	1.481	1.480	+1
Hg 4358	-285.03	1.876	1.876	$\pm 0$

We are indebted to Mr. C. B. Allsop for the following additional measurements.

$p$ .	$\alpha_{5893}$ .	$\alpha_{5780}$ .	$\alpha_{5461}$ .	$\alpha_{4358}$ .	$[\alpha]_{5461}$ .	$\alpha_{4358}/\alpha_{5461}$ .
17.113	-83.35°	-87.43°	-101.04°	-192.28°	-97.37°	-1.903
8.262	-39.26	-41.17	-47.64	-91.04	-95.68	-1.911
3.649	-17.28	-18.17	-21.02	-40.25	-95.97	-1.915
1.943	- 9.21	- 9.72	-11.24	-21.51	-96.2	-1.914
0.991	- 4.71	- 4.92	- 5.70	-10.91	-95.8	-1.914

acetone of mixtures of nicotine with rather more than an equimolecular quantity of butyric or crotonic acid (Tables V and VI) were lævorotatory, and the dispersion ratios were expressed by the same formula as for a solution of the free base in acetone, with  $\lambda_0^2 = 0.06$  (approx.). Although, therefore, the specific rotation of the nicotine was lowered from  $-209^\circ$  to  $-126^\circ$  in the crotonate and to  $-99^\circ$  in the butyrate, its behaviour was like that of the free base instead of a salt. The solvent has therefore prevented the conversion of the base into a kation; but since the rotatory dispersion of the butyrate in acetone (Table V) is almost identical with that of the aqueous base (Table IV), it is possible that it has formed a covalent carbonium salt or ester of the type (II) [compare (I)], with the same rotatory dispersion as the free base but a much lower rotatory power. These formulæ include an additional asymmetric atom, but this would presumably be produced in a partially racemic form, just as in the case of the salts, where the nitrogen atom of the pyrrolidine ring is asymmetric (*Nature*, 1926, **117**, 417).

(e) *isoMethiodide*.—The rotatory power of the *isomethiodide* is

very similar to that of the parent base in water. The specific rotation  $[\alpha]_{5461} = 68.64^\circ$  is again much smaller than that of the anhydrous base, being only about one-third, but the dispersion constant of the two-constant equation,  $\lambda_0^2 = 0.0652$ ,  $\lambda = 2550$ , is nearly the same as in the corresponding equation for the free base. The observed and calculated dispersion ratios for 17 wave-lengths in the visible spectrum are shown in Table VII.

TABLE V.

*Rotatory Dispersion of Nicotine Butyrate in Acetone at 20°.*

6.4480 G. of nicotine to 7.6604 g. of butyric acid; 15.9591 g. of nicotine in 100 g. of solution:  $d_{4^\circ}^{20} = 0.860$ ;  $[\alpha]_{5461} = -99.22^\circ$  (for base),  $= -47.6^\circ$  (for salt);  $[M]_{5461}$  (for base)  $= -160.9^\circ$ ;  $a/a_{5461} = 0.2364/(\lambda^2 - 0.06275)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 4$ ).	$a/a_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	- 33.38°	0.613	0.610	+3
Zn 6363	- 37.62	0.691	0.691	$\pm 0$
Na 5893	- 45.35	0.830	0.831	-1
Cu 5782	- 47.44	0.871	0.870	+1
Hg 5780	- 47.55	0.873	0.871	+2
Cu 5700	- 49.11	0.902	0.902	$\pm 0$
Hg 5461	- 54.44	1.000	1.004	-4
Cu 5218	- 61.43°	1.128	1.128	$\pm 0$
Cu 5152	- 63.43	1.165	1.165	$\pm 0$
Cu 5105	- 64.93	1.193	1.194	-1
Zn 4811	- 76.38	1.403	1.401	+2
Zn 4722	- 80.28	1.475	1.475	$\pm 0$
Li 4602	- 86.29	1.585	1.586	-1
Hg 4358	-101.07	1.877	1.878	-1

TABLE VI.

*Rotatory Dispersion of Nicotine Crotonate in Acetone at 20°.*

2.2078 G. of nicotine to 2.4452 g. of crotonic acid; 5.4377 g. of nicotine in 100 g. of solution:  $d_{4^\circ}^{20} = 0.814$ ;  $[\alpha]_{5461} = -125.9^\circ$  (for base),  $= -61.1^\circ$  (for salt);  $[M]_{5461}$  (for base)  $= -204.1^\circ$ ;  $a/a_{5461} = 0.24074/(\lambda^2 - 0.0575)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 4$ ).	$a/a_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	-13.59°	0.610	0.613	-3
Zn 6363	-15.44	0.693	0.693	$\pm 0$
Na 5893	-18.50	0.830	0.831	-1
Cu 5782	-19.36	0.869	0.870	-1
Hg 5780	-19.38	0.870	0.870	$\pm 0$
Cu 5700	-20.05	0.900	0.900	$\pm 0$
Hg 5461	-22.28	1.000	1.000	$\pm 0$
Cu 5218	-24.92	1.119	1.121	-2
Cu 5153	-25.76	1.156	1.157	-1
Cu 5105	-26.38	1.184	1.185	-1
Zn 4811	-30.84	1.384	1.384	$\pm 0$
Zn 4722	-32.45	1.456	1.454	+2
Zn 4680	-33.22	1.491	1.490	+1
Li 4602	-34.80	1.562	1.560	+2
Hg 4358	-40.53	1.819	1.817	+2



TABLE VII.

