TABLE I

No.	Structure	B.P.	Mm. Hg	n_D^{25}	D_4^{25}	R_D Found	R_D Calcd.[a]	% Si Found	% Si Calcd.	Neut. Equiv. Found	Neut. Equiv. Calcd.
I	$C_6H_5MeCHSiMeCl_2$	121–122	25	1.5197	1.1321	0.2684	0.2650	12.6	12.8	109.8	109.6
II	$C_6H_5CH_2CH_2SiMeCl_2$	137–138	30	1.5107	1.1216	0.2669	0.2650	12.7	12.8	109.9	109.6
III	$C_6H_5MeCHSiMe_3$	111.3	38	1.4959	0.8738	0.3345	0.3307	15.4	15.7		
IV	$C_6H_5CH_2CH_2SiMe_3$[b]	117	40	1.4840	0.8582	0.3329	0.3307	15.6	15.7		
V	$C_6H_5MeCHCH_2SiMeCl_2$	148–149	42	1.5082	1.100	0.2708	0.2690	12.0	11.8	117.2	116.6
VI	$C_6H_5MeCHCH_2SiMe_3$	217	750	1.4841	0.8619	0.3320	0.3308	14.3	14.6		
VII	$(C_6H_5MeCHCH_2SiMeO)_3$	228[c]	1	1.5220	1.041	0.2926	0.2924	16.0	15.8	Viscosity 88–91 cs. at 25°	
VIII	$(C_6H_5MeCHCH_2SiMeO)_4$	270[c]	1	1.5262	1.051	0.2923	0.2924	16.0	15.8	Viscosity 198–202 cs. at 25°	
IX	$(C_6H_5MeCHCH_2SiMe_2)_2O$	162	1	1.5043	0.9487	0.3123	0.3124	15.2	15.1		
X	$C_6H_5MeCHCH_2SiCl_3$	141	30	1.5140	1.218	0.2471	0.2457	11.3	11.1	83.6	83.6

[a] Calculated according to the bond values of A. I. Vogel, W. T. Cresswell, G. H. Jeffrey, and J. Leicester, *J. Chem. Soc.*, 514 (1952); A. I. Vogel, W. T. Cresswell, and J. Leicester, *J. Phys. Chem.*, **58**, 174 (1954). [b] Ref. 1 cites for an authentic sample, b.p. 101° at 20 mm., n_D^{25} 1.4842, D_4^{25} 0.8591. [c] Ebulliometric boiling points. The other boiling points are condensation temperatures taken during distillation.

33% yield with the properties given in Table I, and (II), 1019 g., 53% yield. A viscous polymer (128 g.) remained as residue.

2-Phenylpropylmethyldichlorosilane (V). α-Methylstyrene (354 g., 3.0 mol.) and methyldichlorosilane (380 g., 3.3 mol.) with 2×10^{-5} mol. of chloroplatinic acid were treated as above, and kept overnight at about 140°. Careful fractionation gave 38 g. boiling between the excess methyldichlorosilane and a constant boiling plateau described as V in Table I, 631 g., 90% yield.

2-Phenylpropyltrimethylsilane (VI). Excess methylmagnesium bromide in ether with V formed VI in 85% yield.

(2-Phenylpropyl)methylpolysiloxanes. Hydrolysis of V (700 g., 3.0 mol.) in 2500 ml. of toluene with 1 l. of water was followed by a thorough washing with dilute sodium carbonate and then with water. Distillation at 1 mm. gave 190 g., 36% of the cyclotrisiloxane (VII) n_D^{25} 1.5220–1.5222, viscosity, 88–91 cs. at 25°.

α-Methylstyrene (1182 g., 10.0 mol.) with 2×10^{-4} mol. of chloroplatinic acid was heated to 110° and 1,3,5,7,9-pentamethylcyclopentasiloxane (601 g., 10.0 equivalents) was added slowly. The mixture was kept at 110° overnight and then distilled rapidly from 1 g. of potassium hydroxide at 1 mm. The distillate (1704 g., 96% yield) was a mixture of cyclosiloxanes, n_D^{25} 1.5242, viscosity, 216 cs. at 25°.

