EXPERIMENTAL[9]

p-Fluorobenzyl bromide. To a solution of 11.0 g. (0.10 mole) of *p*-fluorotoluene (Eastman) in 10 ml. of carbon tetrachloride was added 15.0 g. (0.084 mole) of N-bromosuccinimide (Eastman). The mixture was refluxed for 2 hr., and at the end of that time the N-bromosuccinimide which had been at the bottom of the flask had disappeared, and a layer of succinimide was floating on top. The mixture was filtered and the filter cake washed with several portions of carbon tetrachloride.

The filtrate was distilled at atmospheric pressure to remove solvent and a small amount of unreacted *p*-fluorotoluene. Distillation of the remaining liquid at 27 mm. gave 12.8 g. (80.5%) of colorless *p*-fluorobenzyl bromide, b.p. 92–102°, n_D 1.547 (lit.[1] b.p. 93–95°/20 mm., n_D 1.548).

p-Fluorobenzyl cyanide. To a solution of 6.5 g. (0.10 mole) of potassium cyanide dissolved in 12 ml. of water was added, dropwise, 11.9 g. (0.063 mole) *p*-fluorobenzyl bromide dissolved in 30 ml. of 95% ethanol. The mixture was refluxed for 3 hr. The solution was cooled overnight in the refrigerator, and the precipitated inorganic salts were filtered and washed with 95% ethanol. Most of the alcohol was distilled leaving two liquid phases. The aqueous layer was separated and washed with ether and the ether extracts were combined with the organic layer. The solution was dried, the solvent was removed, and the residual oil was distilled at 25 mm. to give 5.3 g. (62%) of *p*-fluorobenzyl cyanide, b.p. 120–129°, n_D 1.499 (lit.[2] b.p. 100–103°/3 mm., n_D 1.501).

p-Fluorotropic acid. Isopropylmagnesium chloride was prepared from 4.2 g. (0.081 mole) of isopropyl chloride and 1.2 g. (0.05 mole) of magnesium in 30 ml. of dry ether. After the addition of the halide, the mixture was refluxed for 45 min. The fluorophenylacetic acid[2] (3.3 g., 0.021 mole) dissolved in 50 ml. of benzene was added to the stirred Grignard reagent during a 20-min. period. The mixture was stirred and refluxed for 3.5 hr. after this addition.

Paraformaldehyde (1.72 g., 0.057 mole), which had previously been dried for several days over phosphorous pentoxide, was heated in an oil bath at 180–200° and the gaseous formaldehyde was carried over the reaction surface in a slow stream of dry nitrogen. The reaction mixture was stirred and ice-cooled during this part of the reaction. Stirring was continued for 30 min. after all of the formaldehyde had been carried over.

The Grignard complex was hydrolyzed by pouring onto a mixture of 100 ml. ice and 7 ml. concentrated sulfuric acid. After standing overnight in the refrigerator, the mixture was stirred for 45 min. and filtered. The layers of the filtrate were separated and the aqueous layer and solid returned to the original reaction flask and heated to boiling. The aqueous layer was then cooled and extracted with five 20 ml. portions of ether. The ether extracts were combined with the benzene layer and the solution concentrated to approximately 25 ml. at which point crystallization occurred.

Filtration and further concentration of the mother liquors gave 2.56 g. (65%) *p*-fluorotropic acid, m.p. 97–100°. Two recrystallizations from benzene gave fine white needles, m.p. 99.5–100°.

Anal. Calcd. for $C_9H_9FO_3$: C, 58.7; H, 4.9; neut. equiv., 184. Found: C, 59.1; H, 5.2; neut. equiv., 189.

Tropine. The method of Findlay[5] was employed with the exception that the sublimation step was omitted. After removal of the ether, white needle-like crystals of tropine were obtained in almost quantitative yield, m.p. 63–64.5° (Findlay reports 87% yield, m.p. 63–65.5°).