*Rotatory Dispersion of Nicotine isoMethiodide in Water at 20°.*

6·8763 G. in 100 g. of solution:  $d_4^{20} = 1.02169$ ;  $[\alpha]_{5461} = -68.64^\circ$ ,  
 $= -128.72^\circ$  (for nicotine as methiodide);  $[M]_{5461} = -208.75^\circ$ ;  $a/\alpha_{5461}$   
 $= 0.23296/(\lambda^2 - 0.0652)$ .

$\lambda$ , Å.U.	$a$ ( $l = 4$ ).	$a/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	-11.58°	0.603	0.606	-3
Cd 6438	-12.86	0.667	0.667	±0
Zn 6363	-13.13	0.681	0.686	-5
Li 6104	-14.48	0.751	0.758	-7
Na 5893	-15.81	0.820	0.826	-6
Hg 5780	-16.70	0.866	0.866	±0
Cu 5700	-17.29	0.896	0.897	-1
Hg 5461	-19.29	1.000	1.000	±0
Cu 5218	-21.66	1.123	1.125	-2
Cu 5153	-22.38	1.160	1.163	-3
Cu 5105	-23.00	1.192	1.192	±0
Cd 5086	-23.24	1.205	1.204	+1
Zn 4811	-27.04	1.402	1.402	±0
Zn 4722	-28.50	1.477	1.477	±0
Zn 4680	-29.15	1.511	1.515	-4
Cd 4678	-29.34	1.521	1.517	+4
Hg 4358	-35.99	1.866	1.868	-2

2. *Positive Rotations.*

Apart from the exceptional magnitude of its optical rotatory power, nicotine is of interest on account of the reversal of sign which takes place when the free base is converted into its salts. The specific rotations and the dispersion constants of the dextrorotatory derivatives of nicotine which have been investigated in the present research are summarised in Table VIII and are given in full in Tables IX to XIII.

TABLE VIII.

*Rotation and Dispersion Constants of Dextrorotatory Derivatives of Nicotine.*

Substance.	Solvent.	Salt.	Base.	$\frac{\alpha_{4358}}{\alpha_{5461}}$ .	$\lambda_0^2$ .	$\lambda_0$ , Å.U.	
		$[\alpha]_{5461}$ .	$[\alpha]_{5461}$ .				$[M]_{5461}$ .
Nicotine (as acetate)	Acetic acid	+25.96°	+45.18°	+73.27°	1.674	0.0272	1650
Nicotine (as butyrate)	Butyric acid	+22.01	+45.92	+74.47	1.668	0.0302	1740
Nicotine (as crotonate)	Water	+16.68	+34.36	+55.73	1.654	0.0302	1740
Zinc chloride compound	Water	+ 8.40	+20.17	+32.71	1.644	0.0217	1480 (about)
Dimethiodide	Water	+17.7	+48.7	+78.9	1.65	0.029	1700
Monomethiodide	Water	+ 6.23	+11.68	+18.95	—	—	—
Dihydriodide	Water	+ 4.78	+12.32	+19.98	—	—	—
Hydriodide of isomethiodide	Water	+ 5.63	+15.00	+24.33	—	—	—

TABLE IX.

*Rotatory Dispersion of Nicotine in Acetic Acid at 20°.*

15.5230 G. of nicotine in 100 g. of solution;  $d_4^{20} = 1.09048$ ;  $[\alpha]_{5461} = +45.18^\circ$ ;  $[M]_{5461} = 73.27^\circ$ ;  $\alpha/\alpha_{5461} = 0.271/(\lambda^2 - 0.02719)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 6$ ).	$\alpha/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	+28.97°	0.631	0.641	-10
Cd 6438	+31.76	0.692	0.700	- 8
Zn 6363	+32.54	0.709	0.718	- 9
Li 6104	+35.63	0.776	0.785	- 9
Na 5893	+38.60	0.841	0.847	- 6
Hg 5780	+40.30	0.878	0.883	- 5
Cu 5700	+41.59	0.906	0.910	- 4
Hg 5461	+45.89	1.000	1.000	$\pm 0$
Cu 5218	+50.90	1.109	1.106	+ 3
Cu 5153	+52.22	1.138	1.137	+ 1
Cu 5105	+53.35	1.162	1.161	+ 1
Cd 5086	+53.78	1.172	1.171	+ 1
Zn 4811	+60.77	1.324	1.327	- 3
Zn 4722	+63.53	1.384	1.384	$\pm 0$
Zn 4680	+64.80	1.412	1.413	- 1
$\alpha$ ( $l = 1$ ).				
Li 4602	+11.21	1.467	1.468	- 1
Hg 4358	+12.79	1.674	1.674	$\pm 0$
Fe 4281	+13.28	1.738	1.737	+ 1
Fe 4202	+13.88	1.817	1.814	+ 3
Fe 4187	+14.00	1.832	1.830	+ 2
Fe 4144	+14.33	1.875	1.875	$\pm 0$
Fe 4132	+14.41	1.886	1.888	- 2

TABLE X.

