ROTATORY POWER AND CHEMICAL CONSTITUTION.

Part I. The Preparation and Resolution of α-Benzyl-α-Capric Acid and some Derivatives.

BY H. R. BURJORJE, KAMAKSHI (MISS), B. K. MENON AND D. H. PEACOCK,
University College, Rangoon.

Received November 21, 1934.

In an earlier paper it was shown that the p-toluene sulphonyl derivative of cinchonicine had a much smaller positive rotatory power than the benzoyl derivative while the picryl derivative had a very large negative rotation and it was suggested that these changes were due to the effect of the substituents upon the intramolecular electrical field of force, and the consequent changes in the forces binding the electrons responsible for optical activity. Looking at these facts from another point of view we see that the dipole produced by the benzoyl group is weaker than that produced by the p-toluene sulphonyl group and this in turn weaker than the three dipoles formed by the three nitro groups in the picryl group and this change first lowers the rotatory power and finally changes its sign. The object of these experiments was to determine whether effects similar to those observed by Flurscheim in reactivity and strengths of acids and bases could also be observed in rotatory powers. Although molecular rotatory powers for one wave-length only are not suitable for absolute comparisons of optical activity yet when the substances examined possess no absorption bands in the neighbourhood of the wave-length used for the measurements, qualitative relationships may at least be hoped for. In this connection it must be pointed out that the high, negative rotation of picryl cinchonicine is possibly bound up with its possessing absorption bands in the visible region of the spectrum.

The effect of a substituent on reactivity is usually considered under three heads: the general polar effect and the electromeric effect both of which are regarded as transmitted through the chain of atoms and a space effect, similar to the general polar effect but transmitted through space. In spirane compounds where no asymmetric atoms in the normal sense of the word are present optical activity may be regarded as due entirely

to effects transmitted through space and the existence of optical activity in such cases shows that the direct or space effect is by no means negligible. The general polar effect of substituents upon rotatory power has been the subject of extensive work by Betti, Rule and others, who have obtained valuable results. The object of the experiments to be described was the search for an alternating effect similar to that observed by Olivier, Lapworth and Shoesmith and others in the reactivity of benzyl halides. For this purpose cinchonicine with its two optically active centres was unsuitable and so were all compounds in which the group whose effect was to be studied was bound to the optically active centre by an oxygen atom because it has been shown that an oxygen atom is generally a very effective barrier to alternating effects. It has, however, been found that in substances of the type \( \text{X.C}_6\text{H}_4\text{CH}_2\text{Y} \) an alternating effect is transmitted to \( \text{Y} \) and therefore it was expected that acids of the type \( \text{X.C}_6\text{H}_4\text{CH}_2\text{CH(R).COOH} \) might show such an alternating effect. Reactivity measurements have shown that, in substances of the type \( \text{X.C}_6\text{H}_4\text{CH}_2\text{Y} \) where \( \text{Y} \) is a halogen, when \( \text{X} \) is a halogen or the methyl group the reactivity is higher with \( \text{X} \) para than with \( \text{X} \) meta but that when \( \text{X} \) is the nitro or carboxyl group the reactivity is lower with \( \text{X} \) para than with \( \text{X} \) meta. There is an exception to this; with trimethyl-amine in benzene para nitrobenzyl chloride reacts faster than does meta nitrobenzyl chloride with aromatic amines the meta compound reacts faster than the para. This discrepancy is not shown by all substituted benzyl halides when they react with aromatic and fatty tertiary amines because Jones and Preston found that with both dimethylaniline and tri-isoamylamine para xylyl bromide reacted faster than meta. The reaction studied by Norrish and Smith seems therefore to be exceptional. The compounds examined below were those of the type \( \text{X.C}_6\text{H}_4\text{CH}_2\text{CH(C}_6\text{H}_9).\text{COOH} \) where \( \text{H} \) was \( \text{H} \), \( \text{Br} \) meta and para, \( \text{COOH} \) meta and para. It was expected that if the change from the meta position to the para position of the bromine atom produced any effect on the rotatory power then the opposite effect would be produced by the carboxyl group. No particular difficulty was observed in resolving \( \alpha\)-benzyl-\( n\)-caproic acid and the meta and para brom derivatives but the resolution of the meta and para carboxy compounds gave capricious results and the rotations observed were very small. The molecular rotations for the acids concerned are given below:

\[ \text{Gazzetta, 1907, 37, 1, 62 and later papers.} \]
\[ \text{J.C.S., 1924, 125, 2168 and later papers.} \]
\[ \text{Norrish and Smith, J.C.S., 1928, 129.} \]
\[ \text{J.C.S., 1912, 101, 1930.} \]
Molecular Rotations of a-Benzyl-n-Caproic Acid and some Derivatives.

