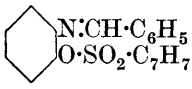
CCLVII.—*The Migration of Acyl Groups in* o-*Aminophenols.*

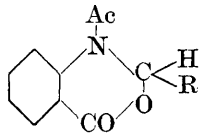
By FRANK BELL.

SINCE the acetyl derivative of *o*-benzylideneaminophenol on hydrolysis gives 2-hydroxyacetanilide (Bell and Kenyon, J., 1926, 1893) it appeared possible that this type of reaction might be utilised to throw light on the migration of acyl groups in *o*-aminophenols (see, *inter alia*, Raiford and Couture, *J. Amer. Chem. Soc.*, 1924, **46**, 2305; Raiford and Lankelma, *ibid.*, 1925, **47**, 1111). An attempt was made to prepare suitable acyl derivatives by interaction of *o*-benzylideneaminophenol with acid chlorides in pyridine solution, but the only isolable product with acetyl, benzoyl, α-naphthoyl, or β-naphthoyl chloride was the corresponding *N*-acyl-*o*-aminophenol. When, however, *p*-toluenesulphonyl chloride was used there was produced a mixture of two isomeric substances. One of these was readily hydrolysed to give 2-*p*-toluenesulphonoxyaniline, from which it could be regained by interaction of this amine with benzaldehyde in alcoholic solution; it must therefore possess the

constitution (I). The other, less soluble, higher-melting isomeride on hydrolysis gave 2-hydroxy-*p*-toluenesulphonanilide, which



(I.)



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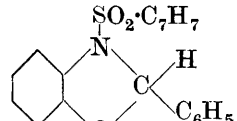
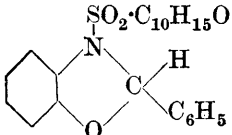


(III.)

indicates that the *p*-toluenesulphonyl residue is already present on the nitrogen atom. Ekeley and his co-workers (*J. Amer. Chem. Soc.*, 1912, **34**, 361; 1913, **35**, 282; 1914, **36**, 603; 1915, **37**, 582; 1922, **44**, 2655) have shown that benzylideneanthranilic acids on treatment with acetic anhydride yield dihydrobenzoxazones of the general formula (II). By analogy, the *N*-*p*-toluenesulphonyl derivative obtained above is probably 2-p-*toluenesulphonyl*-1-*phenyl*-*dihydrobenzoxazole* (III), in which case it contains an asymmetric



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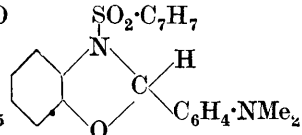

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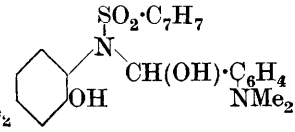
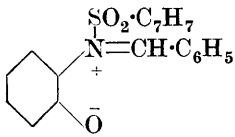


(VI.)

carbon atom. Consequently the corresponding camphorsulphonyl derivative (IV) should be separable into diastereoisomerides, whilst the *p*-dimethylaminobenzylidene analogue (V) should be capable of resolution by combination with optically active acids. Attempts to prepare compound (IV) resulted in the production of viscous gums, whilst compound (V) in contact with acid underwent addition of water to give (VI) (compare Dimroth and Zöppritz, *Ber.*, 1902, **35**, 988). Consequently, conclusive proof of the correctness of the benzoxazole structure is lacking, but it is regarded as more probable



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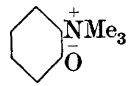
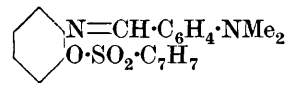


(VIII.)



(IX.)

than the possible alternative of inner ammonium-salt formation (VII), analogous to that in the anhydride of 2-hydroxyphenyltrimethylammonium hydroxide (VIII) described by Griess (*Ber.*, 1880, **13**, 249). The only compound which could be isolated from a pyridine solution of molecular quantities of *p*-benzylideneaminophenol and *p*-toluenesulphonyl chloride was the *O*-*p*-toluene-

sulphonyl derivative. Unfortunately, it was not found possible to prepare *m*-benzylideneaminophenol because *m*-aminophenol reacted very readily with benzaldehyde to give high-melting products (triphenylmethane derivatives ?).