*Rotatory Dispersion of Nicotine in Butyric Acid at 20°.*

14.0793 G. of nicotine in 100 g. of solution;  $d_4^{20} = 1.00108$ ;  $[\alpha]_{5461} = +45.92^\circ$ ;  $[M]_{5461} = +74.47^\circ$ ;  $\alpha/\alpha_{5461} = 0.2682/(\lambda^2 - 0.0302)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 4$ ).	$\alpha/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
Li 6708	+16.54°	0.639	0.639	$\pm 0$
Zn 6363	+18.61	0.719	0.716	+ 3
Li 6104	+20.37	0.787	0.784	+ 3
Na 5893	+21.90	0.846	0.846	$\pm 0$
Hg 5780	+22.83	0.882	0.883	- 1
Cu 5700	+23.67	0.914	0.910	+ 4
Hg 5461	+25.89	1.000	1.001	- 1
Cu 5218	+28.64°	1.106	1.108	- 2
Cu 5153	+29.53	1.141	1.140	+ 1
Cu 5105	+30.20	1.167	1.164	+ 3
Zn 4810	+34.61	1.337	1.333	+ 4
$\alpha$ ( $l = 1$ ).				
Li 4603	+ 9.44	1.477	1.477	$\pm 0$
Hg 4358	+10.66	1.668	1.679	-11

TABLE XI.

*Rotatory Dispersion of Nicotine Crotonate in Water at 20°.*

6.370 G. of nicotine or 13.115 g. of nicotine crotonate in 100 g. of solution;  $d_4^{20^\circ} = 1.01843$ ;  $[\alpha]_{5461} = 34.36^\circ$  (for nicotine),  $= 16.68^\circ$  (for crotonate);  $[M]_{5461}$  (for base)  $= 55.73^\circ$ ;  $\alpha/\alpha_{5461} = 0.2682/(\lambda^2 - 0.0302)$ .

$\lambda$ , Å.U.	$\alpha$ ( $l = 4$ ).	$\alpha/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).*
Li 6708	+ 5.60°	0.629	0.639	-10
Cd 6438	+ 6.15	0.690	0.695	- 5
Zn 6363	+ 6.31	0.708	0.716	- 8
Li 6104	+ 6.94	0.779	0.784	- 5
Na 5893	+ 7.52	0.844	0.846	- 2
Hg 5780	+ 7.88	0.884	0.883	+ 1
Cu 5700	+ 8.12	0.911	0.910	+ 1
Hg 5461	+ 8.91	1.000	1.001	- 1
Cu 5218	+ 9.86	1.107	1.108	- 1
Cu 5153	+10.16	1.140	1.140	$\pm$ 0
Cu 5105	+10.39	1.166	1.164	+ 2
Cd 5086	+10.48	1.176	1.174	+ 2
Zn 4811	+11.94	1.340	1.333	+ 7
Cd 4800	+12.00	1.347	1.343	+ 4
Zn 4722	+12.45	1.397	1.391	+ 6
Zn 4680	+12.70	1.425	1.426	- 1
Hg 4358	+14.74	(1.654)	1.679	(-25)

\* The errors shown in this column are relatively large; but they only correspond with hundredths of a degree in the original readings and appear to be casual rather than systematic in character. The solution had darkened to an extent which made it difficult to read the mercury violet line.

It seemed possible at first that the reversal of sign on passing from nicotine to its salts might be due to the development of asymmetry in the pyrrolidine nitrogen atom on its becoming quinquivalent; but this simple theory was soon disproved when it was found that the same reversal takes place in the formation of the mono- and di-methiodides, where the quaternary nitrogen of the pyrrolidine ring carries *two* methyl groups and cannot therefore be asymmetric. Further experiments showed that, whilst the base retains its levorotatory power when the nitrogen of the pyridine radical becomes quaternary in the isomethiodide, it becomes dextrorotatory whenever the nitrogen of the pyrrolidine ring becomes quaternary, but without regard to the symmetry or asymmetry of this atom. The reversal of sign is therefore not a direct effect of the development of an asymmetric nitrogen atom, but must be due to some secondary action upon the asymmetric carbon atom. If, however, the sign of the rotation has already been reversed by making the pyrrolidine nitrogen quaternary, it is found that (as in the case of the levorotatory base) no further change is effected by making the pyridine nitrogen quaternary. The results as a whole can be summarised by saying that, when the pyrrolidine nitrogen is tervalent

TABLE XII.

