lized as large, dark-orange needles, m.p. 190–191°. *Anal.* Calcd. for $C_{26}H_{24}N_4O_6$: C, 63.02; H, 5.08. Found: C, 63.02; H, 5.01.

***trans*-3,4-Bis-(*p*-methoxyphenyl)-cyclopentanone.**—Methyl *dl*-*β*,*γ*-bis-(*p*-methoxyphenyl)-adipate, m.p. 64–65°, 0.5 g. was subjected to ring closure as described above. The product, purified through Girard reagent and recrystallized from ligroin, was obtained in 66% yield; m.p. 110–111°. *Anal.* Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.85; H, 6.58.

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p-Fluorophenacyl Bromide Salts[1]

In order to obtain a variety of quaternary salts of heterocyclic nitrogen compounds all having the same quaternizing group attached to the nitrogen, so that correlations between structure and biological activity might be studied more conveniently, the salts listed in Table I were prepared for comparison with those previously reported.[2] The methods of preparation were in general the same as those described in the previous publications, care being taken to avoid altering any reactive substituent groups present on the rings. The solid heterocyclic bases which were insoluble in chloroform were treated with *p*-fluorophenacyl bromide in acetone or alcohol. The quinolinium and isoquinolinium salts were only slightly soluble in water, while the pyridinium and pyrazinium compounds were more soluble.

TABLE I

p-FLUOROPHENACYL BROMIDE SALTS

Salt from	Empirical formula	M.p.,[a] °C.	Ionic halogen, % Calcd.	Ionic halogen, % Found
		A. Substituted pyridines		
γ-Picoline	$C_{14}H_{13}BrFNO$	165–168	25.77	25.62, 25.64
2,6-Lutidine	$C_{15}H_{16}BrFNO$	248	24.65	24.30, 24.40
4-*n*-Amylpyridine	$C_{18}H_{21}BrFNO$	181	21.81	21.79, 21.80
2-*n*-Hexylpyridine	$C_{19}H_{23}BrFNO$	180	20.96	20.82, 20.78
2-Propanolpyridine	$C_{15}H_{18}BrFNO_2$	163	22.50	22.27, 22.41
3-Hydroxypyridine	$C_{13}H_{11}BrFNO_2$	223	25.61	25.36, 25.39
3-Aminopyridine	$C_{13}H_{12}BrFN_2O$	200–202	25.68	25.60, 25.70
3-Acetamino-pyridine	$C_{16}H_{14}BrFN_2O_2$	177–179	22.63	22.88, 22.79
3-Acetylpyridine	$C_{15}H_{13}BrFNO_2$	172–173	23.62	23.51, 23.82
3-Cyanopyridine	$C_{14}H_{10}BrFN_2O$	212	24.88	24.87, 24.98
Ethyl nicotinate	$C_{16}H_{15}BrFNO_3$	90	21.70	21.31, 21.36
Nicotinamide	$C_{14}H_{12}BrFN_2O_2$	226–228	23.56	23.23, 23.42
		B. Quinoline and isoquinolines		
Quinoline	$C_{17}H_{13}BrFNO$[b]	235	23.08	23.06, 23.54
Isoquinoline	$C_{17}H_{13}BrFNO$	202	23.08	23.04, 23.01
3-Methylisoquinoline	$C_{18}H_{15}BrFNO$	135–136	22.19	22.15, 21.98
		C. Chloropyrazine		
2-Chloropyrazine[c]	$C_{12}H_9BrClFN_2O$	183		[d]

[a] In nearly all cases the compounds melted with decomposition. [b] The corresponding iodide, $C_{17}H_{13}FINO$, m. p. 190–191°, calcd. I, 32.28: found I, 31.91, 32.45. [c] The product may be either the 3-chloropyrazinium salt or the 2-chloropyrazinium salt, but the former seems more likely since 3-bromopyridine reacts more readily than 2-bromopyridine. [d] Calcd.: C, 43.46; H, 2.74. Found: C, 43.57; H, 2.87.

Samples of these compounds have been submitted to the National Cancer Institute or the Midwest Research Institute for screening against tumors and data showing the variations in biological activity are to be published elsewhere.

We wish to express our thanks to Dr. M. J. Shear and Dr. J. L. Hartwell of the National Cancer Institute and Dr. L. H. Goodson and Dr. W. M. Hoehn of the Midwest Research Institute for their interest in this project, to Dr. J. H. Clark of the American Cyanamid Company for the 2-chloropyrazine used, and to Miss Marguerite Close for carrying out several of the Volhard halogen determinations and to the Microanalytical Laboratory of the National Institute of Health for the carbon and hydrogen analyses.