Tropine hydrobromide was prepared in 95% yield by passing dry gaseous hydrogen bromide into an ethereal solution of the base. The product may be recrystallized from absolute alcohol-petroleum ether. The hydrobromide does not have a sharp characteristic melting point, melting with decomposition between 235° and 260°.

Anal.[4] Calcd. for $C_8H_{16}BrNO$: Br, 36.10. Found: Br, 35.84.

p-Fluoroatropine. p-Fluorotropic acid (0.74 g., 0.004 mole) and a magnetic stirrer were placed in a 20-ml., two necked flask to which a reflux condenser was attached. Freshly distilled acetyl chloride (2 ml.) was added, the mixture was stirred, and after the initial reaction had subsided, it was heated and stirred for 20 min. at 90–95°. After removal of the excess acetyl chloride under reduced pressure, 4 ml. of freshly distilled thionyl chloride was added and the mixture was stirred and heated for 1.5 hr. at 90–95°. The excess thionyl chloride was removed under reduced pressure, 0.80 g. (0.0036 mole) of tropine hydrobromide was added and the mixture was stirred and heated for 1 hr. A drop of concentrated hydrochloric acid and 2 ml. of water were added to the reddish oil and the mixture was heated for 1 hr. at 90–95°. After cooling in ice, 10% sodium hydroxide solution was added until the mixture reached *p*H 10, whereupon an oil precipitated. After standing overnight in the refrigerator, the oil together with the aqueous layer was extracted several times with chloroform. After removal of the solvent from the combined extracts, the oily residue was dissolved in ether and the solution was placed in a refrigerator for several days. The precipitated, crystalline *p*-fluoroatropine (m.p. 87–93°, 0.29 g., 26%) melted at 94–95° after recrystallization from chloroform–petroleum ether (32–63°).

Anal. Calcd. for $C_{17}H_{22}FNO_3$: C, 66.4; H, 7.2. Found: C, 66.5; H, 7.5.

The *picrate* was prepared from a sample of the atropine and recrystallized from ethanol to give yellow powdery crystals, m.p. 181–183°.

Anal. Calcd. for $C_{23}H_{25}FN_4O_{10}$: C, 51.5; H, 4.7. Found: C, 51.0; H, 4.7.

Physiology Division
Directorate of Medical Research
Chemical Warfare Laboratories
Army Chemical Center, Md.

Synthesis of Some Organic Arsonites and Arsonates[1]

Leslie M. Werbel, Thomas P. Dawson,
John R. Hooton, and Theodore E. Dalbey

Received October 8, 1956

Although organic arsenical research has been quite extensive, extending back to the work of Cadet[2] in 1760, little work has been done on alkylarsonate esters. The purpose of this work was to prepare certain methylarsonate esters of the type $CH_3As(O)(OR)_2$ (I).

Several methods for their synthesis appeared to be available: (*1*) reaction of dichloromethylarsine oxide with alcohols, (*2*) alkylation of metallic salts of alkylarsonic acids with alkyl halides, and (*3*) oxidation of alkylarsonites.

Although dichloroarylarsine oxides are known[3,4]

---

[9] All melting points are uncorrected.

(1) Contribution from the Chemical Warfare Laboratories, Directorate of Research, Army Chemical Center, Md.

(2) Cadet de Gassicourt, *Mem. Math. Phys.*, **3**, 363 (1760).

(3) A. E. Goddard and J. N. Friend, *Textbook of Inorganic Chemistry*, Vol. XI, Part II, Charles Griffin and Co., Ltd., London, 1928, p. 131.