*Rotatory Dispersion of Nicotine-Zinc Chloride Compound in Water at 20°.*

17.0079 G. of  $(C_{10}H_{16}N_2)ZnCl_4 \cdot H_2O$  in 100 g. of solution;  $d_4^{20} = 1.07380$ ;  $[\alpha]_{5461} = +20.17^\circ$  (for nicotine),  $= +8.40^\circ$  (for salt);  $[M]_{5461}$  (for base)  $= 32.71$ ;  $\alpha/\alpha_{5461} = 0.275/(\lambda^2 - 0.02187)$ ;  $\lambda_0 = 1479 \text{ \AA.U.}$

$\lambda$ , $\text{\AA.U.}$	$\alpha$ ( $l = 6$ ).	$\alpha/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).*
(a) <i>Visual readings.</i>				
Li 6708	+ 5.79°	0.635	0.642	- 7
Cd 6439	+ 6.27	0.688	0.700	-12
Zn 6363	+ 6.45	0.708	0.718	-10
Li 6104	+ 7.10	0.779	0.784	- 5
Na 5893	+ 7.66	0.841	0.845	- 4
Hg 5780	+ 8.01	0.879	0.881	- 2
Cu 5700	+ 8.26	0.907	0.907	$\pm 0$
Hg 5461	+ 9.11	1.000	0.995	+ 5
Cu 5218	+10.05	1.103	1.098	+ 5
Cu 5153	+10.30	1.130	1.128	+ 2
Cu 5106	+10.52	1.155	1.151	+ 4
Cd 5086	+10.62	1.165	1.161	+ 4
Zn 4810	+11.97	1.314	1.313	+ 1
Zn 4722	+12.46	1.368	1.367	+ 1
Hg 4358	+14.97	1.644	1.636	+ 8
(b) <i>Photographic readings.</i>				
				100 (O-C).
Fe 4245	+15.81°	1.736	1.736	$\pm 0$
Fe 4202	+16.15	1.772	1.777	-1
Fe 4132	+16.67	1.830	1.848	-2
	$\alpha$ ( $l = 1$ ).			
Fe 4003	+ 2.94	(1.94)	1.987	(-5)
Fe 3951	+ 3.04	(1.99)	2.049	(-6)
Fe 3877	+ 3.14	(2.06)	2.140	(-8)

\* The errors shown in this table correspond only to hundredths of a degree in the visual readings and are therefore within the limits of conceivable experimental errors; but they are too regular to be ignored with safety, in view of the fact that the photographic readings (although subject to even larger experimental errors) show a progressive increase in the deviation from the theoretical values as the wave-length is diminished. The regular deviations are, however, too small to make it practicable to deduce the constants of a two-term equation from the experimental data.

(and planar?), the rotatory power of the compound is dominated by a large negative low-frequency term, but that this disappears when the pyrrolidine nitrogen becomes quadricovalent and tetrahedral; the rotation is then produced by a high-frequency term which is smaller in magnitude but positive in sign.

A reversal of sign on salt formation has been observed previously in solutions in chloroform of the salts of brucine with certain unsaturated acids, and of coniine with aromatic acids (Hilditch, J., 1908,

TABLE XIII.

*Rotatory Dispersion of Nicotine Dimethiodide in Water at 20°.*

8.6269 G. of iodide in 100 g. of solution;  $d_4^{20} = 1.03865$ ;  $[\alpha]_{5461} = +48.7^\circ$  (for nicotine),  $= +17.7^\circ$  (for iodide);  $[M]_{5461}$  (for base)  $= 78.9^\circ$   
 $a/\alpha_{5461} = 0.2672/(\lambda^2 - 0.0290)$ .

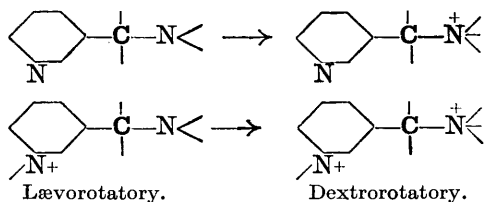
$\lambda$ , Å.U.	$\alpha$ ( $l = 4$ ).	$a/\alpha_{5461}$ .		
		Obs.	Calc.	1000 (O-C).*
Li 6708	+3.99°	0.629	0.635	- 6
Zn 6363	+4.46	0.703	0.711	- 8
Li 6104	+4.88	0.770	0.778	- 8
Na 5893	+5.34	0.842	0.839	+ 3
Hg 5780	+5.59	0.882	0.876	+ 6
Cu 5700	+5.82	0.918	0.903	+15
Hg 5461	+6.34	1.000	0.993	+ 7
Cu 5218	+6.93	1.093	1.098	- 5
Cu 5153	+7.19	1.134	1.130	+ 4
Cu 5106	+7.34	1.158	1.153	+ 5
Zn 4810	+8.36	1.319	1.320	- 1
Zn 4722	+8.81	1.390	1.378	+12
	$\alpha$ ( $l = 1$ ).			
Li 4602	+2.32	(1.468)	1.462	(+ 6)
Hg 4358	+2.60	(1.646)	1.660	(-14)

\* See footnote to Table XI.

93, 700); and a similar reversal occurs when tetrahydroquinaldine,  $[\alpha]_D + 230^\circ$ , is converted into its benzoyl derivative,  $[\alpha]_D - 61.2^\circ$  (Pope and Read, J., 1910, **97**, 2206), or into other derivatives of a similar type (Pope and Winmill, J., 1912, **101**, 2309). No satisfactory explanation of this phenomenon has been given hitherto, but attention can now be directed to two factors which may provide a clue to the origin of the phenomenon: (i) A reversal of sign occurs when the brucine or coniine salts are examined in chloroform, but not when they are examined in water; this change of sign can therefore be attributed to the formation of real molecules (pseudo-salts), although these may be of the same elusive type as the covalent molecules postulated by Moore and Winmill (J., 1912, **101**, 1635) in the hydroxides of the simple amines. (ii) The reversal is specially characteristic of unsaturated and aromatic acids; the experimental data are therefore in harmony with the view that the change depends on the development of an induced asymmetry of opposite sign in unsaturated groups, which are capable in this way of acquiring a very high optical activity, like that of nicotine and its levorotatory derivatives.

