

**258.** *The Different Reaction Velocities of Enantiomers with a Common Optically Active Reagent. Part I. Some New Reactions of *d*- and *l*-Camphor-10-sulphonyl Chlorides.*

By ALFRED S. GALLOWAY and JOHN READ.

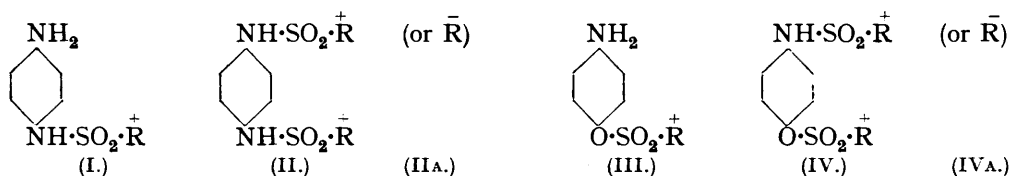
IN the course of work on the stereoisomeric menthylamines, menthols, and *cyclohexanediols*, observations of some interest have been made on the comparative reaction velocities of these substances with certain symmetric reagents (Read and Storey, J., 1930, 2765; Read and Grubb, J., 1934, 1782; Read and Wilson, J., 1935, 1272). Several asymmetric reagents have also been applied in a similar way during these investigations, notably *d*- and *l*-camphor-10-sulphonyl chlorides. Thus, Read and Storey (J., 1930, 2768), in studying the comparative rates of reaction of the *d*- and *l*-rotatory forms of menthylamines, *neomenthylamines*, and *isomenthylamines* with *d*- and *l*-camphor-10-sulphonyl chlorides, found that in all instances the reaction between molecules of opposite optical rotation was more rapid than between the corresponding molecules of similar optical rotation. Moreover, Read and Grubb (J., 1931, 190) observed that *d*-camphor-10-sulphonyl chloride reacted more rapidly with *l*- than with *d*-menthol.

These and other observations suggested a systematic study of several series of such reactions, in an attempt to classify the preferences displayed. Is it possible, for example,

to adduce a sustained and connected series of reactions throughout which a common molecule, or radical, shows a preference in each instance for that form of a second asymmetric molecule having either (1) the same, or (2) the opposite, sense of optical rotation? Can the relative rates of formation of the two diastereoisomeric products of such a reaction be correlated in any way with the comparative physical properties of the two substances? Can the preference be reversed by altering the conditions of the reaction? The researches now inaugurated are designed to explore such ideas, and to throw further light upon related processes of optical resolution.

In the first place it appeared of interest to search for reactions of the general type under notice, in which the molecule of *d*- or *l*-camphor-10-sulphonyl chloride displays a preferential reaction with the form of the second molecule possessing the same sense of optical rotation. Two such reactions are now described. The substances concerned differ in two important respects from those mentioned above. First, the two asymmetric radicals present in the molecule of the final product are separated by the interposition of a benzene ring, instead of being contiguous, as in the earlier examples of the camphor-10-sulphonyl-menthylamines, etc. Secondly, in each instance, the molecule of the reagent presented for reaction with an excess of *dl*-camphor-10-sulphonyl chloride already contains a *d*-camphor-10-sulphonyl radical.

The optically active reagents used were *mono-d-camphor-10-sulphonyl-p-phenylenediamine* (I) and *p-aminophenyl d-camphor-10-sulphonate* (III). The product of the reaction was found to contain in each instance an excess of the substance *D-d*, the mean ratios of *D-d/L-d* being 58 : 42 (II) and 61 : 39 (IV) in the two pairs of experiments described below.



The molecule (II), when the two radicals R are (+) and (−) respectively, becomes symmetric (IIA), and provides an interesting example of internal compensation of the same fundamental type as *d*-bornyl *l*-bornyl fumarate (McKenzie and Abbot, J., 1934, 711).

Upon replacing one ·NH· group by ·O· in this molecule, the two radicals  $\bar{R}$  and  $\bar{R}$  no longer exactly counteract each other's optical rotatory effect, and the new substance (IVA) has  $[\alpha]_D - 2.4^\circ$  in chloroform solution: in this finely balanced yet asymmetric structure the sense of the optical rotation is that of the radical attached to the ·NH· group.