On redistillation of a portion of this material the trisiloxane (VII) was again isolated, n_D^{25} 1.5220, D_4^{25} 1.041, viscosity 88 cs. at 25° (45% yield). After recovering an intermediate portion, presumably a mixture of cyclic trimer and tetramer, there was recovered the cyclotetrasiloxane (VIII), n_D^{25} 1.5262, D_4^{25} 1.051, viscosity 200 cs. at 25° (18% yield). The condensation temperatures recorded during the low pressure distillations were variable and unreliable. The progress of the distillation was followed chiefly by the index of refraction and viscosity of each fraction.

A second portion of this adduct (50 g., 0.28 mol.) was dissolved in 200 ml. of cold concentrated sulfuric acid and saturated with hydrogen fluoride. The upper layer which was assumed to be (2-phenylpropyl)methyldifluorosilane was added to excess methylmagnesium bromide in ether. In the usual way, 2-phenylpropyltrimethylsilane (VI) was isolated in 34% yield. By vapor-liquid phase chromatography this product was judged to be not less than 99% the same as VI, made by methylation of V.

α-Methylstyrene (1040 g., 8.8 mol.), chloroplatinic acid (9×10^{-5} mol.) and 1,3,5,7-tetramethylcyclotetrasiloxane (481 g., 8 equiv.) were heated at 110° overnight. The excess α-methylstyrene was removed at 1 mm. up to a temperature of 315°. The residue then had a viscosity of 211 cs. at 25°. Distillation without the potassium hydroxide gave 1355 g., 95% of a distillate boiling at a flask temperature of 315–320° at 1 mm., n_D^{25} 1.5258–1.5267, viscosity 184–203 cs. at 25°. Most of the distillate had n_D^{25} 1.5263–1.5266, viscosity 193–203 cs. at 25°.

1,3-Bis(2-phenylpropyl)tetramethyldisiloxane (IX). α-Methylstyrene (591 g., 5.0 mol.) and chloroplatinic acid (1 ml. of 0.06*M* solution in dioxane ethanol) were heated to 110° and *sym*-tetramethyldisiloxane (336 g., 2.5 mol.) was added in 50 ml. portions. The reaction proceeded slowly. The mixture was maintained at 110° overnight and distilled through a 1-inch by 3-inch vacuum-jacketed column containing no packing to yield a low boiling fraction (37 g.), b.p. 80° at 1 mm., which gave a positive test for Si-H. This material presumably is 1-(2-phenylpropyl)-1,1,3,3-tetramethyldisiloxane. On continued distillation there was recovered 1,3-bis(2-phenylpropyl)tetramethyldisiloxane (747 g., 81% yield) having the properties given in Table I.

2-Phenylpropyltrichlorosilane (X). α-Methylstyrene (354 g., 3.0 mol.) containing 6×10^{-5} mol. H_2PtCl_6 was kept at 100–110° in a flask equipped with a reflux condenser and a dropping funnel as trichlorosilane (330 ml., 3.3 mol.) was added during 6 hr. The mixture was then maintained at 110° overnight.

Fractionation of the mixture gave 2-phenylpropyltrichlorosilane (505 g., 67% yield) of X.

The residue from the above fractionation (137 g.) contained little hydrolyzable chloride, indicating that it was principally a polymer of α-methylstyrene.

RESEARCH DEPARTMENT
DOW CORNING CORP.
MIDLAND, MICH.

