CCLXXXIV.—*Direct Meta-substitution in the Toluene Nucleus.*

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REACTIONS which result in the entrance of a substituent into the nucleus of the toluene molecule are known to take place normally at the ortho- and para-positions. Results obtained when the Friedel–Crafts reaction is carried out with toluene and various alkyl halides present problems of interest when considered in relation to those obtained from toluene and acyl halides in presence of aluminium chloride, since the nucleus is attacked in the meta- and the para-position by the former and in the para-position by the latter.

An examination of the literature on the subject, however, discloses a number of discrepancies, since Kelbe and Pfeiffer (*Ber.*, 1886, **19**, 1724) reported that *iso*butyl bromide gave with toluene, *m*- and *p*-*iso*butyltoluenes,* whilst Baur (*Ber.*, 1891, **24**, 2833) said that *tert.*-butyl chloride and *iso*butyl bromide gave only *m*-*tert.*-butyltoluene. According to Bialobrzeski (*Ber.*, 1897, **30**, 1773), *tert.*-butyl chloride and toluene with ferric chloride as catalyst produce *p*-*tert.*-butyltoluene.

There is not the same contradiction in the experiments reported on the reaction between acetyl chloride and toluene, which in presence of aluminium chloride results, according to Verley (*Bull. Soc. chim.*, 1897, **17**, 909) and Sorge (*Ber.*, 1902, **35**, 1069), in the formation of *p*-tolyl methyl ketone.

All these experiments were repeated by the authors with a view to discover the quantities of each isomeride produced in the reactions. It was found that each of the alkyl halides reacts with toluene in such a way that both *m*- and *p*-*tert.*-butyltoluenes are formed in a

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* These compounds are really *m*- and *p*-*tert.*-butyltoluenes (compare Shoesmith and Mackie, J., 1928, 2336).

ratio of 65—70 parts of the former to 30—35 of the latter, whether aluminium chloride or ferric chloride is used as catalyst. Hence Bialobrzeski had failed to observe the large quantity of meta-compound produced. It is also noteworthy that Baur had overlooked the quantity of *p*-isomeride formed in presence of aluminium chloride. The results of Verley and Sorge were confirmed.

A reaction between *n*-butyl chloride and toluene in presence of aluminium chloride had not hitherto been carried out. Schramm (*Monatsh.*, 1888, **9**, 621) and Estreicher (*Ber.*, 1900, **33**, 439) have concluded from somewhat unsatisfactory observations that *n*-butyl chloride reacts with benzene to give *sec.*-butylbenzene. It has now been observed that the halide gives with toluene *m*- and *p*-*sec.*-butyltoluenes in a ratio of approximately 75 : 25 respectively. The constitution of these compounds was proved by converting them to sulphonanilides, which were identified with those prepared from authentic specimens of *m*- and *p*-*sec.*-butyltoluenes. Thus, a *sec.*-butyl and not an *n*-butyl radical enters the toluene molecule, which is comparable with the entrance of a *tert.*-butyl radical when the reaction is carried out with an *iso*butyl halide (Baur, *loc. cit.*).

The *sec.*-butyltoluenes were synthesised by the following series of reactions. The Grignard reagent from *m* (or *p*)-bromotoluene and magnesium reacted with methyl ethyl ketone to give an unstable tertiary alcohol, *m*- or *p*-tolylmethylethylcarbinol (I) which with acetic anhydride was converted into β-*m* (or *p*)-tolyl-Δ^{β}-butene (II). The *m*-isomeride was reduced with sodium and ethyl alcohol, and the *p*- with hydrogen iodide and red phosphorus, to the corresponding *sec.*-butyltoluene :

$$\underset{\text{(I.)}}{C_6H_4Me{\cdot}C(OH)MeEt} \xrightarrow{Ac_2O} \underset{\text{(II.)}}{C_6H_4Me{\cdot}CMe{:}CHMe} \xrightarrow{\text{reduction}} C_6H_4Me{\cdot}CHMeEt.$$

These compounds were in turn converted to the *barium sulphonates* and thence to the *sulphonanilides* through the acid chlorides (it was not necessary to determine the position of the sulphonanilido-radical).

EXPERIMENTAL.

The aluminium chloride used during these investigations was a yellow product obtained by subliming commercial aluminium chloride from a wide combustion tube in a current of dry hydrogen chloride.

The Reaction between tert.*-Butyl Chloride and Toluene.*—(a) *In presence of aluminium chloride.* Toluene (125 g. ; b. p. 110—111°), distilled over sodium, was stirred with aluminium chloride (10 g.) in a flask from which moisture was excluded, and cooled to 0°. *tert.*-Butyl chloride (25 g.) was added from a tap-funnel at such a rate that the temperature was maintained at 0—5°. After the addition of the chloride (1 hour) the stirring was continued for a further 4 hours, whereupon the reaction mixture was poured into water, the toluene layer separated, washed first with caustic soda solution and then with water, and dried over calcium chloride. The toluene was removed by distillation and the reaction product fractionated, the portion of b. p. 180—197° being collected separately. This proved to be a mixture (yield 46%) of *m*- and *p*-*tert*.-butyltoluenes, which were separated as follows.