The behaviour of nicotine and its salts can be interpreted in a very simple and satisfactory way by saying that the absorption band at 2650 Å.U., which dominates the rotatory power of the base and its hydrates, as well as of the isomethiodide, becomes optically

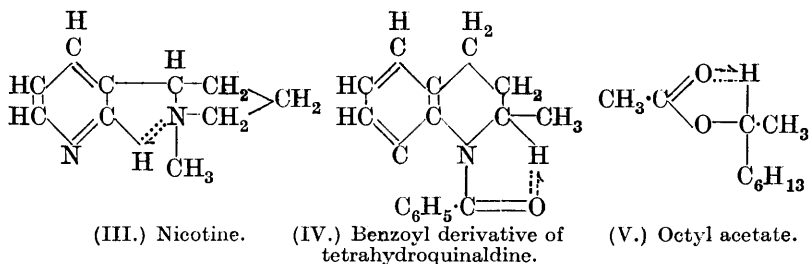
inactive when the pyrrolidine nitrogen has been converted into a quaternary ion, thus :



The fact that this nitrogen atom is attached directly to the asymmetric carbon atom may be an important factor in the abrupt cancellation of the power of the asymmetric carbon atom to set up an induced asymmetry in the aromatic ring; but the experimental data justify a more precise deduction, since the low-frequency term is associated with the presence of a "lone pair" of electrons on the pyrrolidine nitrogen, and vanishes when this lone pair is shared either with a proton in the salts or with a methyl radical in the methiodides.

This purely experimental result lends an unexpected importance to a factor that would have appeared insignificant in the light of the older theories, but which has acquired a new interest in view of the significance that is now attached to "donors" and "acceptors" of electrons as agents in the formation of addition compounds. The logical sequel to these observations would be to postulate a "dative bond" (Menzies, *Nature*, 1928, **121**, 457) between the pyrrolidine nitrogen and the contiguous hydrogen atom of the pyridine ring, as indicated by dotted lines in formula (III), but for the present purpose it is only necessary to suppose that coupling forces exist between the donor and acceptor which are sufficiently strong to prevent "free rotation" about the single bond between the pyridine and pyrrolidine rings. The exceptional rotatory power of the free base could then be attributed to an induction of a more direct and powerful character than that which is transmitted only to an inappreciable extent through the single bond between the two rings in the mono- and di-methiodides. This interpretation can be extended readily to the acyl derivatives of tetrahydroquinaldine (IV), and can also be correlated with the development of complex or anomalous rotatory dispersion in the esters of *secondary* alcohols which themselves give rise to simple rotatory dispersion (Pickard and Kenyon, *J.*, 1914, **105**, 830). The coupling shown in formula (V) (which would prevent "free rotation" about the single bond between alcohol and acid) may also be an essential factor in the resolution of these compounds, since the methods which have been uniformly successful in the case

of the secondary alcohols have failed conspicuously when applied to the simple tertiary alcohols.



### 3. Anomalous Rotatory Dispersion.

Nasini and Pezzolato (*Gazzetta*, 1893, **23**, 43) found that an equimolecular mixture of nicotine and acetic acid with less than five molecules of water was levorotatory,  $[\alpha]_D = -72.2^\circ$ , but that on dilution with water the rotation changed until the value  $[\alpha]_D = +49.68^\circ$  was reached. In the light of the observations made under Sections 1 and 2 above, this change of sign can be attributed to progressive ionisation, although the nature of the levorotatory component is not immediately obvious, since it might be free nicotine, or an un-ionised hydrate or salt. Since, however, nicotine in the free state, as well as in solution in *cyclohexane*, in *acetone*, and in *water*, gives negative specific rotations which can be represented to a fair degree of approximation by a two-constant equation with  $\lambda_0^2 = 0.06$ , whilst the salts give positive rotations with  $\lambda_0^2 = 0.03$ , it was of interest to determine the exact form of the dispersion curves for this series of mixtures, and to compare them with values calculated from a two-term equation with  $\lambda_1^2 = 0.03$ ,  $\lambda_2^2 = 0.06$ . Moreover, the conditions were favourable for verifying our views on anomalous rotatory dispersion by making experiments to realise this phenomenon in a series of compounds of which the dispersion is usually not merely "normal," but at least approximately "simple." For this purpose an equimolecular mixture of nicotine and acetic acid was prepared with only a trace of water, and this mixture was then progressively diluted. The rotations in a 1-dm. tube were as follows :

$p$	=	99.82	84.96	82.69	80.13	79.25	76.74%
$\alpha_{5461}$	=	-96.29°	-21.32°	-17.71°	-10.92°	-3.32°	+5.08°

The general results of Nasini and Pezzolato having thus been confirmed, four solutions were examined over the range  $\lambda$  6708—4358, one of them being designed to exhibit anomalous rotatory dispersion. The numerical results are set in Table XIV and the

TABLE XIV.