The compounds prepared in the course of these experiments were suitable for an extension of the work of Raiford (*loc. cit.*) on the migration of groups in diacylated-*o*-aminophenols, and the following results were obtained. 2-*Acetoxy*-α-*naphthanilide* and 2-α-*naphthoxyacetanilide* were distinct substances although both on hydrolysis gave 2-hydroxy-α-naphthanilide. This is of interest because Raiford and Lankelma have shown that 3-chloro-5-acetamido-*p*-cresol with α-naphthoyl chloride gives the same compound as that obtained by the interaction of 3-chloro-5-α-naphthamido-*p*-cresol with acetic anhydride. In the first case migration only occurs during hydrolysis, whilst in the second it occurs during acylation. Similarly, 2-*benzoxy*-α-*naphthanilide* and 2-α-*naphthoxybenzanilide* were clearly defined substances which both gave 2-hydroxy-α-naphthanilide on hydrolysis. Next, 2-p-*toluenesulphonoxyacetanilide* was distinct from 2-*acetoxy*-p-*toluenesulphonanilide*, and the first on hydrolysis gave pure 2-hydroxyacetanilide and the second pure 2-hydroxy-*p*-toluenesulphonanilide. This normal hydrolysis (inhibition of migration) was obtained with the corresponding α- and β-naphthoyl derivatives. Moreover, 2-d-*camphorsulphonoxyacetanilide* was easily hydrolysed to give pure 2-hydroxyacetanilide. These experiments clearly indicate the marked influence of substituents in determining the migration of acyl groups, and also the dependence of migration on some peculiarity of the ·O·CO· link which is absent from the ·O·SO_2· link. Both of these points will be the subject of a more systematic investigation.

Experimental.

Reduction of 2-*Nitrophenyl* p-*Toluenesulphonate.*—To this compound (20 g.) in alcohol (100 c.c.) was added stannous chloride (50 g.) in concentrated hydrochloric acid (80 c.c.), and the reaction completed by warming on a steam-bath for ½ hour. To the cold solution was added sodium hydroxide (about 80 g. dissolved in a little water), the liberated base was extracted with ether, the extract dried over sodium sulphate, evaporated, and the residue crystallised from alcohol. 2-Aminophenyl *p*-toluenesulphonate, m. p. 102°, was obtained in 75% yield, whilst from the mother-liquor was isolated a small amount of 5(?)-*chloro*-2-*aminophenyl* p-*toluenesulphonate*, stout needles, m. p. 112° (Found : C, 52·2; H, 3·7. $C_{13}H_{12}O_3NClS$ requires C, 52·4; H, 4·0%). With acetic anhydride this readily gave 5(?)-*chloro*-2-*acetamidophenyl* p-*toluenesulphonate* as colourless

cubes, m. p. 168° (Found : C, 52·7; H, 4·2. $C_{15}H_{14}O_4NClS$ requires C, 53·0; H, 4·1%).

4-Aminophenyl *p*-toluenesulphonate, m. p. 145°, and 3-*aminophenyl* p-*toluenesulphonate*, large prisms, m. p. 98° (Found : C, 59·5; H, 5·1. $C_{13}H_{13}O_3NS$ requires C, 59·3; H, 5·0%), were obtained from the corresponding nitro-compounds by the same process. 3-*Nitrophenyl* p-*toluenesulphonate*, obtained by interaction of *m*-nitrophenol and *p*-toluenesulphonyl chloride in pyridine solution, crystallised from alcohol in large prisms, m. p. 112° (Found : C, 53·2; H, 3·9. $C_{13}H_{11}O_5NS$ requires C, 53·2; H, 3·8%).

The following benzylidene derivatives were obtained by interaction of the above bases with benzaldehyde in alcoholic solution: 2-*Benzylideneaminophenyl* p-*toluenesulphonate*, needles, m. p. 98° (Found : C, 68·1; H, 4·9. $C_{20}H_{17}O_3NS$ requires C, 68·4; H, 4·9%); 3-*benzylidene* isomeride, stout needles, m. p. 90° (Found : C, 68·0; H, 5·1%); 4-*benzylidene* isomeride, needles, m. p. 165°, rather sparingly soluble in alcohol (Found : C, 68·3; H, 4·8%).

Interaction of o-*Benzylideneaminophenol with Acid Chlorides.*—Molecular amounts were dissolved in pyridine and the solution, after standing for 12 hours, was poured into water.

(1) p-*Toluenesulphonyl chloride*. The precipitated oil was separated, desiccated, and dissolved in hot benzene. On cooling, 2-p-*toluenesulphonyl*-1-*phenyldihydrobenzoxazole* (III) separated in long needles, m. p. 138° (Found : C, 68·3; H, 5·0. $C_{20}H_{17}O_3NS$ requires C, 68·4; H, 4·9%). The mother-liquor after concentration and dilution with petrol furnished 2-benzylideneaminophenyl *p*-toluenesulphonate (above). This constitution was confirmed by hydrolysis, for when boiled with water for 4 hours the compound lost benzaldehyde and gave pure 2-aminophenyl *p*-toluenesulphonate. The higher-melting compound was neutral, and stable to warm dilute acids, but on being warmed with alcoholic hydrogen chloride for ½ hour it was converted into 2-hydroxy-*p*-toluenesulphonanilide, which was also prepared, m. p. 139°, by interaction of *o*-aminophenol and *p*-toluenesulphonyl chloride (1 mol.) in pyridine solution.