Somewhat similar studies of the interaction of molecules containing the *d*- and *l*-forms of the menthyl and other asymmetric radicals are in progress.

#### EXPERIMENTAL.

*Mono-d-camphor-10-sulphonyl-p-phenylenediamine*.—Upon slowly adding *d*-camphor-10-sulphonyl chloride (80 g.) to a solution of *p*-aminoacetanilide (40 g.) in dry pyridine (100 c.c.), the liquid became deep crimson and heat was evolved. After remaining for 2 days at room temperature, the mixture was poured into dilute hydrochloric acid, and the crimson precipitate was washed with water. The crude *acetylmono-d-camphor-10-sulphonyl-p-phenylenediamine* (97 g.) was decolorised by repeated treatment with norit in boiling alcohol, from which solvent it was eventually obtained in colourless needles, m. p. 136—137°,  $[\alpha]_D + 40.5^\circ$  (*c* 2.0, chloroform) (Found : C, 59.2; H, 6.6.  $C_{15}H_{24}O_4N_2S$  requires C, 59.3; H, 6.6%).

This acetyl derivative (30 g.) was boiled with concentrated hydrochloric acid (150 c.c.) until the products were completely soluble in water (2 hours). The cooled solution was diluted with water (500 c.c.) and neutralised with sodium bicarbonate, the precipitated *mono-d-camphor-10-sulphonyl-p-phenylenediamine* being then washed with water, dried, and recrystallised from pyridine: it formed reddish-brown prisms (14 g.), m. p. 185°,  $[\alpha]_D + 41.1^\circ$  (*c* 2.0, pyridine) (Found : C, 60.0; H, 6.8.  $C_{16}H_{22}O_3N_2S$  requires C, 59.6; H, 6.8%).

*p*-Aminophenyl *d*-Camphor-10-sulphonate.—*p*-Hydroxyacetanilide, m. p. 166° (15 g.), prepared by acetylating commercial *p*-aminophenol by the method of Lumière, Lumière, and Barbier (*Bull. Soc. chim.*, 1905, **33**, 785), was treated as above with *d*-camphor-10-sulphonyl chloride (30 g.) in dry pyridine (75 c.c.). Upon pouring the dark red liquid into 2*N*-hydrochloric acid (600 c.c.), a brown oil separated and gradually solidified to a reddish-brown, crystalline powder. This crude *p*-acetamidophenyl *d*-camphor-10-sulphonate was washed with dilute hydrochloric acid and water, air-dried (36 g.), and decolorised with norit in boiling alcohol, from which it finally crystallised in colourless leaflets (30 g.), m. p. 79°,  $[\alpha]_D + 34.1^\circ$  (*c* 2.0, chloroform) (Found: C, 58.8; H, 6.1.  $C_{18}H_{22}O_5NS$  requires C, 59.1; H, 6.3%).

This acetyl derivative (18 g.) was boiled for an hour with concentrated hydrochloric acid (80 c.c.). The cooled, diluted solution was filtered and rendered slightly alkaline with dilute sodium hydroxide solution in presence of ice. The dirty and somewhat oily precipitate was collected on an asbestos pad and clarified in boiling alcohol (50 c.c.) with successive quantities of norit. Upon dilution with water (10 c.c.), the hot filtered solution deposited colourless *p*-aminophenyl *d*-camphor-10-sulphonate (10 g.) in magnificent, long, straw-like crystals, m. p. 102–103°,  $[\alpha]_D + 42.3^\circ$  (*c* 2.0, chloroform) (Found: C, 59.5; H, 6.6.  $C_{16}H_{21}O_4NS$  requires C, 59.4; H, 6.5%).