(4) G. W. Raiziss and J. L. Gavron, *Organic Arsenical Compounds*, The Chemical Catalog Company, Inc., New York, 1923, p. 235.

the synthesis of dichloromethylarsine oxide (II), $CH_3As(O)Cl_2$, has not been reported. Attempts by the Shell Development Company[5] to prepare II by the chlorination of methylarsonous oxide with chlorine at −35° in methylene chloride were inconclusive, since II was not isolated and the desired product of its reaction with ethanol, $CH_3As(O)(OC_2H_5)_2$, was not obtained. Our attempts to prepare II by the oxidation of dichloromethylarsine with either sulfuryl chloride or sulfur trioxide also were unsuccessful. Silver and sodium salts of methylarsonic acid have been converted to arsonate esters by refluxing with alkyl halides.[6,7]

$$CH_3As(O)(OAg)_2 + 2RI \longrightarrow CH_3As(O)(OR)_2 + 2AgI$$

TABLE I

Preparation of Arsonites $RAs(OR')_2$

R	R′	Yield, %	B.P.	Mm.	d_4^{25}	n_D^{25}	Formula	Analyses Calcd.	Analyses Found
CH_3	C_6H_{11}	78	120	0.01	1.182	1.5005	$C_{13}H_{25}AsO_2$	25.99	25.90
CH_3	$i\text{-}C_3H_7$	62	160	760	1.008	1.4374	$C_7H_{17}AsO_2$	35.99	35.70
$ClCH{=}CH$	C_6H_{11}	35.9	102	0.005	1.250	1.5221	$C_{14}H_{24}AsClO_2$[a]	22.38	22.42
$o\text{-}NO_2C_6H_4$	$i\text{-}C_3H_7$	14.6	94	0.04			$C_{12}H_{18}AsNO_4$	23.77	23.79

[a] Anal. Calcd.: Cl, 10.50. Found: Cl, 10.52.

TABLE II

Preparation of Arsonates, $RAs(O)(OR')_2$

R	R′	Yield, %	B.P.	Mm.	d_4^{25}	n_D^{25}	Formula	Analyses Calcd.	Analyses Found
CH_3	$i\text{-}C_3H_7$	83	82	3	1.2133	1.4420	$C_7H_{17}AsO_3$	33.39	33.94
CH_3	$n\text{-}C_4H_9$[a]	49	105[b]	2			$C_9H_{21}AsO_3$	29.67	29.00

[a] Prepared by Method B. [b] Lit. b.p. 160.3–161.3°/13 mm., E. J. Salmi, K. Merivuori, E. Laaksonen, *Suomen Kemistilehti*, **19B,** 102 (1946).

This method was also employed successfully by us to prepare alkylarsonates. In general, the silver salts could be obtained in a purer state and were more reactive than the sodium salts.

Dichloromethylarsine has been employed to prepare arsonites by reaction with sodium alkoxides.[8]

$$CH_3AsCl_2 + 2NaOR \longrightarrow CH_3As(OR)_2 + 2NaCl$$

In the current investigation the alkoxide was replaced by a mixture of the desired alcohol and an equimolar quantity of triethylamine.

$$CH_3AsCl_2 + 2ROH + 2(C_2H_5)_3N \longrightarrow CH_3As(OR)_2 + 2(C_2H_5)_3N{\cdot}HCl$$

This procedure gave better yields than the alkoxide method. The alkylarsonite was then oxidized to the arsonate with selenium dioxide. The arsonate prepared by this method was more difficult to purify than the arsonate prepared by the silver salt method. The oxidized product contained traces of an organic selenium compound which necessitated an additional distillation for its removal.

Several miscellaneous methods which are more or less standard for the preparation of analogous phosphorus compounds were also tried without success. These reactions included the Arbusov Rearrangement[9] and the oxidative chlorination of a dialkyl alkylarsonite with phosgene.[10]

The arsonites and arsonates prepared, together with their properties and analytical data, are summarized in Tables I and II.

EXPERIMENTAL

Arsonites. To a stirred solution of the appropriate alcohol and triethylamine (1.0 mole each) in 400 ml. of *n*-hexane, a solution of 0.5 mole of dichloromethylarsine in 200 ml. of *n*-hexane was added dropwise with sufficient cooling to maintain the temperature at 40–50°. After completing the addition the reaction mixture was stirred until cool, filtered free of amine hydrochloride, and the filter cake washed with additional *n*-hexane. The *n*-hexane solution of the product was then dried over anhydrous calcium sulfate, the solvent was stripped off and the residue was distilled under vacuum in an atmosphere of dry nitrogen.

