Di-(*p*-chlorophenyl)-pentafluoroethylcarbinol.—From the Grignard solution, prepared with 38.5 g. of *p*-chlorobromobenzene, the ether was distilled off and a solution of 15.4 g. of ethyl pentafluoropropionate in 25 ml. of toluene added. The carbinol is an oil, which boils at 165–175° (4 mm.), and was purified by chromatography; yield 16.0 g. (54%), n^{25}_D 1.5270, d^{25}_4 1.4700, *MR* calcd. 77.10, *MR* found 77.57.

Anal. Calcd. for $C_{15}H_9Cl_2F_5O$: C, 48.5; H, 2.4; F, 25.6; Cl, 19.2. Found: C, 48.8; H, 2.4; F, 25.0; Cl, 19.1; ultraviolet spectrum: 227.5 (4.30); 260.0 (3.37).

Ethyl Heptafluorobutyrate.—When a mixture of 90 g. of perfluorobutyric acid, 50 ml. of anhydrous alcohol and 25 ml. of concd. sulfuric acid was refluxed for 2 hours, the ester separated. Upon distillation in presence of phosphorus pentoxide, it boiled at 95–96°; yield 92%.[22]

Di-(*p*-chlorophenyl)-heptafluoropropylcarbinol (V).[23]—A Grignard solution, prepared from 5.3 g. of magnesium turnings and 42 g. of *p*-chlorobromobenzene in 70 ml. of ether was freed from the solvent, and a solution of 24.2 g. of the preceding ester in 25 ml. of toluene added. The mixture was heated at 100° for one hour and worked up as usual. The fraction boiling at 165–175° (5–6 mm.) was subjected to chromatography and the carbinol V obtained as a yellowish oil; yield 23 g. (55%), n^{22}_D 1.5072, d^{22}_{22} 1.51, *MR* calcd. 82.2, *MR* found 83.0.

Anal. Calcd. for $C_{16}H_9Cl_2F_7O$: C, 45.6; H, 2.1. Found: C, 46.2; H, 2.5.

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[22] A. L. Henne and W. C. Fiancis, THIS JOURNAL, **75**, 992 (1953).

[23] The chlorine-free carbinol has recently been described by O. R. Pierce, J. C. Siegle and E. T. McBee, *ibid.*, **75**, 6324 (1953).

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The Reactions of Perfluoropropionic Acid and Tetrafluoroethylene with Phenyllithium in Refluxing Ether

BY THOMAS F. MCGRATH[1] AND ROBERT LEVINE

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In a previous paper[2] it was reported that the reaction of trifluoroacetic acid with phenyllithium gave none of the expected trifluoroacetophenone. Instead a mixture of the cleavage products, benzoic acid, benzophenone, triphenylmethane and tetraphenylethylene, was obtained. The present report is concerned with the reaction of perfluoropropionic acid with phenyllithium in refluxing ether.

When perfluoropropionic acid was added to three equivalents of an ethereal solution of phenyllithium, only the following three compounds were obtained: benzophenone (52%), *sym*-diphenyldifluoroethylene (37%) and triphenylfluoroethylene (6%).

Elemental analyses and molecular weight determinations were used in elucidating the composition of the olefins. The structure of *sym*-diphenyldifluoroethylene was established further by its oxidation to benzoic acid.

The initially formed lithium perfluoropropionate probably is decarboxylated to give carbon dioxide, which reacts with phenyllithium to give benzophenone and C_2F_5Li, which undergoes β-elimination to give lithium fluoride and tetrafluoroethylene (I). Then I reacts with more phenyllithium to give the olefins II and III.

$$C_2F_5Li \longrightarrow C_2F_4(I) + LiF \qquad (1)$$

$$I + 2C_6H_5Li \longrightarrow C_6H_5CF{=}CFC_6H_5(II) + 2LiF \qquad (2)$$

$$II + C_6H_5Li \longrightarrow (C_6H_5)_2C{=}CFC_6H_5(III) + LiF \qquad (3)$$

Support for reaction 1 is available from the work of McBee and co-workers,[3] who found that refluxing an ethereal solution of perfluoro-*n*-propyllithium gave a 97% yield of the olefin, hexafluoropropene. That reactions 2 and 3 are plausible was shown by bubbling tetrafluoroethylene, prepared by the pyrolysis of sodium perfluoropropionate,[4] through three equivalents of phenyllithium and isolating *sym*-diphenyldifluoroethylene (55%) and triphenylfluoroethylene (13%).