*Specific Rotation of Nicotine Acetate in Water at 20°.*

$\lambda$ , Å.U.	$a$ ( $l = 1$ ).	$a/a_{5461}$ .		
		Obs.	Calc.	1000 (O-C).
<i>Solution A.</i> $p = 99.82\%$ ; $d_4^{20} = 1.05789$ ; $c = 105.598$ g./100 c.c.;				
$a/a_{5461} = +0.2615/(\lambda^2 - 0.06) - 0.02613/(\lambda^2 - 0.03)$ .				
Zn 6363	- 67.47°	0.689	0.689	$\pm 0$
Cu 5782	- 84.87	0.867	0.867	$\pm 0$
Hg 5780	- 85.01	0.868	0.868	$\pm 0$
Cu 5700	- 87.92	0.898	0.899	-1
Hg 5461	- 97.93	1.000	1.000	$\pm 0$
Cu 5218	- 109.84	1.122	1.124	-2
Zn 4722	- 143.65	1.467	1.468	-1
Zn 4680	- 147.31	1.504	1.506	-2
Hg 4358	- 181.11	1.849	1.849	$\pm 0$
<i>Solution B.</i> $p = 10.1332$ ; $d_4^{20} = 1.0137$ ; $c = 10.2720$ g./100 c.c.;				
$a/a_{5461} = -0.04505/(\lambda^2 - 0.06) + 0.3189/(\lambda^2 - 0.03)$ .				
100 (O-C).				
Li 6708	+2.16*	0.620	0.644	-2
Zn 6363	+5.17†	0.742	0.720	+2
Li 6104	+2.67*	0.767	0.788	-2
Hg 5780	+6.18†	0.887	0.885	$\pm 0$
Cu 5700	+6.46†	0.927	0.912	+2
Hg 5461	+6.97†	1.000	1.001	$\pm 0$
Cu 5218	+3.86*	1.108	1.105	$\pm 0$
Cu 5153	+4.01*	1.151	1.136	+1
Zn 4811	+4.72*	1.355	1.322	+3
Hg 4358	+5.71*	1.639	1.649	-1
<i>Solution C.</i> $p = 76.737$ ; $d_4^{20} = 1.10254$ ; $c = 84.61$ g./100 c.c.;				
$a/a_{5461} = -1.058/(\lambda^2 - 0.06) + 1.459/(\lambda^2 - 0.03)$ .				
100 (O-C).				
Li 6708	+3.75	0.738	0.761	-2
Zn 6363	+4.12	0.812	0.825	-1
Li 6104	+4.37	0.862	0.877	-1
Na 5893	+4.60	0.907	0.917	-1
Hg 5780	+4.76	0.938	0.938	$\pm 0$
Hg 5461	+5.08	1.000	1.000	$\pm 0$
Cu 5218	+5.41	1.065	1.040	+2
Hg 4358	+4.99	0.983	0.983	$\pm 0$
<i>Solution D.</i> $c = 29.17$ ; $a/a_{5461} = 0.2626/(\lambda^2 - 0.06) - 0.02753/(\lambda^2 - 0.03)$ .				
1000 (O-C).				
Li 6708	-12.34	0.603	0.608	- 5
Zn 6363	-14.04	0.686	0.689	- 3
Li 6104	-15.43	0.754	0.760	- 6
Hg 5780	-17.74	0.867	0.867	$\pm 0$
Cu 5700	-18.37	0.897	0.898	- 1
Hg 5461	-20.47	1.000	1.000	$\pm 0$
Cu 5218	-23.05	1.126	1.123	+ 3
Cu 5105	-24.13	1.179	1.190	-11
Zn 4811	-28.41	1.388	1.395	- 7
Li 4602	-31.93	1.560	1.579	-19
Hg 4358	-37.85	1.849	1.849	$\pm 0$

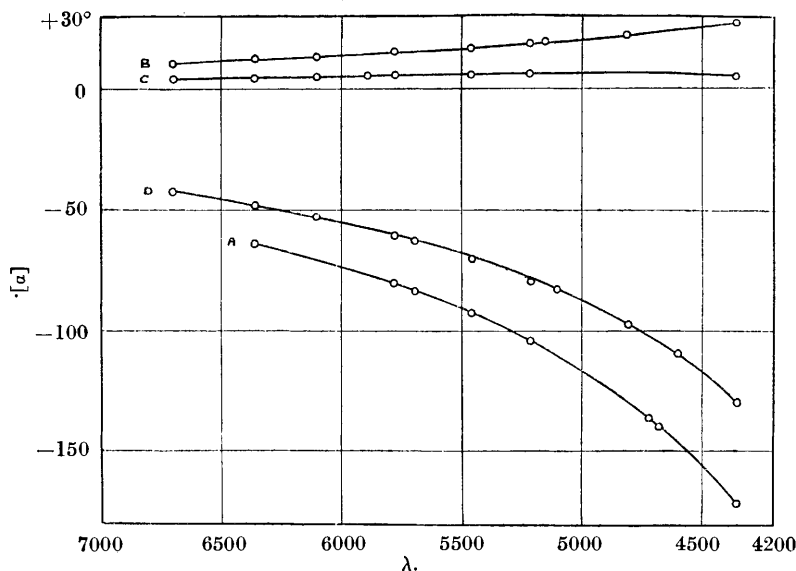
\*  $l = 2$ .†  $l = 4$ .