*Comparative Reaction Velocities of d- and l-Camphor-10-sulphonyl Chlorides with Mono-d-camphor-10-sulphonyl-p-phenylenediamine.*—The two pure reference compounds were prepared by the interaction of mono-*d*-camphor-10-sulphonyl-*p*-phenylenediamine (1 g.) and *d*- or *l*-camphor-10-sulphonyl chloride (1 g.) in dry pyridine (5 c.c.). The solution was kept at room temperature over-night and poured into an excess of dilute hydrochloric acid. The resulting crimson solid was washed with water, dried at 100°, and dissolved in chloroform. The solution was decolorised by boiling under reflux with several quantities of norit. Crystallisation of the product of the first reaction from chloroform–light petroleum gave colourless needles of *di-d-camphor-10-sulphonyl-p-phenylenediamine*, m. p. 188°,  $[\alpha]_D + 52.3^\circ$  (*c* 2.0, pyridine) (Found: C, 57.9; H, 6.8.  $C_{26}H_{36}O_8N_2S_2$  requires C, 58.2; H, 6.8%). Similarly, the second reaction yielded *d-camphor-10-sulphonyl-l-camphor-10-sulphonyl-p-phenylenediamine*, m. p. 206°,  $[\alpha]_D \pm 0.0^\circ$  (*c* 2.0, pyridine) (Found: C, 58.0; H, 6.7%).

A known amount (4.5582 g. and 4.3326 g. in two separate experiments) of *dl*-camphor-10-sulphonyl chloride was dissolved in pure dry pyridine in a small methylating flask contained in a thermostat at 31.0°, and the solution was stirred mechanically. When the temperature was constant at 31.0°, considerably less than 1 mol. of mono-*d*-camphor-10-sulphonyl-*p*-phenylenediamine dissolved in dry pyridine was run slowly into the flask from a burette. After 3 hours' further stirring, the contents of the flask were transferred to an excess of dilute hydrochloric acid, and the mixture was kept over-night. The precipitate was then collected, washed well with dilute hydrochloric acid and with water, drained with suction, and dried at 100°. The solution of this product in chloroform was decolorised by boiling it under reflux with several portions of animal charcoal; each portion of spent charcoal was well washed with chloroform, and the united filtrate and washings were treated anew. Upon finally distilling away the chloroform, a colourless residue was obtained, of which the weight and value of  $[\alpha]_D$  in chloroform (*c* 2.0) were noted (1.7086 g., + 29.8°; 1.5179 g., + 31.0°).

The composition of this reaction product, calculated from its optical rotatory power, in the two closely similar experiments indicated above, was (1) 57% and 43%, (2) 59% and 41%, of the compounds *D-d* and *L-d*, respectively. Hence *d*-camphor-10-sulphonyl chloride reacted more rapidly than its enantiomorphous *l*-form with mono-*d*-camphor-10-sulphonyl-*p*-phenylenediamine, under the conditions adopted.

*Comparative Reaction Velocities of d- and l-Camphor-10-sulphonyl Chlorides with p-Aminophenyl d-Camphor-10-sulphonate.*—The reference compounds were prepared similarly to the two di-derivatives of *p*-phenylenediamine described above. *p-d-Camphor-10-sulphonamidophenyl d-camphor-10-sulphonate* crystallised from methyl alcohol in rosettes of colourless needles, m. p. 133°,  $[\alpha]_D + 69.9^\circ$  (*c* 2.0, chloroform) (Found: C, 57.7; H, 6.6.  $C_{26}H_{35}O_7NS_2$  requires C, 58.1; H, 6.5%); and the *l*-ester had m. p. 135°,  $[\alpha]_D - 2.4^\circ$  (*c* 2.0, chloroform) (Found: C, 57.9; H, 6.6%).

An excess of *dl*-camphor-10-sulphonyl chloride (4.6936 g. and 4.4342 g. in two separate experiments) was treated in dry pyridine, as described above, with *p*-aminophenyl *d*-camphor-10-sulphonate. The mixed product was isolated in the usual manner, and the weight and value of  $[\alpha]_D$  in chloroform (*c* 2.0) were noted (2.1522 g., + 41.2°; 1.9134 g., + 42.6°). The composition of the reaction product in the two experiments was (1) 60% and 40%, (2) 62% and 38%, of the compounds *D-d* and *L-d*, respectively. Hence, as in the preceding example, *d*-camphor-

10-sulphonyl chloride reacted more rapidly than its enantiomer with *p*-aminophenyl *d*-camphor-10-sulphonate.

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THE UNIVERSITY, ST. ANDREWS.

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