Action of Trifluoroacetic Acid on Peptide Bonds

KENNETH D. KOPPLE AND ELISABETH BÄCHLI

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In view of the utility of anhydrous trifluoroacetic acid as a protein solvent, a report on its reactivity toward peptide bonds may be of interest. Simple amides such as *N*-acetyl-β-phenylethylamine and acetanilide can be recovered unchanged

after prolonged heating in this solvent, but *N*-acyl amino acids and polypeptides undergo extensive trifluoroacetolysis. For example, during 20 hr. at reflux (71°) *N*-acetyl-L-leucine in 0.03 *M* solution was converted to a mixture of partially racemized leucine, *N*-trifluoroacetyl-L-leucine and acetyl-DL-leucine. After similar treatment of *N*-acetyl-DL-phenylalanine, phenylalanine and *N*-trifluoroacetyl phenylalanine were isolated; hippuric acid was converted to benzoic acid, *N*-trifluoroacetyl glycine and glycine. From L-leucine itself after 24 hours' heating with trifluoroacetic acid only traces of trifluoroacetyl L-leucine were isolated.[1]

Several amino acid polymers were treated with refluxing trifluoroacetic acid. Each was converted to a mixture of *N*-trifluoroacetyl amino acid plus trifluoroacetylated peptides, but complete degradation was not achieved.

Although the conditions under which trifluoroacetolysis occurs are relatively severe, these observations indicate a necessity for caution in using trifluoroacetic acid as a solvent for peptides and proteins, even when specifically acid labile residues such as serine[2] and tryptophane[3] are lacking.

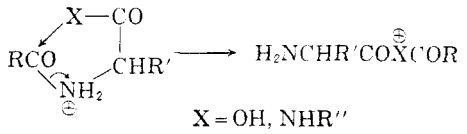
The trifluoroacetolysis reaction, which is probably similar to the hydrogen chloride catalyzed acetolysis of insulin reported by Vadja,[4] is apparently an equilibrium; experiments with hippuric acid indicate that the conversion to benzoic acid increases with increasing dilution. Catalytic quantities (0.1 mol. equiv.) of triethylamine, sulfuric acid, or trifluoroacetic anhydride did not affect the conversion after 24 hours' heating. The following reactions are probably involved.[5]

$$RCONHR' + CF_3COOH \rightleftharpoons RC\overset{\oplus}{O}NH_2R' + CF_3COO\ominus \quad (1)$$

$$RC\overset{\oplus}{O}NH_2R' + CF_3COO\ominus \rightleftharpoons RCOOCOCF_3 + (R'NH_2) \rightleftharpoons RCOO\ominus + CF_3C\overset{\oplus}{O}NH_2R' \quad (2)$$

$$RCOOCOCF_3 + CF_3COOH \rightleftharpoons RCOOH + (CF_3CO)_2 \quad (3)$$

Racemized products are formed by the usual interaction of α-acylamino acids and the anhydrides present in the medium.[6] The reactivity of α-acylamino acids and peptides is not explained by reactions (1) and (2) but might be accounted for by participation of the carboxyl or carboxamide group as in Equation 4.[7]



$$X = OH, NHR'' \quad (4)$$

Weygand and co-workers have reported the cleavage of peptides by trifluoroacetic anhydride in trifluoroacetic acid.[8] In the presence of the anhydride cleavage occurs more rapidly than under the conditions reported here. The direct *N*-acylation of amide groups suggested for reaction with the anhydride[8] seems less likely in pure trifluoroacetic acid, however.

EXPERIMENTAL

Reaction of hippuric acid with trifluoroacetic acid. Hippuric acid, m.p. 187–188°, (2.0 g.) was dissolved in commercially obtained anhydrous trifluoroacetic acid and the solution, protected from atmospheric moisture, was heated to reflux for 24 hr. Solvent was then removed by distillation at room temperature. The resulting oil was poured into 50 ml. of water and stored several hours at room temperature. A crystalline precipitate of benzoic acid, m.p. 122°, was collected and dried. The mother liquors were concentrated to 15 ml. and stored at 0–5° before a second crop of crystals, crude hippuric acid, m.p. 172–180° was collected. Extraction of these mother liquors with ether allowed isolation of crude trifluoroacetyl glycine, m.p. 95–106°, which could be recrystallized from benzene to m.p. 114°.[9]

When 40 ml. of trifluoroacetic acid solvent was used, the yield of benzoic acid was 50%, of trifluoroacetyl glycine 32%, and of recovered hippuric acid, 33%. When 250 ml. of solvent was used 92% of benzoic acid was isolated. Prolonged heating did not affect these yields.

