of sodium methacrylate with 2,4-dinitro-, or 2,4,6-trinitrochlorobenzene[3] (see Table I).

Aromatic amines with free ortho-position reacted smoothly with methacrylyl chloride; ortho-substituted arylamines, *e.g.*, 2-nitroaniline and 2,6-disubstituted anilines, failed to react. Diamines yielded only the corresponding diamides with methacrylyl chloride, even when a large excess of the diamine was employed. Equally, *p*-aminophenol gave only the amide–ester. The products are described in Table II.

Polymerization of the new esters and amides was studied both in solution and in bulk, and the intrinsic viscosity of the polymers was determined. Turbidimetric determination of the molecular weight of poly-4-nitrophenyl methacrylate (31,000) led to the conclusion, that multiplication of the intrinsic viscosity data (Table III) by $10^5$ gives a good approximation for the molecular weights of the polymers.

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### Experimental

**Methacrylyl chloride** was prepared from methacrylic acid and benzoyl chloride in accordance with the directions given for the preparation of acrylyl chloride[4]; b.p. 93–94° (700 mm.), yield 85–90%.

**Procedure for the Preparation of Aryl Methacrylates** (Table I).—The phenol (0.04 mole) was dissolved in an excess of aqueous sodium hydroxide (5%); the solution cooled in an ice-bath, and 4.2 g. (0.04 mole) of methacrylyl chloride added with stirring in the course of 5–10 minutes. Stirring was continued with cooling for ten minutes, and then at room temperature for 30 minutes. The resulting ester was purified either by crystallization or by distillation.

**4-Methacrylylamidophenyl methacrylate** was obtained by the above procedure from 0.04 mole of 4-aminophenol and 0.04 mole of methacrylyl chloride, in 24.5% yield; m.p. (from dilute ethanol), 126–127°.

*Anal.* Calcd. for $C_{14}H_{15}O_3N$: C, 68.6; H, 6.2; N, 5.7. Found: C, 67.8; H, 6.0; N, 5.9.

**Procedure for the Preparation of N-Arylmethacrylamides** (Table II).—To a saturated solution of the amine (0.04 mole) in ether or benzene, there was added at room temperature and with stirring 0.04 mole of methacrylyl chloride in the course of 5–10 minutes. Stirring was continued for 20–30 minutes, the mixture filtered, and both precipitate and filtrate washed with dilute hydrochloric acid and water. The solvent was then evaporated, and the residue recrystallized together with the precipitate. Some of the methacrylonitroanilides gave stable molecular compounds with the parent amines; only by prolonged shaking with hydrochloric acid could they be separated into the components. Two molecules of XIII gave a compound, m.p. 95°, with one molecule of 3-nitroaniline. *Anal.* Calcd. for $C_{26}H_{26}O_8N_6$: C, 56.7; H, 4.8; N, 15.3. Found: C, 57.6; H, 4.9; N, 14.9. One molecule of XV gave a compound, m.p. 84°, with one molecule of 2-methyl-5-nitroaniline. *Anal.* Calcd. for $C_{18}H_{20}O_5N_4$: C, 58.1; H, 5.4; N, 15.0. Found: C, 57.9; H, 5.4; N, 15.4.

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[3] The claim of R. F. Cellini (*Anales real. soc. espan. fis. y quim.*, **45B**, 1131 (1949), *C. A.*, **44**, 8859 (1950)), that picryl methacrylate can be prepared by refluxing methacrylyl chloride with picric acid, could not be substantiated.

[4] G. H. Stempel, *et al.*, THIS JOURNAL, **72**, 2299 (1950).

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## Phenylalanylphenylalanine Ethyl Ester Synthesis by Chymotrypsin

BY HENRY TAUBER

It previously has been reported that insoluble high molecular weight (250,000–500,000) protein-like substances are synthesized by chymotrypsin from protein-free peptic digests.[1–3] Recently Brenner and associates[4] found by filter paper chromatography that soluble peptides form when chymotrypsin is added to certain $\alpha$-amino acid esters at an alkaline *p*H. It has now been observed that L-phenylalanine ethyl ester is rapidly converted to the water-insoluble and readily crystallizable phenylalanylphenylalanine ethyl ester by chymotrypsin. The compound has been isolated in pure crystalline form. The reaction probably occurs in the following manner

L-phenylalanine ethyl ester + phenylalanine ⟶
phenylalanylphenylalanine ethyl ester

**Enzymic Synthesis.**—In a 50-ml. beaker were placed 3 g. of L-phenylalanine ethyl ester hydrochloride and 12 ml. of distilled water. Sodium hydroxide (2 *N*) was added to yield a solution of *p*H 8.8. Salt-free chymotrypsin (Worthington), (12 mg.) in 1 ml. of distilled water was added, and the volume was made up to 24 ml. The beaker was kept at 37° and the mixture was stirred occasionally. Precipitation began in 10 minutes. Sodium hydroxide was added during the remaining 30 minutes of the reaction period to maintain the *p*H above 8.6. The yield of dipeptide ester decreases in a less or more alkaline medium.