(2) *Acetyl chloride*. The precipitated oil was rubbed with alcohol, and 2-hydroxyacetanilide, m. p. 205°, was isolated in 25% yield.

(3) *Benzoyl chloride* [compare (2)]. 2-Hydroxybenzanilide, m. p. 167°, was isolated in about 50% yield.

(4) α-*Naphthoyl chloride* [compare (2)]. 2-*Hydroxy*-α-*naphthanilide*, m. p. 194°, was isolated in 75% yield, and its constitution was confirmed by its preparation from *o*-aminophenol and α-naphthoyl chloride (1 mol.) in pyridine solution (Found : 77·5; H, 5·0. $C_{17}H_{13}O_2N$ requires C, 77·6; H, 4·9%). The α-naphthoyl chloride was obtained by interaction of α-naphthoic acid and thionyl

chloride, and after distillation (b. p. 163°/10 mm.) rapidly set to a colourless solid, m. p. 26°. This appears to be the first time it has been obtained in a solid condition.

(5) β-*Naphthoyl chloride* [compare (2)]. 2-*Hydroxy*-β-*naphthanilide*, m. p. 194°, was isolated in 75% yield; it depressed the m. p. of the α-isomeride above, and was alternatively prepared as follows. A solution of β-naphthoyl chloride (3·5 g.) and *o*-aminophenol (2·0 g.) in pyridine was left over-night and then poured into water. The resultant gum was solidified by rubbing with alcohol, separated (3·6 g.), and boiled with chloroform; the naphthanilide (1·3 g.) was left undissolved (Found: C, 77·8; H, 4·9. $C_{17}H_{13}O_2N$ required C, 77·6; H, 4·9%). The chloroform solution was evaporated and the residue after crystallisation from alcohol gave 2-β-*naphthoxy*-β-*naphthanilide*, m. p. 150° (Found: C, 80·7; H, 4·5. $C_{28}H_{19}O_3N$ requires C, 80·6; H, 4·6%). β-Naphthoyl chloride, from the acid and thionyl chloride, separated from benzene–light petroleum as a crystalline powder, m. p. 51°.

2-p-*Toluenesulphonyl*-1-*dimethylaminophenyldihydrobenzoxazole* (V).—A pyridine solution of *p*-dimethylaminobenzylidene-*o*-aminophenol (5 g.) and *p*-toluenesulphonyl chloride (4 g.) was left overnight and then poured into water. The sticky precipitate was filtered off, dried on a porous plate, and boiled with alcohol. The insoluble *substance* (m. p. *ca.* 180°) after recrystallisation from alcohol formed needles, m. p. 186° (3·3 g.) (Found: C, 67·2; H, 5·6. $C_{22}H_{22}O_3N_2S$ requires C, 66·9; H, 5·6%). 2-Hydroxy-*p*-toluenesulphonanilide was the only compound isolated from the mother-liquor. To a solution of *d*-camphorsulphonic acid (1·7 g.) in alcohol was added compound (V) (2·8 g.). On dilution with water there were obtained needles of the N-p-*toluenesulphonyl* derivative of *p*-dimethylaminobenzaldehyde-*o*-hydroxyaniline [*o*-(*p*-dimethylamino-ω-hydroxybenzyl)aminophenol] (VI), m. p. 92° (2·9 g.), optically inactive and unchanged in m. p. after recrystallisation from aqueous alcohol or benzene (Found: C, 64·0; H, 5·6. $C_{22}H_{24}O_4N_2S$ requires C, 64·1; H, 5·8%). This compound rapidly dissolved in sodium hydroxide solution but was reprecipitated as 2-hydroxy-*p*-toluenesulphonanilide, m. p. 139°. The *d*-camphorsulphonic acid used in the above experiment could be replaced by acetic acid without affecting the result.

2-p-*Dimethylaminobenzylideneaminophenyl* p-*toluenesulphonate* (IX), prepared by condensation of *p*-dimethylaminobenzaldehyde and 2-aminophenyl *p*-toluenesulphonate in alcohol solution, formed pale yellow needles, m. p. 135° (Found: C, 67·2; H, 5·7. $C_{22}H_{22}O_3N_2S$ requires C, 66·9; H, 5·6%).