Theoretically one can visualize that the fluorinated olefins are formed by two routes: (1) Wurtz–Fittig type coupling and/or (2) successive addition–elimination reactions whereby phenyllithium adds to tetrafluoroethylene to give $C_6H_5CF_2CF_2Li$, which then eliminates lithium fluoride to give α,β,β-trifluorostyrene. This styrene might then react with more phenyllithium to give the fluorinated olefins. We prefer the addition–elimination mechanism since tetrafluoroethylene, which may be regarded as a vinyl halide, would not be expected to function as an alkylating agent.

Recently, Tarrant and Warner[5] have shown that the treatment of trifluorochloroethylene with an equivalent of phenylmagnesium bromide for four days in a reactor packed in Dry Ice gives only one product, 1-chloro-1,2-difluoro-2-phenylethylene in 16.6% yield. It was therefore of interest to treat tetrafluoroethylene with an equivalent and a considerable excess (five equivalents) of phenyllithium to determine the nature of the reaction products. *A priori*, equivalents of this olefin and phenyllithium might be expected to give some α,β,β-trifluorostyrene, while the use of excess phenyllithium might give some tetraphenylethylene and perhaps pentaphenylethane. However, as may be seen in Table I, only *sym*-diphenyldifluoroethylene and triphenylfluoroethylene were obtained. Therefore, if any of the styrene is formed it reacts immediately with more phenyllithium to give the substituted olefins, and apparently triphenylfluoroethylene does not react further with phenyllithium under our experimental conditions.

TABLE I

REACTIONS OF TETRAFLUOROETHYLENE WITH PHENYLLITHIUM

Moles of base per mole of olefin	Products, yield, %	
	sym-Diphenyldifluoroethylene	Triphenylfluoroethylene
1	32	10
3	55	13
5	53	17

Experimental

Reaction of Phenyllithium with Perfluoropropionic Acid.—To phenyllithium (0.9 mole in 900 ml. of ether), contained in a 2000-ml., three-neck, round-bottom flask equipped with a mercury-sealed stirrer, a water-cooled reflux condenser and an addition funnel, perfluoropropionic acid (0.3 mole, 67.2 g.), dissolved in 150 ml. of anhydrous ether, was added dropwise with rapid stirring. After the acid was added and the spontaneous refluxing of the ether ceased, the reaction mixture was refluxed for two more hours. After cooling to room temperature, the reaction mixture was quenched by cautiously pouring it onto a mixture of ice and excess con-

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[1] Monsanto Chemical Co. Fellow, 1953–1954.

[2] T. F. McGrath and R. Levine, THIS JOURNAL, **77**, 3656 (1955).

[3] O. R. Pierce, E. T. McBee and G. F. Judd, *ibid.*, **76**, 474 (1954).

[4] J. D. LaZerte, L. J. Hals, T. S. Reid and G. H. Smith, *ibid.*, **75**, 4525 (1953).

[5] P. Tarrant and D. A. Warner, *ibid.*, **76**, 1624 (1954).

centrated hydrochloric acid. The ether and aqueous phases were separated, the aqueous phase extracted several times with ether and the combined ether extracts dried over Drierite. After the solvent and the low boilers were removed at atmospheric pressure, the residue was distilled in vacuum to give *sym*-diphenyldifluoroethylene (24.2 g., 37%, b.p. 120–123° at 2 mm., m.p. 73.8–74.2° from 60–70° petroleum ether; *Anal.*[6] Calcd. for $C_{14}H_{10}F_2$: C, 77.78; H, 4.63; F, 17.59; mol. wt., 216. Found: C, 77.96; H, 4.57; F, 17.11; mol. wt., 222, 225 (using a McCoy apparatus and benzene as the solvent)); benzophenone (28.7 g., 52%, b.p. 125–127° at 2 mm., m.p. 48.2–48.8°, 2,4-dinitrophenylhydrazone, m.p. 237–239°)[7] and triphenylfluoroethylene (2.3 g., 6%, b.p. 150–155° at 2 mm., m.p. 103.6–104.2° from 60–70° petroleum ether; *Anal.*[6] Calcd. for $C_{20}H_{15}F$: C, 87.59; H, 5.47; F, 6.93; mol. wt., 274. Found: C, 87.23; H, 5.83; F, 7.02; mol. wt., 286, 287).