**Isolation of the Dipeptide Ester.**—The insoluble product was collected by centrifuging for 10 minutes at 3000 r.p.m. It was washed twice with 20 ml. of distilled water and extracted three times, each time with 25 ml. of acetone in which most dissolved. The acetone extract was concentrated *in vacuo* to 20 ml. The slight amorphous precipitate which formed was removed and discarded. When the acetone was removed 280 mg. of white powder was obtained. It was extracted with 20 ml. of ether. The ether-soluble fraction was discarded. The ether insoluble portion was extracted with 20 ml. of acetone in which almost all dissolved. To the acetone solution distilled water was added to obtain a 45% acetone concentration. The solution was kept for 3 days at room temperature; the dipeptide ester separated in the form of microscopic needles which were collected by centrifuging and dried *in vacuo*, m.p. 188–190° with decomposition.

*Anal.* Calcd. for $C_{20}H_{24}N_2O_3$: C, 70.56; H, 7.10; N, 8.23. Found: C, 70.07; H, 6.99; N, 8.14.

**Identification of Phenylalanine.**—About 10% of the L-phenylalanine ethyl ester employed in the synthesis was converted to L-phenylalanine and was isolated as such from the supernatant of the enzyme reaction mixture. It was identified by filter paper chromatography.

**General Properties of the Dipeptide Ester.**—The phenylalanylphenylalanine ethyl ester is soluble in glacial acetic acid and in acetone, but insoluble in water, 2.5 *N* sodium hydroxide and 2.5 *N* sulfuric acid. The dipeptide (phenylalanylphenylalanine) itself, however, is readily soluble in dilute acids and alkalies.[5] The dipeptide ester gives a much lighter ninhydrin spot test than L-phenylalanine, it is hydrolyzed by mold peptidase and is slightly hygroscopic.

**Enzymic Hydrolysis.**—Enzymic hydrolysis, 0.75 mg. of the compound in 0.3 ml. of acetone was mixed with 0.7 ml. of distilled water and 1.0 ml. of phosphate buffer (*p*H 7.5). A flocculent precipitate was produced. To this mixture was added 1.0 ml. (10 mg.) of mold peptidase. The final *p*H was 7.7. Toluene (0.1 ml.) was added to prevent bacterial growth. The mixture was kept at 37°. The precipi-

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[1] H. Tauber, THIS JOURNAL, **71**, 2952 (1949).

[2] H. Tauber, *ibid.*, **73**, 1288 (1951).

[3] H. Tauber, *ibid.*, **73**, 4965 (1951).

[4] M. Brenner, H. R. Müller and R. W. Pfister, *Helv. Chim. Acta*, **33**, 568 (1950).

[5] E. Fischer, *Ber.*, **37**, 3068 (1904).

tate disappeared completely after 18 hours. A control without added enzyme remained turbid. Crystalline trypsin and chymotrypsin produced no visible effect on the mixture.

Cysteine ethyl ester, glycine ethyl ester and arginine methyl ester were not converted to insoluble compounds by chymotrypsin. Crystalline trypsin and crystalline carboxypeptidase did not produce insoluble compounds from L-phenylalanine ethyl ester.

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## The Fluorination of Thiophene with Cobalt Trifluoride

BY JULIUS SCHULTZ AND MURRAY HAUPTSCHEIN

The fluorination of thiophene over cobalt trifluoride in a Fowler-type[1] apparatus resulted in extensive cleavage of the molecule with the formation of various low boiling sulfur fluorides and fluorocarbon cleavage products. Two compounds of interest were isolated, one a sulfur-free fluorinated butane derivative, and the other a fluorine-free sulfur-containing polymer.

A series of ten fluorinations was carried out in the usual manner. In each case a 21-g. sample of thiophene was introduced at the rate of 30.0 g. per hour in a stream of dry nitrogen at a rate of 30–35 cc. per minute. The reactor temperature was varied from 150–250°, and 350 g. of cobalt trifluoride was used in each case. Nearly complete reduction to cobalt difluoride was noted. The yield of products was not very much dependent on the temperature of the reaction, which on the introduction of the charge would increase suddenly from 30 to 50° due to the very exothermic reaction.

The two products of interest were isolated from the two traps closest to the system, cooled in water–ice and Dry Ice–acetone, respectively. The average weight of products collected in these traps was 59 g. resulting from the fluorination of 21 g. of thiophene. Approximately 16 g. of product boiling at 30–40° was recovered. On further rectification of this fraction, most of the product boiled at 36.5–37°, f.p. app. −55°, $d^{0}_{4}$ 1.5653, $d^{10.5}_{4}$ 1.5404, $\Delta d/\Delta t$ −0.0024, and corresponded to the dihydride $C_4H_2F_8$.

