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CYCLODEHYDRATION OF DIPHENYL-TRIFLUOROMETHYL-CARBINOLS

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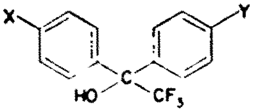
Abstract—The halochromic product from di-(*p*-fluorophenyl)-trifluoromethylcarbinol and sulphuric acid gives with ethyl mercaptan 3-ethylthio-6 fluoro-9-trifluoromethylfluorene. Analogous reactions have been observed with (*p*-chlorophenyl)-(*p*-fluorophenyl)-, with (*p*-fluorophenyl)-phenyl-, and with diphenyl-trifluoromethyl-carbinol.

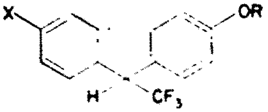
The infra-red spectra of the fluorene derivatives formed are discussed.

DI-(*p*-HALOGENOPHENYL)-TRIFLUOROMETHYL-CARBINOLS (I), when treated successively with concentrated sulphuric acid and water (or methanol) are converted into 3-halogeno-6-hydroxy (or methoxy)-9-trifluoromethylfluorenes (II), by a mechanism which has been discussed previously,[1,2]

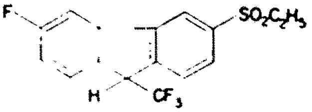
In the present paper an attempt is made to determine the scope of this reaction. (*p*-Chlorophenyl)-(*p*-fluorophenyl)-trifluoromethyl-carbinol, prepared from *p*-chloro-ω,ω,ω-trifluoroacetophenone and *p*-fluorophenylmagnesium bromide, was transformed under the above conditions into 3-chloro-6-methoxy-9-trifluoromethylfluorene (II, X Cl; R CH$_3$); the fluorine atom is thus exchanged in preference to the chlorine atom. (*p*-Fluorophenyl)-phenyl-trifluoromethylcarbinol, prepared analogously from ω,ω,ω-trifluoroactophenone, when treated with sulphuric acid and then with methanol or water, gave 3-methoxy- and 3-hydroxy-9-trifluoromethylfluorene (II, X H, R CH$_3$ or H), respectively; the previously suggested reaction mechanism explains adequately this course of the reaction.



I



II



III

(*o*-Chlorophenyl)-phenyl-trifluoromethyl-carbinol, obtained from ω,ω,ω-trifluoroacetophenone and *o*-chlorophenylmagnesium bromide, gave qualitatively the same picture as the carbinols studied before (strong halochromism, quickly fading in colour); however, no defined product could be obtained upon treatment of the resulting solution with water or methanol.

It is interesting that also the unsubstituted diphenyl-trifluoromethyl-carbinol undergoes a cyclodehydration reaction, when treated with concentrated sulphuric acid. According to its analysis and spectrum, the product, obtained in low yield, is 9-trifluoromethylfluorene. This reaction is analogous to the conversion of benzilic to fluorene-9-carboxylic acid.[3]

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[1] S. Cohen, *J. Amer. Chem. Soc.* **79**, 1499 (1957).
[2] S. Cohen and A. Kaluszyner, *Experientia* **13**, 236 (1957).
[3] D. Vorlaender, *Ber. Dtsch. Chem. Ges.* **44**, 2467 (1911).

The product formed from di-(*p*-fluorophenyl)-trifluoromethyl-carbinol and sulphuric acid underwent with *ethyl mercaptan* a reaction analogous to that occurring with water or alcohols. Although the expected 3-ethylthio-6-fluoro-9-trifluoromethylfluorene could not be induced to crystallize, the corresponding sulphone (III), formed from the crude reaction product with hydrogen peroxide, was well-defined and gave correct analytical figures.

The previously described[4] di-(*p*-chlorophenyl)-pentafluoroethyl- and -heptafluoropropyl-carbinols behave exactly like the corresponding trifluoromethyl compound. Successive treatment with sulphuric acid and methanol gave two compounds which according to their analyses and spectra, were 3-chloro-6-methoxy-9-pentafluoroethyl- and -9- heptafluoropropyl-fluorene, respectively.