2-p-*Toluenesulphonoxy*-α-*naphthanilide*, prepared by interaction

of either (*a*) 2-hydroxy-α-naphthanilide and *p*-toluenesulphonyl chloride or (*b*) 2-*p*-toluenesulphonoxyaniline and α-naphthoyl chloride in pyridine solution, crystallised from alcohol in needles, m. p. 125° (Found : C, 69·0; H, 4·5. $C_{24}H_{19}O_4NS$ requires C, 69·1; H, 4·6%). It was hydrolysed by boiling under reflux with 5*N*-sodium hydroxide and gave 2-hydroxy-α-naphthanilide.

2-p-*Toluenesulphonoxy*-β-*naphthanilide*, prepared as above, crystallised from acetic acid in needles, m. p. 125° (Found : C, 69·2; H, 4·4%), depressed on admixture with the α-isomeride. On hydrolysis it furnished 2-hydroxy-β-naphthanilide.

2-*Acetoxy*-p-*toluenesulphonanilide*, prepared by warming 2-hydroxy-*p*-toluenesulphonanilide with acetic anhydride, crystallised from acetic acid in needles, m. p. 123° (Found : C, 58·6; H, 4·9. $C_{15}H_{15}O_4NS$ requires C, 59·0; H, 4·9%). It was rapidly hydrolysed by warm 3*N*-sodium hydroxide to give 2-hydroxy-*p*-toluenesulphonanilide.

2-p-*Toluenesulphonoxyacetanilide*, prepared (*a*) by solution of 2-*p*-toluenesulphonoxyaniline in acetic anhydride or (*b*) from 2-hydroxyacetanilide and *p*-toluenesulphonyl chloride, crystallised from acetic acid in prisms, m. p. 134° (Found : C, 58·6; H, 5·0%). On being warmed with 3*N*-sodium hydroxide for several hours, it gave 2-hydroxyacetanilide.

2-p-*Toluenesulphonoxy*-p-*toluenesulphonanilide*, prepared by interaction of (*a*) 2-*p*-toluenesulphonoxyaniline or (*b*) 2-hydroxy-*p*-toluenesulphonanilide with *p*-toluenesulphonyl chloride in pyridine solution, crystallised from acetic acid in large prisms, m. p. 143° (Found : C, 57·6; H, 4·2. $C_{20}H_{19}O_5NS_2$ requires C, 57·3; H, 4·6%).

2-*Acetoxy*-α-*naphthanilide*, prepared by solution of 2-hydroxy-α-naphthanilide in acetic anhydride, crystallised from aqueous acetic acid or chloroform–light petroleum in long needles, m. p. 153° (Found : C, 74·4; H, 4·9. $C_{19}H_{15}O_3N$ requires C, 74·7; H, 4·9%). It was equally readily obtained by use of acetyl chloride in pyridine as the acetylating agent. Hydrolysis with sodium hydroxide readily gave 2-hydroxy-α-naphthanilide.

2-α-*Naphthoxyacetanilide*, prepared by interaction of 2-hydroxyacetanilide and α-naphthoyl chloride in pyridine solution, crystallised from aqueous acetic acid in needles, m. p. 139° (Found : C, 75·0; H, 4·9%). Hydrolysed as above, it gave pure 2-hydroxy-α-naphthanilide.

2-*Benzoxy*-α-*naphthanilide*, prepared by interaction of 2-hydroxy-α-naphthanilide and benzoyl chloride in pyridine solution, crystallised from acetic acid in needles, m. p. 176° (Found : C, 78·2; H, 4·7. $C_{24}H_{17}O_3N$ requires C, 78·5; H, 4·6%). Hydrolysis gave 2-hydroxy-α-naphthanilide.

2-α-*Naphthoxybenzanilide*, prepared by interaction of 2-hydroxybenzanilide and α-naphthoyl chloride in pyridine solution, crystallised from acetic acid in needles, m. p. 170° (Found : C, 78·1; H, 4·8%). Hydrolysis gave 2-hydroxy-α-naphthanilide.

2-*Acetoxy*-β-*naphthanilide* (compare α-isomeride) formed needles, m. p. 149° (Found : C, 75·2; H, 5·1%). Hydrolysis gave 2-hydroxy-β-naphthanilide.

2-d-*Camphorsulphonoxyacetanilide*, prepared by interaction of 2-hydroxyacetanilide and *d*-camphorsulphonyl chloride in pyridine solution, crystallised from benzene in large needles, m. p. 133°, $[\alpha]_{5461}$ + 60·9° in acetone ($c = 2·53$) (Found : C, 59·5; H, 6·2. $C_{18}H_{23}O_5NS$ requires C, 59·2; H, 6·3%). It was easily hydrolysed by sodium hydroxide to give 2-hydroxyacetanilide. *o*-Aminophenol with *d*-camphorsulphonyl chloride (1 mol.) in pyridine gave an uncrystallisable gum.

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