Reaction of N-acetyl L-leucine with trifluoroacetic acid. N-Acetyl L-leucine, m.p. 196–198°[10] (1.0 g.) was treated as above with 200 ml. of trifluoroacetic acid. The oily reaction product was extracted three times with boiling benzene and the benzene extracts were concentrated to yield, after crystallization from ethyl acetate, 110 mg. of *N*-acetyl leucine, m.p. 154–165° (reported 157–158°),[11] $[\alpha]_D^{25}$ = 0.0°. The residue from the benzene extraction was taken up in ethyl acetate and filtered free of insoluble, ninhydrin positive material, 145 mg. (19%) which proved to be partially racemized L-leucine, m.p. 273–279° d., $[\alpha]_D^{25}$ = +8.5° (c = 2.02 in 6*N* hydrochloric acid, pure enantiomer +15.1°).[12] The material extracted into ethyl acetate was a mixture of acetyl and trifluoroacetyl leucine which exhibited carboxyl and trifluoroacetamido infrared absorption at 1730 cm.$^{-1}$, acetamido absorption at 1640 cm.$^{-1}$, and C—F absorption at 1160, 1185, and 1210 cm.$^{-1}$ Vacuum distillation afforded about 50 mg. of trifluoroacetyl-

(1) Similar treatment of L-leucine with acetic acid leads to acetyl-DL-leucine in 75% yield. E. A. Bell, *J. Chem. Soc.*, 2423 (1958).

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(10) M. Bergmann and J. Tietzman, *J. Biol. Chem.*, **155**, 535 (1944), report m.p. 189–190°.

(11) E. Fischer, *Ber.*, **34**, 444 (1901); a partially racemized acetyl-L-leucine, m.p. 155–167° is reported by A. Karrer, K. Escher, and R. Widmer, *Helv. Chim. Acta*, **9**, 322 (1926).

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L-leucine, m.p. 68°[13] and about 200 mg. of crude acetyl leucine, characterized by its infrared spectrum.

Reaction of Poly-L-leucine with trifluoroacetic acid. Poly-L-leucine (2.0 g.) was dissolved in 250 ml. of trifluoroacetic acid and treated as above. The reaction product was digested with ether and the material extracted by ether was distilled at 70–100° and 0.1 mm. pressure. The distillation yielded 0.4 g. of trifluoroacetyl-L-leucine, $[\alpha]_D^{25} = -35.2°$ (c = 1.0 in water, reported −39.4°[13]) (11%) and a non-volatile residue (0.64 g.) with the infrared spectrum of polyleucine. The ether insoluble residue, washed with aqueous sodium bicarbonate and with water, weighed 0.90 g. and exhibited infrared absorption due to CF_3— groups at 1160, 1185 and 1210 cm.$^{-1}$, in addition to the bands of the polyleucine spectrum.

Other trifluoroacetolyses. From 2.0 g. (0.01 mol.) of *acetyl-DL-phenylalanine* was obtained, after 36 hr. at reflux in 60 ml. of trifluoroacetic acid, 0.95 g. of *N*-trifluoroacetyl phenylalanine, m.p. 130°[9] after recrystallization from water, plus an undetermined amount of phenylalanine.

Acetanilide and *acetyl-β-phenylethylamine* were both recovered quantitatively after 24 hr. at reflux in 5% solutions.

Polyglycine and a *copolymer of DL-alanine and L-glutamic acid* were also treated with excess trifluoroacetic acid and the reaction product extracted with organic solvents. From these extracts were isolated *N*-trifluoroacetyl glycine and *N*-trifluoroacetyl-DL-alanine, respectively.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CHICAGO
CHICAGO, ILL.