5 G. of the product were vigorously agitated at the ordinary temperature with concentrated sulphuric acid (8 c.c.); heat was developed, and after 4 hours the mixture was cooled, poured into water, and unchanged oil extracted with ether. On removal of the ether, 1·5 g. (afterwards proved to be *p*-isomeride) of hydrocarbon remained. From the solution of the sulphonic acid, 3 g. (afterwards proved to be *m*-compound) were recovered by adding an equal volume of concentrated sulphuric acid and distilling the hydrocarbon in a current of superheated steam.

The reaction products were identified by their oxidation with nitric acid (*d* 1·2) to the corresponding *tert*.-butylbenzoic acids. From the acid-soluble portion, the oxidation product had m. p. 126·5—127°, which proved that the main reaction product was *m*-*tert*.-butyltoluene; the insoluble portion yielded on oxidation an acid of m. p. 162—163°, proving the hydrocarbon to be *p*-*tert*.-butyltoluene (compare Baur, *loc. cit.*).

A second method of separation employed was slightly more accurate but more laborious, and depended on a marked difference in the solubilities of the *barium sulphonates* of the hydrocarbons. The mixture of *tert*.-butyltoluenes (18·5 g.) was vigorously agitated with 37 c.c. of concentrated sulphuric acid for ½ hour, and dissolution of the oil was completed by heating the mixture on the water-bath, after which it was poured into water, and heated in a porcelain basin until almost boiling. Barium carbonate was added, and the neutral aqueous solution filtered from the solid while still hot; the latter was extracted with 5 litres of boiling water in two portions, and the solid separated. The liquid was mixed with the original filtrate and the water evaporated. A salt began to crystallise when the volume of the solution had been reduced to about 5 litres, and when only one litre of solution remained, the solid which had crystallised was filtered off. The solution was then evaporated to 150—200 c.c. and the very small quantity of salt which had crystallised was again removed. This, together with that already obtained, weighed 23 g. [Found: Ba, 23·0. $(C_{11}H_{15}SO_3)_2Ba$ requires Ba, 23·2%]. No further solid separated until the filtrate was evaporated to dryness, and 12·5 g. of the more soluble barium sulphonate were recovered (Found : Ba, 23·4%). The difference in the solubilities of the two sulphonates was clearly marked and a good separation was obtained. The weight of barium salts obtained denoted the presence of *m*- and *p*-*tert.*-butyltoluenes in a ratio of 62 : 38 respectively.

The hydrocarbons were recovered from the two barium sulphonates by the passage of a current of superheated steam through a mixture of the salt with hot sulphuric acid (50%).

The more insoluble salt yielded the theoretical quantity of *m*-*tert.*-butyltoluene (b. p. 188·5—190°) whilst the more soluble gave a 60% yield of *p*-*tert.*-butyltoluene. The constitution of the hydrocarbons was proved by oxidation to the *tert.*-butylbenzoic acids.

(b) *In presence of ferric chloride.* This reaction was carried out in the same way as that in (a), and the yield of monosubstituted derivatives was 75% of that expected. 30 G. on sulphonation yielded 20 g. (70% of the total) of *m*-*tert.*-butyltoluene and 8·5 g. (28%) of *p*-*tert.*-butyltoluene, identified by oxidation to the corresponding acids. By the barium sulphonate method of separation, the proportions were discovered to be $m : p = 67 : 33$.

(c) *In presence of nitrobenzene–aluminium chloride.* The aluminium chloride in this experiment was first dissolved in twice its weight of nitrobenzene and added to the reaction mixture. The mode of operation differed from that employed in the reaction with aluminium chloride alone since it was necessary to remove the nitrobenzene from the reaction product by reduction to aniline which was eliminated with acid. The yield of hydrocarbons was 70% of that expected, and the sulphonation method of separation showed the ratio of *m*- to *p*-*tert.*-butyltoluene to be 67 : 33.

Reaction between iso*Butyl Bromide and Toluene in Presence of Aluminium Chloride.*—The products of the reaction were obtained in a yield of 30% and consisted of *m*- and *p*-*tert.*-butyltoluenes, the latter forming 30% of the total, but the separation was not so satisfactory in this case.

n-*Butyl Chloride and Toluene in Presence of Aluminium Chloride.*—The reaction was carried out as in previous cases and from the product, a liquid, afterwards proved to be a mixture of *m*- and *p*-*sec.*-butyltoluenes, distilling chiefly at 198—202° (yield 45%), was obtained. When the mixture was sulphonated at room temperature, 25% of it remained unchanged (*p*-compound) and was separated; b. p. 200—203° (Found : C, 89·0; H, 10·9. Calc. for $C_{11}H_{16}$: C, 89·1; H, 10·9%). The hydrocarbon recovered from the solution of the sulphonic acid (*m*-compound) had b. p. 197—200° (Found : C, 89·2; H, 10·9%). These fractions were respectively oxidised to tere- and *iso*-phthalic acids, in turn identified by conversion to their dimethyl esters, m. p.'s 140·5—141° and 63—64°, respectively.