*Anal.*[2] Calcd. for $C_4H_2F_8$: C, 23.76; H, 1.00; F, 75.24; mol. wt., 202. Found: C, 23.67; H, 1.08; F, 75.76; mol. wt., 203.

The dihydrofluorocarbon is alkali resistant, reduces permanganate, and is chlorinated slowly in the vapor phase under ultraviolet illumination, to form the corresponding dichloride, b.p. 62–63°, mol. wt., found, 270; mol. wt., calcd. for $C_4Cl_2F_8$: 271.

The other product isolated in the first copper trap cooled in water–ice was a brown solid (5 to 6 g.), which was formed only when the system did not include a sodium fluoride tube for removing the hydrogen fluoride formed. No evidence was found for the formation of this solid in either the fluorinator or the copper tubing connecting lines. After washing this solid with dilute bicarbonate solution to remove any hydrogen fluoride, it was extracted with hot glacial acetic acid to remove any copper contamination. The insoluble powder was then freed of acid and exhaustively extracted with ether. The ether extracts were negligible. The dried powder, which was essentially insoluble in the common organic solvents (except carbon disulfide in which it was slightly soluble) as well as in 10% acid and alkali, could be dissolved in hot fuming nitric acid. Analysis[2] of the purified product gave on an ash-free basis C, 55.8; H, 3.92; S, 40.3. This corresponds closely to the formula $(C_4H_{3.4}S_{1.1})_x$. This formula does not differ greatly from that for a polymer of thiophene, *i.e.*, $(C_4H_4S)_x$, but the deficiency in hydrogen may be significant.

**Acknowledgment**.—The authors wish to express their sincere appreciation to the U. S. Air Force, Air Materiel Command, for their financial support of part of this work.

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[1] R. D. Fowler, *et al.*, *Ind. Eng. Chem.*, **39**, 292 (1947).

[2] Analysis by Clark Microanalytical Laboratory, Urbana, Ill.

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## Perfluoroalkyl Halides Prepared from Silver Perfluoro-Fatty Acid Salts. III. 1,3-Dibromohexafluoropropane and 1,3-Dichlorohexafluoropropane

BY MURRAY HAUPTSCHEIN, CHARLES S. STOKES AND ARISTID V. GROSSE

In our first paper of this series[1] we reported the preparation of an 18% yield of 1,3-diiodohexafluoropropane by the thermal degradation of silver hexafluoroglutarate by an excess of iodine. That reaction was shown to proceed mainly with formation of perfluorobutyrolactone probably through cyclization of the intermediate gamma iodo salt, $ICF_2CF_2CF_2CO_2Ag$. We have now treated silver hexafluoroglutarate with bromine and chlorine by the method previously described[2] and have isolated the new compound 1,3-dibromohexafluoropropane and 1,3-dichlorohexafluoropropane in 80.3 and 64.5% yield, respectively. No evidence was found for the formation of any perfluorobutyrolactone. The larger size of the iodine atom, *i.e.*, the closer spacial proximity to the silver atom, may be the principal factor in favoring cyclization and lactone formation in the previous case only.

Since the yield of AgBr was 100% and that of AgCl was 90% of theory (*vide infra*), it is likely that similar proportions of dihalides were formed in the reaction, and the lower yields actually isolated resulted from losses in the recovery processes.

The infrared spectra[3] are shown in Figs. 1 and 2. It is of interest to note the absence of any prominent bands below 7.85 microns in the spectra of these 1,3-dihaloperfluoropropanes. This picture is consistent with that for 1,3-diiodohexafluoropropane given previously,[1] and in marked contrast with that for perfluoroalkyl halides containing $-CF_3$ groups where intense absorption bands appear at 7.3 to 7.52 microns.[1,2]

### Experimental

**Preparation of $CF_2BrCF_2CF_2Br$.**—A 45.38-g. (0.10 mole) sample of finely powdered silver hexafluoroglutarate reacted with 42 g. (0.26 mole) of bromine. The reaction was carried out at 80–90° and was completed in four hours. The yield of AgBr was 37.5 g. (100%). There was obtained 24.84 g. (80.3% yield) of washed and dried dibromide. 1,3-Dibromohexafluoropropane is a water-white liquid, b.p. 74.2°, $n^{0.5}D$ 1.3684, $n^{30.2}D$ 1.3536, $d^{0.0}_{4}$ 2.1966, $d^{27.8}_{4}$ 2.1162, *MR* (found) 31.81, $AR_F$ 1.14.

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[1] M. Hauptschein and A. V. Grosse, THIS JOURNAL, **73**, 2461 (1951).

[2] M. Hauptschein and A. V. Grosse, XIIth International Congress of Pure and Applied Chemistry, New York City, September 10–13, 1951.

[3] Determined with a Baird Associates Infrared Recording Spectrophotometer of Samuel P. Sadtler & Sons, Inc., Philadelphia.