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RECEIVED MARCH 24, 1952

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[1] This research was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] C. T. Bahner, W. K. Easley, M. D. Pickens, H. D. Lyons, L. L. Norton, B. G. Walden and G. E. Biggerstaff, THIS JOURNAL, **73**, 3499 (1951); C. T. Bahner and L. L. Norton, *ibid.*, **72**, 2881 (1950).

Methyl Esters of Substituted Benzoic Acids[1]

Methyl *p*-phenoxybenzoate.—*p*-Phenoxybenzoic acid was prepared by carbonation of the Grignard reagent made in the usual way from 25 g. of *p*-bromodiphenyl ether. Pouring the Grignard solution onto crushed dry ice gave only very small amounts of the desired acid, but carbonation by the method of Hussey[2] yielded 7.5 g. (35%) of *p*-phenoxybenzoic acid, m.p. 158–160°. The methyl ester was prepared by boiling 5.15 g. of the acid with 70 ml. of methyl alcohol and 7 ml. of sulfuric acid for two hours, distilling off most of the methanol and washing the solid product with a solution of sodium bicarbonate and then with water. Recrystallization from methanol–water mixture yielded 4.0 g. (65%) of colorless crystalline methyl *p*-phenoxybenzoate, m.p. 59.5–60°. The ester is biaxial, crystallizing in the orthorhombic system, optically positive with $2V = 85°$; α, 1.515; β, 1.573; γ, 1.667 (calculated), exhibiting prismatic habit and irregular cleavage.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.90; H, 5.34.

Methyl *p*-Ethoxybenzoate.—A similar esterification with *p*-ethoxybenzoic acid gave the methyl ester in 75% yield. Recrystallization was effected from methanol–water and from ligroin. This ester forms colorless crystals melting at 37.5–38° to a colorless liquid which boils at 260°. The crystals are orthorhombic, with $2V = 85\text{–}90°$, showing prismatic habit and irregular fracture.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.71; H, 6.71.

Methyl anisate was found to have crystallographic properties similar to the two preceding esters. Microscopic examination showed crystals of this compound to be biaxial, orthorhombic, optically negative, with $2V = 70\text{–}75°$, exhibiting irregular prismatic habit and platy cleavage.

Methyl 3,4-Dichlorobenzoate.—Although it has been mentioned in a patent,[3] no properties of this compound have been reported. It was prepared in 81% yield from the corresponding acid by a similar Fischer esterification, followed by recrystallization from methanol. The ester crystallizes in long colorless prismatic needles, also in the orthorhombic system; m.p. 46.5–47.5°; b.p. 248°.

Anal. Calcd. for $C_8H_6O_2Cl_2$: C, 46.86; H, 2.95. Found: C, 46.97; H, 3.15.

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[1] All temperatures are corrected.

[2] A. S. Hussey, THIS JOURNAL, **73**, 1364 (1951).

[3] R. S. Long (to American Cyanamid Co.) U. S. Patent 2,392,167 (1946).

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RECEIVED JULY 31, 1951

Preparation of Cerous Ammonium Acetylacetonate

To 6 ml. (0.058 mole) of refluxing acetylacetone was added 6 ml. (0.091 mole) of concentrated ammonium hydroxide and the mixture refluxed for ten minutes. A solution of 500 mg. (0.0012 mole) of cerous nitrate hexahydrate in 3 ml. water was then introduced dropwise and the resulting solution refluxed for ten minutes. The solution was allowed to cool slowly and crystals formed after ten minutes standing at room temperature. After one hour the crystals were separated by filtration, dried, and washed with petroleum ether. A 90% yield of hexagonal yellow crystals was obtained. The material melted with decomposition at 143–144° and was found to be soluble (> 1 mg./ml.) in carbon tetrachloride, acetone and benzene, and insoluble in petroleum ether, hexane and isoöctane.

The analysis of this compound was carried out with a Sargent microcombustion apparatus. The water was absorbed by a tube filled with anhydrone and the carbon dioxide by ascarite. Final temperatures in each ignition were 850° and all were carried out in an atmosphere of commercial grade oxygen. The cerium was determined gravimetrically as the dioxide and the nitrogen by a modified Kjeldahl procedure.

Anal. Calcd. for $Ce(C_5H_7O_2)_3 \cdot 2NH_4C_5H_7O_2$: Ce, 20.9; C, 44.7; H, 6.46; N, 4.17. Found: Ce, 21.1; C, 44.8; H, 6.29; N, 4.28; molar ratios, C/Ce, 24.8; N/Ce, 2.03.

