TABLE I

DATA CONCERNING *N*-PHENYLPIPERAZINIUM SALTS DERIVED FROM VARIOUS ORGANIC ACIDS

Acids	Yield (%)	Melting Point (°C. corr.)	Nitrogen, % Calcd.	Found	Acids	Yield (%)	Melting Point (°C. corr.)	Nitrogen, % Calcd.	Found
p-Anisic	91.0	158.3–159.3	8.91	8.88	Isovaleric	70.0	78.9–80.4	10.59	10.25
Cyclohexanebutyric	92.0	87.7–88.6	8.42	8.29	Caprylic	40.0	58.4–60.6	9.13	8.87
Cyclohexaneacetic	93.0	79.4–80.9	10.85	10.82	Valeric	85.5	50.5–52.5	10.59	10.27
Cyclohexanecaproic	91.0	91.6–93.4	12.85	12.80	Phenoxyacetic	97.7	117.9–119.0	8.92	8.84
Cyclohexanevaleric	90.0	67.8–68.9	8.12	7.95	Propanoic	33.0	58.9–59.8	12.35	12.00
Cyclohexanepropionic	96.0	85.2–87.2	8.80	8.77	Salicylic	96.0	184.8–185.8	9.34	9.36
Acetic	91.0	82.0–83.0	12.61	12.50	Hendecanoic	50.0	50.5–52.5	8.04	8.38
Enanthic	40.0	56.1–57.5	9.56	9.43	Malonic	93.5	111.8–113.8	13.10	13.12
Caproic	35.5	65.2–67.3	10.05	9.85	Oxalic	95.0	226.7–227.2	12.45	12.47
Lauric	89.0	60.6–61.5	7.74	7.74	Isophthalic	97.0	184.4–185.8	11.41	11.26
Levulinic	65.5	82.8–84.2	10.12	10.32	Phthalic	98.0	188.3–189.9	11.41	11.25
Formic	75.5	112.6–113.6	13.71	13.68					

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Substituted α,α,α-Trifluoroacetophenones, α-Trifluoromethylbenzyl Alcohols, and α-Chloro-α-trifluoromethyltoluenes

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As part of a study of substituent effects in nucleophilic displacement reactions at electron-deficient, saturated carbon atoms, a series of five *meta* and *para* substituted α-chloro-α-trifluorotoluenes have been prepared. Three new substituted α,α,α-trifluoroacetophenones were obtained by the reaction of arylmagnesium bromides with trifluoroacetic acid.[1] The ketones were reduced by hydrogen or sodium borohydride to α-trifluoromethylbenzyl alcohols, which were converted to the corresponding chlorides by reaction with thionyl chloride. Preliminary studies indicate a very low reactivity of the chlorides toward the strong nucleophilic reagents iodide, thiosulfate, phenoxide, and butoxide ions, and towards alcoholic silver nitrate. In all cases *p*-methoxy-α-chloro-α-trifluoromethyltoluene was more reactive than the *p*-chloro, *m*-trifluoromethyl, or unsubstituted analogs.

TABLE I

α,α,α-TRIFLUOROACETOPHENONES, $YC_6H_4COCF_3$

Y	B.p., °C/Mm.	Yield, %	n_D^{30}	Formula	Calcd. C	Calcd. H	Found C	Found H
H[a]	66–67/33	67	1.4528					
p-CH_3[b]	81–82.5/22	66	1.4645					
p-CH_3O	70–70.5/2	56	1.4944	$C_9H_7O_2F_3$	52.9	3.5	53.2	3.6
p-Cl[c]	84/24	56	1.4852	$C_8H_4OClF_3$	46.1	1.9	48.9	2.3
m-CF_3	65–67.5/24	68	1.4100	$C_9H_4OF_6$	44.6	1.7	44.5	1.7
			α-Trifluoromethylbenzyl Alcohols, $YC_6H_4CHOHCF_3$					
H[d]	53–54.5/2	87	1.4550					
p-CH_3	74.5–75/2.5	72	1.4626[e]	$C_9H_9OF_3$	56.8	4.8	57.3	5.0
p-CH_3O	87–88/1	91	1.4743	$C_9H_9O_2F_3$	52.4	4.4	52.6	4.5
p-Cl	71–73/1.9	82	1.4785	$C_8H_6OClF_3$	45.6	2.9	45.7	3.1
m-CF_3	95–97/24	80	1.4133	$C_9H_6OF_6$	44.3	2.5	44.9	3.1
			α-Chloro-α-trifluoromethyltoluenes, $YC_6H_4CHClCF_3$					
H	70–71/27	73	1.4540	$C_8H_6F_3Cl$	49.4	3.1	49.2	3.3
p-CH_3	89–90/27	66	1.4590	$C_9H_8F_3Cl$	51.8	3.9	52.0	4.2
p-CH_3O	57.5–59.5/1	73	1.4746	$C_9H_8OClF_3$	48.1	3.6	47.9	3.9
p-Cl	95–95.5/24	67	1.4778	$C_8H_5Cl_2F_3$	41.9	2.2	41.6	2.4
m-CF_3	75.5–76.5/25	54	1.4128	$C_9H_5ClF_6$	41.1	1.9	40.9	2.2

[a] J. H. Simons and E. O. Rambler, *J. Am. Chem. Soc.*, **65**, 389 (1943). [b] J. D. Park, H. A. Brown, and J. R. Lacher, *J. Am. Chem. Soc.*, **73**, 709 (1951). [c] Impure sample. [d] E. T. McBee, O. R. Pierce, and J. F. Higgins, *J. Am. Chem. Soc.*, **74**, 1736 (1952). [e] 25°.