- a-Benzyl Acid... \([\alpha]_{D}^{20} + 57.6^\circ\)
- a-\(p\)-Brombenzyl Acid... \(+ 116.3^\circ\)
- a-\(m\)-Brombenzyl... \(+ 57.0^\circ\)
- a-\(p\)-Carboxybenzyl... \(+ 14.5^\circ\)
- a-\(m\)-Carboxybenzyl... \(+ 23.1^\circ\)

All rotations were measured in benzene solution.

The para brom acid has a greater molecular rotation than the meta acid, thus the effect of the position of the bromine atom on rotatory power is similar to its effect on the rate of hydrolysis of brombenzyl bromides. Assuming that a similar relationship holds for the carboxyl group we should expect the effect of this group upon the rate of hydrolysis of the carboxybenzyl bromides (\(\omega\)-brom toluic acids) to be similar to the effect on the rotatory powers of meta and para carboxybenzyl-n-caproic acids so that the rotatory power of the para acid should be less than that of the meta. This is found to be the case but the rotations of the carboxybenzyl acids are so small that we do not wish to stress this agreement until the results have been confirmed. The present results can be regarded as approximate only.

When we compare the rotations of the benzyl, \(p\)-brombenzyl and \(p\)-carboxybenzyl acids we see that the order is \(p\) Br > H > COOH. The general polar effects of both the bromine atom and the carboxyl group are the same, both are electron attracting so that the difference in the behaviour of these two groups may tentatively be ascribed to the electro-metric effect of the bromine atom.

Experimental.

dl-\(\alpha\)-benzyl-n-caproic acid.—Sodium (18.4 grs.) was dissolved in absolute alcohol (225 grs.) and ethyl aceto-acetate (130 grs.) and \(n\)-butyl bromide (110 grs.) added. The mixture was boiled under reflux for 28 hours but was still faintly alkaline; it was acidified with acetic acid and the product worked up in the usual way; yield 78 grams, b.p. 124–7\(^\circ\) C./35 mm. This was converted to the sodium derivative and condensed with benzyl chloride by boiling under reflux for 6 hours. The crude ester obtained was saponified by concentrated caustic potash solution and the acid obtained in the usual way, b.p. 181–2\(^\circ\) C./5 mm. (Found: C, 75.75; H, 8.47; \(C_{13}H_{19}O_2\) requires C, 75.71; H, 8.74%). The silver salt was insoluble in water (Found: Ag, 34.28; \(C_{13}H_{17}O_2Ag\) requires Ag, 34.59%).

dl-\(\alpha\)-benzyl-n-caproamide.—The acid was converted to the chloride by means of thionyl chloride and from the acid chloride the amide was prepared...
by the action of concentrated aqueous ammonia; crystals from boiling water and from dilute alcohol m.p. 97°C. (Found: N, 6.95; C₁₃H₁₉ON requires N, 6.82%). The anilide prepared by the action of aniline on the acid chloride had m.p. 97°C. from aqueous alcohol (Found: N, 4.69%; C₁₃H₂₂ON requires N, 4.98%).

**d-a-benzyl-n-caproic acid.**—The acid (16.48 grams, 0.4 M) was dissolved in benzene and a hot solution of quinine (12.8 grs. 0.2 M) in benzene added. After some time crystals of the quinine salt separated, m.p. 95°C. These were crystallised twice from benzene; m.p. 95°C. 

\[ [\alpha]_D^{\circ} = 9^\circ \pm 96^\circ \] for each crop of crystals. (Found: N, 5.57; C₃₂H₄₂O₄ requires N, 5.28%). The free acid was prepared from the salt and the rotation in benzene solution determined, 

\[ [\alpha]_D^{\circ} + 28^\circ, \quad (M)^{29}_D, + 57.6^\circ \] The acid recovered from the mother liquors of the original benzene solution had

\[ [\alpha]_D^{\circ} = 10.5^\circ \]