The structure of the products obtained in the cyclodehydration reactions was deduced from the infra-red and ultra-violet spectra. The latter resemble closely that of fluorene derivatives.[1,2] It was found that the compounds II (R = CH_3, X = H or Cl) showed an infra-red C—H frequency at about 3400 cm^{-1}. It is suggested that this frequency is due to the C—H bond in the 9-position. Acetylene, too, has an unusually high C—H frequency (3270–3305 cm^{-1}).[5] Experiments of our own have shown that fluorene has a peak at 3330 cm^{-1}, and methyl fluorene-9-carboxylate, which is structurally similar to II, at 3400 cm^{-1}; 9,9-diphenylfluorene, which lacks a hydrogen atom in the 9-position, has no band beyond 3000 cm^{-1}.[6]

EXPERIMENTAL

(p-*Chlorophenyl*)-(p-*fluorophenyl*)-*trifluoromethyl-carbinol* (I, X = Cl, Y = F). To a Grignard solution prepared from magnesium (2·45 g) and *p*-fluorobromobenzene (17·5 g) in ether (150 cc), dry toluene (100 cc) was added and the ether distilled off. Then *p*-chloro-ω,ω,ω-trifluoroacetophenone[4] (10·4 g) was added dropwise and with stirring to the hot mixture (80–90°) over a period of 20 min. Refluxing was continued for an additional 30 min, then the mixture was cooled, decomposed with ice and sulphuric acid and extracted with ether. Distillation of the ethereal layer yielded the desired *compound* as a yellowish oil, b.p. 131–135°/2 mm. Yield, 12·5 g (82%); n_D^{24} 1·5301, d_{24}^{24} 1·395. MR, Found: 67·54; MR, Calc.: 67·35. $\tilde{\nu}_{max}^{liq.}$ 3550 (hydroxyl), 1165 (CF_3), 1068 (C—F), 752 (C—Cl) cm^{-1}. (Found: C, 55·6; H, 3·2. $C_{14}H_9ClF_4O$ requires: C, 55·2; H, 3·0%).

3-*Chloro-6-methoxy-9-trifluoromethylfluorene* (II, X = Cl, R = CH_3). A mixture of the foregoing carbinol (2·8 g) and conc sulphuric acid (20 cc) was shaken for 3 hr, kept overnight, and the coloured solution added, dropwise and with stirring, to an excess of methanol at 5–10°. Crushed ice was added and the precipitated material collected and recrystallized from methanol (charcoal) to yield 1 g (36%) of 3-*chloro-6-methoxy-9-trifluoromethylfluorene*, m.p. 97–99° (lit:[1,4] 95–96°). No depression was observed in the m.p. of a mixture of this compound with an authentic sample. λ_{max}^{EtOH} 217 (4·39); 240 (4·21); 302 (3·70); 308 (3·74); 310 mμ (3·85). $\tilde{\nu}_{max}^{KBr}$ 3420 (C—H), 1265 (Ar—O—CH_3), 1165 (CF_3), 1038 (C—F), 744 (C—Cl) cm^{-1} (Found: C, 60·7; H, 3·5; F, 19·3%. Calc. for $C_{15}H_{10}ClF_3O$: C, 60·3; H, 3·4; F, 19·1%).

(p-*Fluorophenyl*)-*phenyl-trifluoromethyl-carbinol* (I, X = H, Y = F). To a solution of the Grignard reagent, prepared from magnesium (2·4 g), and *p*-fluorobromobenzene (17·5 g) in ether (150 cc), a solution of ω,ω,ω-trifluoroacetophenone[7] (15 g) in ether (75 cc) was added dropwise and with stirring over a period of 15 min, so that the mass was kept boiling. It was then refluxed for 15 min, cooled and poured into a mixture of crushed ice and sulphuric acid. The organic layer was separated, and the aqueous layer extracted once with ether. The combined ether extracts were dried over sodium sulphate and distilled. The *carbinol* forms a colourless oil of b.p. 120–125°/3 mm. Yield, 15 g (71%).

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[4] A. Kaluszyner, S. Reuter and E. D. Bergmann, *J. Amer. Chem. Soc.* **77**, 4164 (1955).

[5] R. N. Jones and C. Sandorfy, *Chemical Applications of Spectroscopy* p. 387. Interscience, New York (1956).