dispersion curves are shown in Fig. 1. It will be seen (i) that the dispersion curves can be calculated on the assumption that the solutions contain two optically active components of opposite sign and unequal dispersion, and (ii) that the expected anomaly is developed in solution C, which exhibits a maximum rotatory power in the green region of the spectrum. It is, moreover, clear that only a slight change of composition would be required to bring the reversal of sign or the inflexion into the visible spectrum. In the case of solution C the calculated wave-lengths of the anomalies are as follows: Inflexion 5700 Å.U., maximum 4800 Å.U., reversal of sign 3730 Å.U.

FIG. 1.

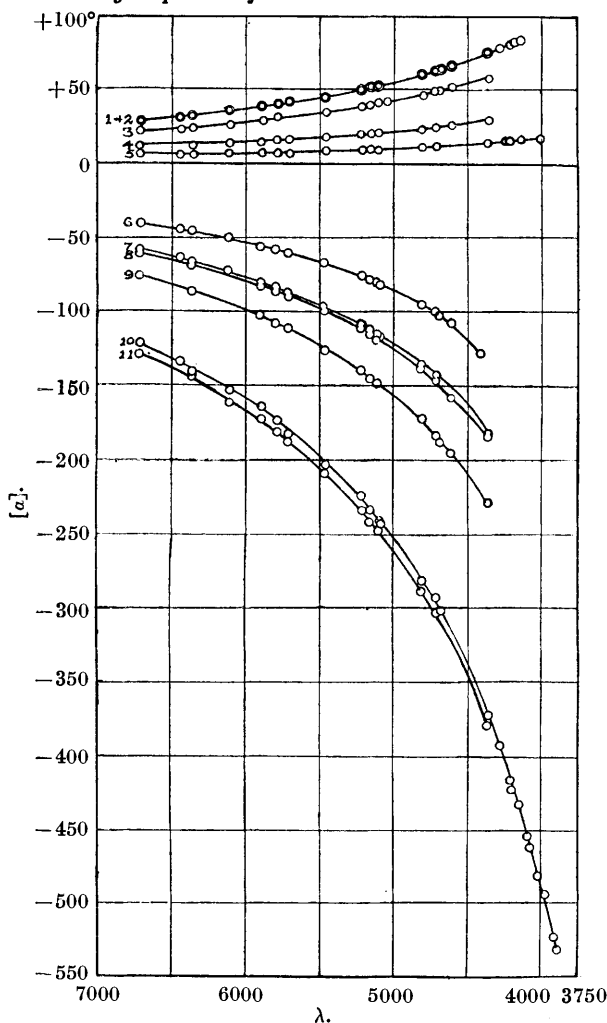
*Rotatory dispersion of nicotine acetate.*



#### 4. Characteristic Diagrams.

The dispersion curves for nicotine and its derivatives (with the exception of the acetate solutions of Fig. 1) are plotted in Fig. 2. The curves form a simple continuous series or family, in which the relationships are even simpler than in the case of methyl or ethyl tartrate (J., 1915, **107**, 1173, 1187), since none of the curves intersects another. The data now under consideration therefore provide a particularly favourable opportunity for a critical review of the "rectilinear diagrams" (Darmon, *Compt. rend.*, 1908, **147**, 195; *Ann. Chim. Phys.*, 1911, **22**, 247; compare Lucas, Thesis, Paris, 1927) and "characteristic diagrams" (Armstrong and Walker,

FIG. 2.

*Rotatory dispersion of nicotine and its derivatives.*

1. Nicotine in excess butyric acid.
2. Nicotine in excess acetic acid.
3. Nicotine + excess crotonic acid in water.
4. Nicotine dimethiodide in water.
5. Nicotine-zinc chloride compound in water.
6. Nicotine isomonomethiodide in water.
7. Nicotine in water.
8. Nicotine + excess butyric acid in acetone.
9. Nicotine + excess crotonic acid in acetone.
10. Nicotine.
11. Nicotine in acetone.

*Proc. Roy. Soc.*, 1913, *A*, **88**, 388; compare Pickard and Kenyon, *J.*, 1914, **105**, 844, 845, 847, 1118; Patterson, *J.*, 1916, **109**, 1182; 1925, **127**, 2441), which have been used from time to time to correlate the rotatory dispersions of a series of solutions or of related compounds.