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β-Arylglutaconic Acids. II.[1] Imides of Certain β-Arylglutaconic and Glutaric Acids

J. J. NERURKAR,[2] R. N. JOSHI, AND V. M. BHAVE

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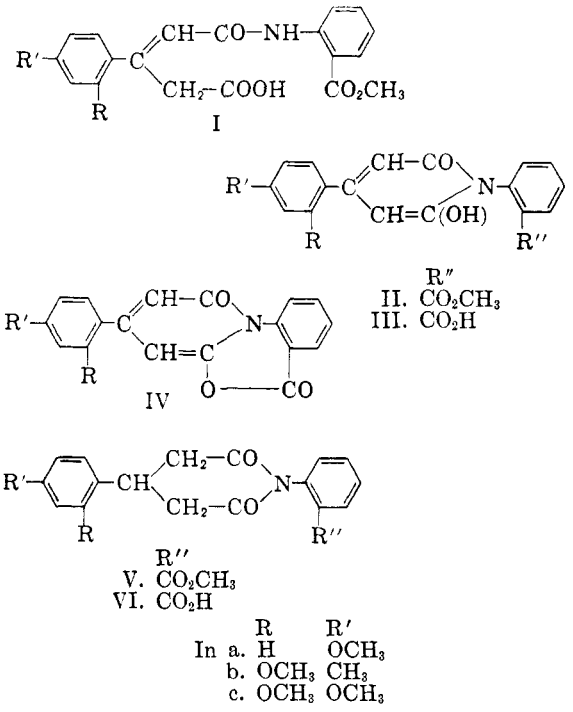
The anhydrides of β-arylglutaconic acids on treatment with equimolar quantities of methyl anthranilate in refluxing benzene solution give rise to the corresponding *cis*-semianilides (I).[1] In the present studies, the *cis*-semianilides were found to undergo dehydration when heated above 170–180° to give the corresponding imides (II) in 75–80% yield and a small quantity (5%) of a neutral substance which was later characterized as the *trans*-decarboxylation product.[3] The yield of the imides (II) was increased to 90–92% by heating at reflux temperature the β-arylglutaconic anhydrides with an excess of methyl anthranilate. The β-arylglutaconic anhydrides are in part enolic in nature, as indicated through production of a purple color with alcoholic ferric chloride solution and by the fact that they can be titrated as monobasic acids with standard alkali. The imides (II) should therefore exist partially in the enolic form. This fact was confirmed by a positive ferric chloride test and by titration with standard alkali. From the resulting alkaline solution the imides could be recovered by acidification in the cold.



Since we were interested in studying the chemical properties of these weakly acidic compounds, imides IIa, b, and c were synthesized from (a) β-(4-methoxyphenyl)glutaconic acid,[4] (b) β-(2-methoxy-4-methylphenyl)glutaconic acid,[5] and (c) β-(2,4-dimethoxyphenyl)glutaconic acid.[6]

When the carbomethoxy substituted hydroxyimides (IIa, b, and c, respectively) were boiled with strong sodium hydroxide solution (12.5*N*), they were hydrolyzed to the corresponding carboxyimides (IIIa, b, and c, respectively). Unlike the carbomethoxyimides (IIa, b, and c), these acids did not give any coloration with ferric chloride solution but did titrate as dibasic acids with standard alkali, indicating the presence of an enol group. This was further confirmed by treating the carboxyimides with acetic anhydride at reflux temperature. From the reaction mixture, neutral substances (40 to 50% yields) were isolated and after purification were characterized as the lactones (IVa, b, and c, respectively). When they were dissolved in dilute sodium hydroxide solution and the alkaline solution was neutralized, the starting carboxyimides (IIIa, b, and c, respectively) were recovered. This behavior confirms the

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(2) Present address: Laboratory of Pharmaceutical Chemistry, The University of Kansas, Lawrence, Kan.
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