Arsonates. Method A: Oxidation of the arsonite with SeO_2. To 0.11 mole of freshly prepared SeO_2 in 400 ml. of dry benzene at reflux temperature, 0.19 mole of the diester was added dropwise during a 20 min. period. The reaction mixture turned light brown, red, and finally black. After heating for 3 hr., the metallic selenium was filtered off, the solvent stripped off and the product distilled under vacuum in an atmosphere of dry nitrogen. Analysis of the once-distilled product revealed the presence of traces of organic selenium (0.1–0.2%), which necessitated an additional distillation to obtain a pure product. The arsonate esters are extremely sensitive toward moisture.

Method B: Reaction of the silver salt of the arsonic acid with an appropriate alkyl iodide. The appropriate alkyl iodide

---

(5) Shell Development Company, ETF-100-29/Task 5, Army Chemical Center, Md., 1954.

(6) G. Meyer, *Ber.*, **16**, 1440 (1883).

(7) A. J. Quick and R. Adams, *J. Am. Chem. Soc.*, **44**, 805 (1922).

(8) Y. F. Komissarov, A. Y. Maleeva, and A. S. Sorokoumov, *Compt. rend. acad. sci., U.R.S.S.*, **55**, 719 (1947).

(9) A. Arbusov, *Chem. Zentr.*, **77**, (II) 1639 (1906).

(10) A. H. Ford-Moore, *J. Chem. Soc.*, 1776 (1953).

(0.5 mole) was added to the silver salt (0.25 mole) in 1-l. of dry benzene. The mixture was stirred and heated under reflux for about 24 hr. The silver iodide was filtered off, the benzene solvent stripped off, and the product distilled under vacuum in an atmosphere of dry nitrogen. The arsonate prepared by this method is much purer than when prepared by method A, only one distillation being required to obtain a pure product.

Chemical Research Division
Army Chemical Center, Md.

Preparation of *N*-1,1-di-H-perfluoroalkyl Amines

Harvey A. Brown and George Van Dyke Tiers

Received October 8, 1956

The preparation of *N*-1,1-di-H-trifluoroethyl aniline ($C_6H_5NHCH_2CF_3$) and *N*-1,1-di-H-heptafluorobutyl aniline ($C_6H_5NHCH_2C_3F_7$) has been described in the literature.[1,2] The first of these was prepared by reacting 1,1-di-H-trifluoroethyl chloride with aniline in a sealed ampoule at 185° for 24 hr., while the latter material was prepared in poor yield by the lithium aluminum hydride reduction of heptafluorobutyranilide.

Earlier we reported the preparation of various 1,1-di-H-perfluoroalkyl tosylates (*p*-toluenesulfonates) and their reactions with various alkali halides to give excellent yields of the corresponding 1,1-di-H-perfluoroalkyl halides.[3] It was reasonable to suppose that analogous reactions might occur between these tosyl esters and aliphatic or aromatic amines.

We have found that good yields of pure *N*-1,1-di-H-heptafluorobutyl aniline are readily obtained by heating a mixture of aniline and 1,1-di-H-heptafluorobutyl tosylate for 24 hr. at 230°. It would appear that the previously reported preparation,[2] a liquid, was seriously impure, as our product melted at 38°-39.5°. The corresponding *N*-substituted piperidine was prepared in similar fashion. The use of lower temperatures or shorter reaction times resulted in lower yields of the desired product.

Attempts to react the tosyl ester with ammonia or diethyl amine under similar conditions gave tarry, decomposed mixtures from which the desired products could not be isolated. Similarly, reactions of the iodide, n-$C_3F_7CH_2I$, with aniline at 250° led only to decomposition, none of the desired amine being found.

A highly fluorinated amide has been prepared by treating *N*-1,1-di-H-heptafluorobutyl aniline with heptafluorobutyric anhydride.