[6] G. W. H. Scherf and R. K. Brown, *Canad. J. Chem.* **38**, 697 (1960).

[7] A. Sykes, J. C. Tatlow and C. R. Thomas, *Chem. & Ind.* 630 (1955).

n_D^{20} 1·5180; d_{20}^{20} 1·331. MR, Found: 61·46; MR, calc.: 61·82. $\tilde{\nu}_{max}^{liq}$: 3450 (hydroxyl), 1163 (CF_3), 1065 (C—F) cm^{-1}. (Found: C, 62·6; H, 4·1. $C_{14}H_{10}F_4O$ requires: C, 62·2; H, 3·7%).

The *acetate* was prepared by heating for 3 hr at 100° a mixture of the carbinol (0·5 g), acetic anhydride (4 cc) and sulphuric acid (2 drops), decomposition with ice and recrystallization of the organic product from methanol. M.p. 70–71°. $\tilde{\nu}_{max}^{KBr}$ 1770 (carbonyl), 1175 (CF_3), 1024 (C—F) cm^{-1}. (Found: C, 61·7; H, 4·3. $C_{16}H_{12}F_4O_2$ requires: C, 61·5; H, 3·9%).

3-*Methoxy-9-trifluoromethylfluorene* (II, X – H, R – CH_3). A mixture of the foregoing carbinol (1 g) and conc sulphuric acid (20 cc) was shaken for 1 hr and the coloured solution added, dropwise and with stirring, to an excess of methanol at 5–10°. Crushed ice was added, whereupon crystals of 3-*methoxy-9-trifluoromethylfluorene* separated. The compound was purified by recrystallization from methanol or petroleum ether and formed silky needles of m.p. 87–88°. Yield, 0·6 g (61%). $\tilde{\nu}_{max}^{KBr}$ 3400 (C_9—H), 1235 (Ar—O—CH_3) 1165 (CF_3), 1038 (C—F) cm^{-1}. λ_{max}^{EtOH} 213 (4·43); 235 (4·31); 262 (4·14); 270 (4·15); 288 (3·50); 298 (3·62); 303 (3·64); 310 mμ (3·85) (Found: C, 68·3; H, 4·3. $C_{15}H_{11}F_3O$ requires: C, 68·2; H, 4·2%).

3-*Hydroxy-9-trifluoromethylfluorene* (II, X – R – H). The product from the carbinol (I, X – H, Y – F) and conc sulphuric acid (20 cc) was poured onto crushed ice. The compound was extracted with ether and the ether residue recrystallized from carbon tetrachloride to yield 0·3 g (32%) of the *compound*, m.p. 174–176°. $\tilde{\nu}_{max}^{KBr}$ 3280 [hydroxyl and C_9—H(?)], 1165 (CF_3) cm^{-1}. λ_{max}^{EtOH} 213 (4·34); 236 (4·26): 263 (4·14); 270 (4·15); 290 (3·45); 305 (3·65); 312 mμ (3·73). (Found: C, 66·8; H, 3·7; F, 22·3. $C_{14}H_9F_3O$ requires: C, 67·2; H, 3·6; F, 22·8%).

(o-*Chlorophenyl*)-*phenyl-trifluoromethyl-carbinol*. To a solution of the Grignard reagent, prepared from magnesium (2·9 g) and *o*-bromochlorobenzene (23 g) in ether (100 cc), dry toluene (70 cc) was added and the ether removed. Then a solution of *ω*,*ω*,*ω*-trifluoroacetophenone (17·4 g) in toluene (40 cc) was added with stirring, at the b.p. of the mixture, over a period of 20 min; refluxing was further maintained for 30 min. After decomposition with ice and sulphuric acid, separation of the ethereal layer and distillation, the *carbinol* was obtained as a yellowish oil, b.p. 139–141°/2 mm; yield, 9 g (31%). $\tilde{\nu}_{max}^{liq}$: 3580 (hydroxyl), 1165 (CF_3); 1040 (C—F); 752 (C—Cl) cm^{-1}. (Found: F, 19·7. $C_{14}H_{10}ClF_3O$ requires: F, 19·9%).