**d-a-p-brombenzyl-n-caproic acid.**—This was prepared in the usual way from p-brombenzyl bromide and ethyl a-aceto-n-caproate. The crude ester was saponified by boiling for 24 hours with 50% caustic potash solution. The crude acid was purified by distillation: b.p. 209°C./5 mm., m.p. 62°C. from a mixture of benzene and petrol ether. (Found: Br, 27.58; C₁₃H₁₇O₂Br requires Br, 28.07%). The silver salt was prepared in the usual way (Found: Ag, 27.3%; C₁₃H₁₆O₂BrAg requires Ag, 27.5%). The amide, m.p. 138°C. from alcohol (Found: Br, 28.21; C₁₃H₁₅ONBr requires Br, 28.17%) and the anilide, m.p. 116°C. from aqueous alcohol (Found: Br, 22.53; C₁₉H₂₂ONBr requires Br, 22.22%) were also prepared.

**d-a-p-brombenzyl-n-caproic acid.**—dl-a-p-brombenzyl-n-caproic acid (71.2 grs. 0.25 M) was dissolved in benzene and quinine (40.5 grs. 0.125 M) added gradually to the hot solution. The solution was cooled, ether added and the mixture allowed to stand for some days in a refrigerator. The separated salt was crystallised from aqueous ethyl alcohol until the rotation was constant and the acid isolated. The free acid had 

\[ [\alpha]_D^{\circ} + 40.8^\circ \]

\[ [M]_D^{30} + 116.3^\circ. \]

**dl-a-m-brombenzyl-n-caproic acid.**—This was prepared similarly to the para acid; b.p. 217°C. C./8 mm. (Found: Br, 27.52; C₁₃H₁₇O₂Br requires Br, 28.07%). The silver and barium salts were prepared in the usual way. (Found: Ag, 26.9; C₁₃H₁₆O₂BrAg requires Ag, 27.5%; Ba, 19.54; (C₁₃H₁₆O₂Br)₂Ba requires Ba, 19.48%). The amide crystallised from aqueous alcohol; m.p. 91°C. (Found: Br, 27.80; C₁₃H₁₅ONBr requires Br, 28.17%). The anilide also crystallised from aqueous alcohol; m.p. 119°C. (Found: Br, 22.42; C₁₉H₂₂ONBr requires Br, 22.22%).
d-α-m-brombenzyl-n-caproic acid.—The dl acid was resolved similarly to the benzyl acid. The free acid had $[\alpha]_D^{20} + 20.08^\circ$, $[\beta]_D^{30} + 57^\circ$.

dl-α-p-carboxybenzyl-n-caproic acid.—p-cyan-benzyl chloride was condensed with the sodium derivative of ethyl α-aceto-β-caproate in the usual way. The crude ester was saponified with concentrated caustic potash solution when the nitrile group was at the same time hydrolysed. The free acid was very soluble in acetone, ethyl acetate and chloroform, soluble in ether, benzene, ethyl and methyl alcohols, sparingly soluble in petrol ether; m.p. 160°C. (Found: E (by titration), 127.9; C, 67.33; H, 6.78; C$_{14}$H$_{18}$O$_4$ requires E, 125; C, 67.2; H, 7.2%). The silver salt was prepared. (Found: Ag, 46.99; C$_{14}$H$_{18}$O$_4$Ag$_2$ requires Ag, 46.53%).

dl-α-p-carboxybenzyl-n-caproic acid.—The dl acid was resolved by means of the normal quinine salt. The free acid had $[\alpha]_D^{20} + 5.8^\circ$, $[\beta]_D^{30} + 14.5^\circ$. These results need confirmation.

dl-α-m-carboxybenzyl-n-caproic acid.—This was prepared similarly to the para acid; m.p. 115°C. (Found: equivalent, by silver salt, 125.1; C$_{14}$H$_{18}$O$_4$ requires 125).

dl-α-m-carboxybenzyl-n-caproic acid.—The dl acid was resolved by means of the normal brucine salt. The free acid had $[\alpha]_D^{20} + 9.2^\circ$; $[\beta]_D^{30} + 23.1^\circ$. These figures can only be regarded as approximate.

We have to thank the University of Rangoon for a grant towards the expenses of this investigation which is being continued.

**Summary.**

The following acids have been prepared and resolved: α-benzyl, β-brombenzyl, m-brombenzyl, p-carboxybenzyl, m-carboxybenzyl-n-caproic acids. The molecular rotatory powers have been measured in order to see whether any alternating effect on rotatory power could be detected. It is possible that such an effect exists but the results obtained we only put forward tentatively.