Reaction of Phenyllithium with Tetrafluoroethylene.—The apparatus used in this reaction was the same as that in the previous experiment except that the water-cooled condenser was replaced by a Dry Ice condenser charged with a slurry of Dry Ice and ether as the coolant. Dry powdered sodium perfluoropropionate (0.3 mole, 55.8 g.) was pyrolyzed by heating the flask containing it to 250–290° in a metal-bath. The tetrafluoroethylene[4] thus formed was passed in succession through a safety trap, two traps containing 30% aqueous potassium hydroxide (to trap the carbon dioxide formed during the pyrolysis), a trap containing concentrated sulfuric acid (to remove any moisture), a second safety trap and then into the reactor containing 0.9 mole of phenyllithium. After the tetrafluoroethylene was added, the Dry Ice condenser was replaced by a water-cooled condenser and the mixture then was refluxed for 30 minutes. The reaction was then processed as described above to give 35.2 g. (55%) of *sym*-diphenyldifluoroethylene, m.p. 73.7–74.2°, and 10.2 g. (13%) of triphenylfluoroethylene, m.p. 103–104.2°. Mixed melting points between each of these compounds and the corresponding compounds prepared in the previous experiment showed no depression.

Oxidation of *sym*-Diphenyldifluoroethylene.—To 0.027 mole (4.3 g.) of potassium permanganate, dissolved in 200 ml. of water, was added 0.02 mole (4.3 g.) of *sym*-diphenyldifluoroethylene. The reaction mixture was stirred and heated at 100° for six hours, stirred for 20 hours at room temperature and then made acid with concentrated hydrochloric acid. The mixture was extracted with several portions of ether, the combined ether extracts dried over Drierite and the solvent distilled. The crystalline residue was extracted with boiling water to give an aqueous solution and a residual oil. On cooling the aqueous solution there was obtained 1.8 g. (37%) of benzoic acid, m.p. 120.6–121.2° alone and when mixed with an authentic sample. The oil crystallized on standing to give 1.2 g. (28%) of recovered *sym*-diphenyldifluoroethylene, m.p. 73.6–74.2°.

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(6) Analysis by Clark Analytical Laboratory, Urbana, Ill.

(7) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., Third Edition (1948).

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If an Enzyme–Substrate Modifier System Exhibits Non-competitive Interaction, then, in General, its Michaelis Constant is an Equilibrium Constant

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Recently, Botts and the author[1] derived the expression for the steady-state reaction velocity, $v = \mathrm{d}(\text{products})/\mathrm{d}t$, in the system shown below. Here E stands for enzyme ([E₀] for total enzyme concentration), S for substrate, and Y for any rate-modifying substance ("modifier") *e.g.*, H^+, an inhibitor, an activator, etc. The expression is

$$\frac{v\,([\mathrm{S}],[\mathrm{Y}])}{[\mathrm{E}_0]} = \frac{k_2\bar{K}_1[\mathrm{S}] + k_2'K_0'\bar{K}_1[\mathrm{Y}][\mathrm{S}] + k_2'(\Delta_{\mathrm{ES}}/\Delta) + k_2'(\Delta_{\mathrm{SEY}}/\Delta)}{1 + \bar{K}_1[\mathrm{S}] + K_0[\mathrm{Y}] + K_0'\bar{K}_1[\mathrm{Y}][\mathrm{S}] + (\Delta_{\mathrm{EY}} + \Delta_{\mathrm{ES}} + \Delta_{\mathrm{SEY}})/\Delta} \quad (1)$$