EXPERIMENTAL

N-1,1-di-H-heptafluorobutyl aniline. Two hundred grams (2.15 moles) of aniline and 354.2 g. (1.0 mole) of 1,1-di-H-heptafluorobutyl *p*-toluenesulfonate[3] were allowed to react in a 180-ml. Aminco stainless steel autoclave for 24 hr. at 230°. After cooling, the contents of the autoclave were washed out with ether; the mixture was filtered and 200.5 g. (75.5%) of anilinium *p*-toluenesulfonate was obtained. To remove unreacted aniline the filtrate was washed with 250 ml. of 5% hydrochloric acid and then with several portions of water. The ether was boiled off and the residue was subjected to vacuum distillation. One hundred eighty-seven grams of the desired product, n-$C_3F_7CH_2NHC_6H_5$, was obtained, b.p. 86-95° (7-8 mm.), 68% yield. It solidified on cooling, and upon recrystallization from 70% alcohol, melted at 38-39.5°.

Anal. Calcd. for $C_{10}H_8F_7N$: C, 43.6; N, 5.08. Found: C, 43.4; N, 5.08.

N-1,1-di-H-heptafluorobutyl piperidine. In a $^3/_4$-inch o.d. heavy-walled Pyrex No. 7740 ampoule of approximately 30 ml. volume was sealed a mixture of 12.8 g. (0.036 mole) of 1,1-di-H-heptafluorobutyl *p*-toluenesulfonate and 6.2 g. (0.073 mole) of piperidine. The ampoule, placed in an iron pipe shield for safety, was rocked continuously at 175° for 20 hr. The ampoule, still in the iron pipe, was cautiously cracked open at liquid air temperature. After warming to room temperature, the reaction product was treated with petroleum ether and the slurry was filtered to remove piperidinium *p*-toluenesulfonate. The solution was fractionally distilled at 148°-151° and had n_D^{25} 1.3576; there was obtained 4.2 g. (44% yield).

Anal. Calcd. for $C_9F_7H_{12}N$: N, 5.25; F, 49.8. Found: N, 5.10; F, 49.6.

Attempted reaction of aniline with $C_3F_7CH_2I$. In the first two attempts, the sealed, 80-ml. heavy-walled Pyrex ampoules burst when 20 g. (0.064 mole) of $C_3F_7CH_2I$ and 12 g. of (0.129 mole) aniline were heated to 250°. The third reaction was carried out for 24 hr. at 250° in a 43-ml. Aminco stainless steel autoclave, the same quantities of the reactants being used. The reaction product was black and very tarry and none of the desired amine, n-$C_3F_7CH_2NHC_6H_5$, could be isolated by vacuum distillation.

N-1,1-di-H-heptafluorobutylheptafluorobutyranilide. A mixture of 19 g. (0.07 mole) of *N*-1,1-di-H-heptafluorobutylaniline and 41 g. (0.1 mole) of heptafluorobutyric anhydride was refluxed for 7 hr. The mixture was then poured into 250 ml. of water and was neutralized with sodium carbonate. The product was taken up in two 50-ml. portions of ether, washed twice with water, and dried over magnesium sulfate. After distilling off the ether, the product was distilled under reduced pressure, b.p. 90-91° (3 mm.), m.p. 21°, n_D^{20} 1.3834 (supercooled). The yield of pale yellow amide was 20.3 g. (0.043 mole) or 61%.

Anal. Calcd. for $C_{14}H_7F_{14}NO$: C, 35.66; N, 2.97. Found: C, 35.7; N. 2.89.

Acknowledgment. The authors thank Dr. L. C. Krogh for furnishing the data concerning *N*-1,1-di-H-heptafluorobutyl heptafluorobutyranilide.

Central Research Department
Minnesota Mining and Manufacturing Co.
St. Paul, Minn.

---

[1] J. B. Dickey, U. S. Pat. 2,618,630, Nov. 18, 1952.

[2] J. B. Dickey, *Ind. Eng. Chem.*, **46**, 2213-2220 (1954).

[3] G. V. D. Tiers, H. A. Brown, and T. S. Reid, *J. Am. Chem. Soc.*, **75**, 5978-79 (1953).