These devices are merely a graphical expression of Biot's mixture rule, according to which the rotatory power of a binary mixture for any wave-length can be calculated by simple proportion from the rotatory powers of the two components for the same wave-length. Conversely, therefore, if the lines in Darmois's rectilinear diagram are accurately congruent, or if the points in the characteristic diagram of Armstrong and Walker fall accurately upon a series of straight lines, we may conclude that the rotations in question can be expressed as the weighted mean of those of two limiting components. The easiest case to understand is that in which these limiting components are real compounds, and exhibit simple rotatory dispersion; the rotatory powers of mixtures in various proportions can then be expressed by a general formula of the type

$$\alpha = \frac{x}{\lambda^2 - \lambda_1^2} \pm \frac{1-x}{\lambda^2 - \lambda_2^2},$$

where  $x$  is the fraction by weight of one component in the mixture.\* These numbers would obviously give rise to accurate linear diagrams, and this would still occur if the limiting components in the diagram did not represent two pure substances but merely two limiting mixtures, or if one or both of the limiting components exhibited a complex rotatory dispersion. The same result would follow also if a diagram were plotted for a single pure compound in which two partial rotations were developed in varying proportions according to the nature of the medium or the physical conditions of temperature and pressure; but the rule would no longer hold good if one partial rotation could be increased without a corresponding decrease in the other, since Biot's mixture rule would obviously fail if the specific rotations of the components were variable even if their dispersion ratios remained constant. In the case of nicotine, we have seen that the specific rotation falls to one-half when the base is dissolved in water, but

\* This family of curves has been plotted for the case in which  $\lambda_1^2 = 0.03$ ,  $\lambda_2^2 = 0.06$  (*J.*, 1915, **107**, 1200). In this figure Patterson's "rational zero" depends on finding a curve on which the ordinate  $\alpha$  has equal values for two selected values of the abscissa  $\lambda^2$ , which must obviously lie on opposite sides of a maximum, e.g.,  $\alpha = +2^\circ$  for  $\lambda^2 = 0.1$  or  $0.2$  on the curve  $0.7A-0.3B$ . In this ideal case, in which only two components are possible and no deviations from Biot's mixture law are admitted, the "dispersion ratio" with respect to Patterson's "rational zero" is then identical with the dispersion ratio calculated in the ordinary way for the difference between the two limiting components *A* and *B*.

without any substantial change in the dispersion ratios. The data for anhydrous and aqueous nicotine would therefore be congruent with those of a compound of zero rotatory power at all wave-lengths, or of a compound (either dextrorotatory or lævorotatory) which had the same dispersion ratios as the base; but they could not be congruent with the data for a dextrorotatory salt with much smaller dispersion ratios. The fact that in the case of nicotine, both in the homogeneous state and when dissolved in nitrotoluene, quinoline, water, formamide, or sulphuric acid, "the data obtained lie in a fairly satisfactory manner on the lines of the diagram" (Patterson and Fulton, J., 1925, **127**, 2441) shows that this method of examination is subject to the same limitations as the graphical method of detecting simple rotatory dispersion, *e.g.*, that it will show up the more obvious deviations from the rule, but in other cases can only be regarded as preliminary to a precise algebraic analysis of the data. Thus, whilst the characteristic diagram for nicotine and its derivatives appears to be compatible with a two-component scheme such as that represented by the equation  $\alpha = x/(\lambda^2 - 0.03) - (1 - x)/(\lambda^2 - 0.06)$ , algebraic analysis reveals the existence on the one hand of a series of lævorotatory molecules with an almost constant high dispersion but with very variable specific or molecular rotations, and, on the other hand, of a series of dextrorotatory ions with an almost constant low dispersion but again with very variable rotatory powers; and it is only in exceptional cases that these two types of partial rotation coexist in such proportions as to give rise to dispersion curves which are too complex to exhibit a linear relation between  $1/\alpha$  and  $\lambda^2$  in a merely graphical analysis. Whilst, therefore, the dispersion curves for tartaric acid and its esters are conspicuously anomalous, the curves for nicotine and its salts, with almost identical values for the high- and low-frequency dispersion constants (0.03 and 0.06), nearly all exhibit at least a pseudo-simple rotatory dispersion, and only become anomalous under specially selected conditions.

#### *Summary.*

(a) The rotatory dispersion of nicotine is nearly (but not quite) simple, with  $\lambda_1^2 = 0.06$ ; the characteristic wave-length is rather less than that of the maximum of selective absorption.

(b) The hydrate in water, and the butyrate and crotonate in acetone, have nearly the same dispersion ratios as free nicotine, but their rotatory powers are much less. It is possible that nicotine forms a pseudo-base, like those investigated by Decker in the *iso*-quinoline series, and a series of pseudo-salts with weak acids.

(c) The *isomethiodide* is lævorotatory, but its hydriodide and methiodide are dextrorotatory with a nearly simple dispersion for

which  $\lambda_2^2 = 0.03$ . The zinc chloride compound of nicotine is also dextrorotatory with very similar dispersion ratios.

(d) The reversal of sign on salt formation, which has been noticed also in brucine and coniine, and on benzylation of tetrahydroquinoline, is associated in nicotine with the saturation of a lone-pair of electrons on the pyrrolidine nitrogen, and is perhaps dependent on the elimination of an incipient dative bond between the two rings.

(e) A solution showing anomalous rotatory dispersion has been prepared by diluting nicotine acetate with water.

(f) The significance of Darmois's rectilinear diagram and Armstrong and Walker's characteristic diagram is discussed.

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