where

$$r = k_2/k_{-1};\ r' = k_2'/k'_{-1} \quad (2)$$

$$\bar{K}_1 = k_1/(k_{-1} + k_2) \quad (3)$$

$$\mathfrak{D} = (r - r')k'_{-1}K_0'\bar{K}_1[\mathrm{Y}][\mathrm{S}] \quad (4)$$

$$\Delta = k_{-0}k'_{-1}(1 + r')\{k_0'[\mathrm{Y}] + k_{-1}(1 + r)\} + k'_{-0}k_{-1}(1 + r)\{k_1'[\mathrm{S}] + k_{-0}\} \quad (5)$$

$$\Delta_{\mathrm{EY}} = -k'_{-0}k_{-1}\,(1 + r)\mathfrak{D} \quad (6)$$

$$\Delta_{\mathrm{ES}} = k_{-0}k'_{-0}\mathfrak{D} \quad (7)$$

$$\Delta_{\mathrm{SEY}} = k_{-0}\{k_0'[\mathrm{Y}] + k_{-1}(1 + r)\}\mathfrak{D} \quad (8)$$

Since all the perturbation terms in equation 1 contain $\mathfrak{D}$ as a factor, $v/[\mathrm{E}_0]$ assumes simple forms whenever $\mathfrak{D} = 0$. We have remarked[1] that $\mathfrak{D}$ will vanish in, (a) the absence of modifier, *i.e.*, $[\mathrm{Y}] = 0$, whence equation (1) reduces to the familiar Michaelis–Menten equation, (b) the case of "competitive" interaction, *i.e.*, $K'_0 = K'_1 = 0$, and (c) the coincidence that $r = r'$. We have also reported that equation 1 will reduce to that of "non-competitive" interaction if both $K_0 = K'_0$ (or, because of free energy balance, $K_1 = K_1'$), and the enzyme–substrate reactions are at quasi-equilibrium, *i.e.*, $r \rightarrow 0$, and $r' \rightarrow 0$. It is the purpose of this note to examine the inversion of these latter conditions.

A plot of $1/v$ against $1/[\mathrm{S}]$ will be straight throughout the range of [S] if and only if the perturbation terms of equation 1 vanish. Simple algebraic arguments show that, in turn, this will be so if and only if $\mathfrak{D}$ vanishes. Therefore, the straightness of the plot may be taken to mean that $\mathfrak{D}$ is, for some reason, equal to zero. As is well-known, the intercept of the plot on the $(1/v)$-axis will be independent of [Y] in "competitive" interaction. If the system does not meet this test, then we can presume that $\mathfrak{D}$ vanishes for reasons other than (a) or (b) above. We may then ask if varying [Y] varies the intercept and the slope of the plot by the same factor. If it does not, then it is likely that the system is characterized by the coincidence (c). If varying [Y] does affect intercept and slope by the same factor, then we may presume that $K_0 = K'_0$ (and $K_1 = K'_1$), and that the system is governed by the equation

$$\frac{1}{v([\mathrm{S}],[\mathrm{Y}])} = \left\{\frac{1 + K_0[\mathrm{Y}]}{v(\infty, 0) + K_0[\mathrm{Y}]v(\infty, \infty)}\right\}\left\{1 + \frac{1}{\bar{K}_1[\mathrm{S}]}\right\} = \left\{\frac{(1 + K_0[\mathrm{Y}])v(\infty, 0)}{v(\infty, 0) + K_0[\mathrm{Y}]v(\infty, \infty)}\right\}\frac{1}{v([\mathrm{S}], 0)} \quad (9)$$

We suggest that compliance with equation 9 be taken as the operational definition of "non-competitive" interaction. Clearly, "non-competitive inhibition" is a special case wherein $v\,(\infty, \infty) = 0$.

The foregoing remarks show that for a system exhibiting non-competitive interaction, $\mathfrak{D} = 0$, but in general $K'_0\bar{K}_1[\mathrm{Y}][\mathrm{S}] \neq 0$; in other words, the quantity, $k'_{-1}\,(r - r') = 0$. This quantity vanishes in just three cases: I, the coincidence (c),

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(1) D. J. Botts and M. F. Morales, *Trans. Faraday Soc.*, **49**, 696 (1953).