Synthesis of m- *and* p-sec.-*Butyltoluenes.*—m- *and* p-*Tolylmethylethylcarbinols.* Methyl ethyl ketone (1 mol.) in dry ether was slowly added to an ethereal solution of *m*- or *p*-tolyl magnesium bromide (1 mol.). After 12 hours the reaction mixture was treated in the usual way with ice and dilute hydrochloric acid, the ethereal layer separated, and dried over sodium sulphate. During removal of the ether, drops of water separated, probably due to the decomposition of the tertiary alcohol to the unsaturated hydrocarbon, β-*m* (or *p*)-tolyl-Δ^{β}-butene. The reaction product was distilled under reduced pressure and converted to the butene by boiling for 3 hours with 2½ times its weight of acetic anhydride. The mixture was poured into water, and the oily layer separated, washed first with aqueous caustic soda then with water, and dried. The oil was fractionated in a vacuum and the fraction of (*m*-) b. p. 90—94°/12 mm. or (*p*-) b. p. 90—94°/10 mm. was collected separately. (Rupe and Burgin give b. p. 93·5—94°/10 mm. for the *p*-compound.)

m-sec.-*Butyltoluene.* β-*m*-Tolyl-Δ^{β}-butene was reduced in solution in 10 times its volume of absolute alcohol by addition of its own weight of sodium in small portions so that the mixture was maintained at the boiling point. The product was poured into water, and the oil extracted with ether. After the removal of the latter, the oily *m-sec.*-butyltoluene was distilled, and the fraction of b. p. 194—198° collected.

p-sec.-*Butyltoluene.* Reduction of the corresponding butene with sodium and alcohol or sodium amalgam did not proceed to completion. β-*p*-Tolyl-Δ^{β}-butene (3 parts), hydriodic acid (b. p. 127°; 12 parts), and red phosphorus (1 part) were heated to the boiling point, whereupon a vigorous reaction took place and some free iodine was liberated. After boiling for some time, the mixture was poured into water, the phosphorus filtered off and washed with ether, and the washings added to an ethereal extract of the filtrate, the whole being washed with aqueous caustic soda, dried, and the ether removed. The residual oil was distilled over sodium to remove iodine, and *p-sec.*-butyltoluene, b. p. 195—197°, collected (Wallach, *Annalen*, 1917, **414**, 211, gives b. p. 196—197°).

Sulphonanilides of the Synthetic sec.-*Butyltoluenes and of those obtained by the Friedel–Crafts Reaction.*—The hydrocarbon (1 part) was vigorously agitated with concentrated sulphuric acid (3 parts) at the ordinary temperature in the case of the *m*-compound, and at 90° in the case of the *p*-compound; the sulphonated hydrocarbon was converted to the barium sulphonate, which was converted by phosphorus pentachloride into the sulphonyl chloride and hence by excess of aniline into the sulphonanilide. The constants of the various derivatives are given below, (S) denoting those obtained synthetically and (F) those from the Friedel–Crafts reaction :

m-sec.-Butyltoluene-(?)-sulphonyl chloride (F), b. p. 160—164°/9 mm. (Found : Cl, 14·1. $C_{11}H_{15}O_2SCl$ requires Cl, 14·4%) ; m-sec.-*butyltoluene-(?)-sulphonyl chloride* (S), b. p. 164—165°/11 mm. (Found : Cl, 14·3%).

p-sec.-Butyltoluene-(?)-sulphonyl chloride (F), b. p. 166—170°/14 mm. (Found : Cl, 14·4%) ; p-sec.-*butyltoluene-(?)-sulphonyl chloride* (S), b. p. 162—164°/12 mm. (Found : Cl, 14·2%).

m-sec.-Butyltoluene-(?)-sulphonanilide (F), m. p. 119·5—120° (Found : N, 4·45, 4·52. $C_{17}H_{21}O_2NS$ requires N, 4·62%) ; m-sec.-*butyltoluene-(?)-sulphonanilide* (S), m. p. 120·5—121°. A mixed m. p. of these compounds, which both crystallised in rhombic prisms from aqueous alcohol, was 119·5—120·5°.

p-sec.-Butyltoluene-(?)-sulphonanilide (F), m. p. 123·5—124·5° (Found : N, 4·54, 4·55%) ; p-sec.-*butyltoluene-(?)-sulphonanilide* (S), m. p. 124·5—125°. A mixed m. p. of these compounds, which also crystallised in rhombic prisms from aqueous alcohol, was 123·5—124·5°.

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