The *acetate* prepared from the carbinol, acetic anhydride and sulphuric acid, melted at 45–47°. (Found: C, 58·3; H, 3·5. $C_{16}H_{12}ClF_3O_2$ requires: C, 58·5; H, 3·7%).

The carbinol (3 g) and conc sulphuric acid (20 cc) gave a deep-purple solution; the colour changed within a few minutes to a dirty green. No defined material could be obtained by either treating this product with crushed ice or cold methanol.

9-*Trifluoromethylfluorene*. Conc sulphuric acid (60 g) was added in portions to powdered diphenyl-trifluoromethyl-carbinol[4] (10 g) in a mortar and the mass triturated till the red-brown colour did no longer appear. The grey mass was then added to an excess of ice and the precipitate filtered off and dried to yield 9·7 g of m.p. 58–100°. The product was extracted with hot methanol; from the filtered solution separated, upon concentration, 9-*trifluoromethylfluorene* which was purified by recrystallization from glacial acetic acid; yield, 0·7 g (7·5%), m.p. 170·5–171°. λ_{max}^{EtOH} 235 mμ (3·90); 271 mμ (3·90); 294 mμ (3·23); 306 mμ (3·16). (Found: C, 71·8; H, 4·0; F, 24·5. $C_{14}H_9F_3$ requires: C, 71·8; H, 3·9; F, 24·3%).

3-*Chloro-6-methoxy-9-pentafluoroethyl-fluorene*. A mixture of di-(*p*-chlorophenyl)-pentafluoroethyl-carbinol[4] (7·4 g) and conc sulphuric acid (60 cc) was shaken mechanically for 3 hr, allowed to stand overnight and added, dropwise and with stirring, to methanol (200 cc) at 5–10°. The methanolic solution was poured onto crushed ice and the *product* recrystallized from petroleum ether (b.p. 60–90°), m.p. 89–91°; yield, 2·1 g (30%). λ_{max}^{EtOH} 218 mμ (4·66); 238 mμ (4·48); 265 mμ (4·24); 292 mμ (3·75); 302 mμ (3·85); 314 mμ (3·98). (Found: C, 55·3; H, 3·1. $C_{16}H_{10}ClF_5O$ requires: C, 55·1; H, 2·9%).

3-*Chloro-6-methoxy-9-heptafluoropropyl-fluorene*. This compound was obtained from di-(*p*-chlorophenyl)-heptafluoropropyl-carbinol[4] (8·4 g) and conc sulphuric acid (60 cc), as described above. Yield, 2·2 g (27%), m.p. 84–85·5° (from pet ether b.p. 60–90°). λ_{max}^{EtOH} 240 mμ (4·32); 266 mμ (4·00); 273 mμ (4·00); 314 mμ (3·88). (Found: C, 51·2; H, 2·8. $C_{17}H_{10}ClF_7O$ requires: C, 51·2; H, 2·5%).

3-*Ethylsulphonyl-6-fluoro-9-trifluoromethylfluorene* (III). A mixture of di-(*p*-fluorophenyl)-trifluoromethyl-carbinol (2·9 g) and conc sulphuric acid (30 cc) was shaken mechanically for 3 hr, then added, dropwise and with stirring, to ethyl mercaptan (100 g) at 0°. The colour of the first drops faded quickly, but soon a second layer was formed, and vigorous stirring was required to bring about this change. The mixture was added to excess cold water, the organic layer separated and subjected to distillation, first at atmospheric pressure, then *in vacuo* in order to remove some diethyl disulphide. The residual oil could not be induced to crystallize; it was dissolved in glacial acetic acid (20 cc) and oxidized to the sulphone with 30% hydrogen peroxide (5 cc) on the water bath for 30 min. After 12 hr. at room temp, the solution was diluted with water and neutralized partially with sodium bicarbonate, whereupon crystals of *3-ethylsulphonyl-6-fluoro-9-trifluoromethylfluorene* (III) separated; yield, 1·1 g (32%). They were purified by recrystallization from a petroleum ether-chloroform mixture and subsequently from ether; b.p. 137–138·5°. (Found: C, 55·6; H, 3·4. $C_{16}H_{12}F_4O_2S$ requires: C, 55·8; H, 3·5%).