(1) K. T. Dishart and R. Levine, *J. Am. Chem. Soc.*, **78**, 2268 (1956).

EXPERIMENTAL

α-Trifluoromethylbenzyl alcohols. α,α,α-Trifluoroacetophenones were prepared by the procedure of Levine,[1] using the Grignard reagent from 1.0 mole of aryl bromide and 0.40 mole of trifluoroacetic acid. Hydrogenation of α,α,α-trifluoroacetophenone at 25 lbs. pressure using platinum oxide catalyst afforded α-trifluoromethylbenzyl alcohol in 48% yield. A better yield was obtained by sodium borohydride reduction in aqueous dioxane, so this procedure was used to prepare all of the substituted alcohols.

α-Chloro-α-trifluoromethyltoluenes. The α-trifluoromethylbenzyl alcohols (0.28 mole) were stirred at 150° for 2–3 hr. with 0.29 mole of pyridine and 0.29 mole of thionyl chloride. The reaction mixtures were poured into water, washed with dilute sulfuric acid, water, dilute sodium bicarbonate, and again with water, dried, and distilled.

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Carbamates and Dimethanesulfonates of Some New Glycols[1]

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The inhibitory effect of Myleran, 1,4-butanediol dimethanesulfonate[2] and urethane on the development of various tumors has been noted previously.[3] The availability of a series of previously unknown glycols has prompted our preparation of their dimethanesulfonates and dicarbamates as part of a program on cancer chemotherapy. The glycols were made available through the generosity of the Tennessee Eastman Company. Typical procedures for the preparation of the two types of compounds are given in the experimental section. Data for the preparation and characterization of all samples are given in Tables I and II. Dimethanesulfonates were obtained for all the glycols. Dicarbamates were obtained from most but not all. Available test data from the evaluation of these compounds in tumor retardation studies using Sarcome 180 has thus far disclosed no significant activity in any.[4]

EXPERIMENTAL[5]

Cyclohexane-1,4-dimethanol dimethanesulfonate. A solution of 2.8 g. (0.02 mole) of cyclohexane-1,4-dimethanol in 10 ml. of pyridine was cooled to 5–10°. Methanesulfonyl chloride, 5.7 g. (0.05 mole), was added dropwise with stirring. The reaction mixture was poured onto dilute hydrochloric acid and the precipitated product was collected, washed, dried, and recrystallized from benzene-petroleum ether to give 3.3 g. (56%) of the dimethanesulfonate, m.p. 162–163°.

Cyclohexane-1,4-diol dicarbamate. A solution of 2.3 g. (0.02 mole) of cyclohexane-1,4-diol in 25 ml. of dry acetone was added dropwise to a solution of 5 g. (0.05 mole) of phosgene in 35 ml. of dry acetone at −10°. The solution was warmed to 10° for 30–60 min., cooled to −20°, and treated with 100 ml. of concentrated ammonium hydroxide. The

TABLE I
GLYCOL DIMETHANESULFONATES

Glycol	M.P. (°C.)	Yield (%)	Solvent[a]	Analysis: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Cyclohexane-1,2-diol	136	76	AW	35.29	35.34	5.88	6.00
Cyclohexane-1,4-diol	148	45	AW	35.29	35.36	5.88	6.14
Cyclopentane-1,1-dimethanol	91	81	AW	37.76	37.86	6.29	6.37
Cyclohexane-1,1-dimethanol	54	66	MW	40.00	39.92	6.67	6.51
Cyclohexane-1,4-dimethanol	163	56	BP	40.00	39.92	6.67	6.68
3-Cyclohexene-1,1-dimethanol	87	100	AW	40.27	40.30	6.04	5.97
Norcamphane-2,2-dimethanol	112	80	AW	42.31	42.24	6.41	6.71
Norcamphane-2,3-dimethanol	115	36	MW	42.31	42.27	6.41	6.46
Norcamphane-2,5-dimethanol	136	49	MW	42.31	42.40	6.41	6.46
2,2′-(1,5-Naphthylenedioxy)-diethanol	189	90	N	47.52	47.81	4.95	5.20
Perhydro-1,4-naphthalenediol	152	30	MW	44.17	44.02	6.75	6.78
2,2′-(2,5-Dichloro-*p*-phenylenedioxy)diethanol	160	83	AW	34.04	34.15	3.78	3.76
2,2′-(2,5-Di-*t*-butyl-*p*-phenylenedioxy)diethanol	175	92	AW	51.50	51.58	7.30	7.50
2,2′-(4,4′-Sulfonyldiphenoxy)-diethanol	134	87	AW	43.72	43.68	4.45	4.46
5-Hydroxymethyl-β,β-5-trimethyl-2-*m*-dioxaneethanol	86	90	MW	40.00	39.92	6.67	6.72
β,β,β′,β′-Tetramethyl-2,4,8,10-tetraoxaspiro[5.5]undecane-3,9-diethanol	184	84	AW	44.35	44.45	6.96	7.16

[a] Solvent for recrystallization: B, benzene; P, petroleum ether; A, acetone; W, water; M, methanol; N, nitromethane.

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(2) This compound is indexed by *Chemical Abstracts* under methanesulfonic acid, tetramethylene ester.