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RECEIVED FEBRUARY 25, 1952

Preparation of Praseodymium Ammonium Acetylacetonate

To 6 ml. (0.058 mole) of refluxing acetylacetone was added 6 ml. (0.091 mole) of concentrated ammonium hydroxide and the mixture refluxed for ten minutes. A solution of approximately 500 mg. of praseodymium nitrate (from the oxide in concentrated nitric acid evaporated to dryness) in 3 ml. of water was then introduced dropwise and the resulting solution refluxed for five minutes. The solution was allowed to cool slowly at room temperature and crystals formed within a few minutes. These crystals were a mixture of praseodymium acetylacetonate and the double salt with ammonia, and after being allowed to stand in the solution for one day were completely converted to the double salt. The solid was then separated by filtration, dried, and washed with petroleum ether. A 90% yield of hexagonal green crystals was obtained. The material melted at 145° and was found to be soluble (> 1 mg./ml.) in carbon tetrachloride and acetone, and insoluble in petroleum ether, hexane and isoöctane.

The analysis of this compound was carried out with Sargent microcombustion apparatus. The water was absorbed by a tube filled with anhydrone and the carbon dioxide by ascarite. Final temperatures in each ignition were 850° and all were carried out in an atmosphere of commercial grade oxygen. The praseodymium was determined gravimetrically as Pr_6O_{11} and the nitrogen by a modified Kjeldahl procedure.

Anal. Calcd. for $Pr(C_5H_7O_2)_3 \cdot 2NH_4C_5H_7O_2$: Pr, 20.9; C, 44.6; H, 6.45; N, 4.17. Found: Pr, 20.7; C, 44.8; H, 6.33; N, 4.03; molar ratios, C/Pr, 25.4; N/Pr, 1.96.

DEPARTMENT OF CHEMISTRY
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RECEIVED FEBURARY 25, 1952

COMMUNICATIONS TO THE EDITOR

CHROMATOGRAPHY OF STEREOISOMERS WITH "TAILOR MADE" COMPOUNDS

Sir:

Two years ago F. H. Dickey[1] published the results of his experiments on specific adsorption of silica gels prepared according to Pauling's suggestions[2] in the presence of the molecules for which specificity is desired. Since then no other news has appeared on this subject, in spite of the great interest in this new field. In previous work[3] we have established the conditions for the preparation of highly specific silica gels, which we used as chromatographic adsorbents. The influence of the acid used for the preparation of silica gel has been studied (we obtained good results with acetic acid and with cation exchange resins); it has also been pointed out that the most alkaline sodium silicate is the best starting material. Temperature has to be kept constant and at the same value at which the chromatographic experiments will be carried out.

Optical antipodes of camphorsulfonic and mandelic acids have been separated[4] using specific silica gels. An enrichment of 30% 1-camphorsulfonic acid was obtained in the percolate by only one passage through a column containing 5 g. of silica gel specific to *d*-camphorsulfonic acid; 200 ml. of 0.01 *m* *dl*-camphorsulfonic acid was used in this experiment. This gel had been prepared by adjusting the *p*H of 30 ml. of sodium silicate (d = 1.4; $Na_2O:SiO_2$ = 3.34), in which 2 g. of *d*-camphorsulfonic acid had been dissolved, to 4 and diluting with 250 ml. of water. The acid was extracted with methanol at room temperature and, since no optical activity was observed, we proceeded with the chromatography of *dl*-camphorsulfonic acid. Twenty-ml. fractions of the percolates were submitted to polarimetric measurements. A levo activity was observed to such an extent to leave no possible doubt of the effectiveness of the method. This activity increases in the second and third fraction of eluate; then it decreases, reaching the value of zero after 200 ml. has been chromatographed. The maximum of activity observed is of the order of a half degree, which corresponds to a 30% enrichment in *l*-camphorsulfonic acid. The apparent incongruence of an activity that increases passing from the first to the second and third fraction of percolate may be explained by the fact that a gel is not completely unadsorbent for the antipode opposite to the one for which the gel is specific.

Another series of experiments with mandelic acid confirmed the general applicability of this method, though the efficiency of the adsorbent was not as good as before, reaching now the value of 10% in the best fraction of percolate.

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(1) F. H. Dickey, *Proc. Nat. Acad. Sci.*, **35**, 229 (1949).

(2) *Chem. Eng. News*, **27**, 913 (1949).

(3) R. Curti, U. Colombo and F. Clerici, in press.

(4) R. Curti and U. Colombo, Communication at the Meeting of the Italian Chem. Soc. (Emilian Section) Dec., 1949.