

a multiplet for CH at 7.5, and $C_{ar}-H$ at 2.96 in a ratio of 9:10:1:10. The spectrum was identical with that of an authentic sample separated by v.p.c. from the partial alkaline desilylation of IV.

Alkaline Desilylations. Phenyl-1,2-bis(trimethylsilyl)ethane (I).—Heating 27 g. of I, 90 ml. of ethanol, 6 ml. of water, and 60 g. of potassium hydroxide at reflux (115°) for 24 hr., dilution with water, extraction with ether, and fractional distillation gave 17 g. (88.5%) of 1-phenyl-2-trimethylsilylethane: b.p. 117° (40 mm.), n_D^{25} 1.4840; lit.²⁵ b.p. 117° (40 mm.), n_D^{25} 1.4840. The infrared and H^1 n.m.r. spectra were identical with that of an authentic sample.²⁵

1,4-Diphenyl-1,4-bis(trimethylsilyl)butane (III).—Heating 5 g. of III, 60 ml. of ethanol, 4 ml. of water, and 40 g. of potassium hydroxide at reflux for 5 days, dilution with water, and recrystallization from methanol gave 2.2 g. (74%) and 2.3 g. (78%) of 1,4-diphenylbutane, m.p. 53°, lit.²⁶ 52.3° (infrared spectrum identical with reported spectrum²⁷), from IIIA and IIIB, respectively.

2,5-Diphenyl-2,5-bis(trimethylsilyl)hexane (IV).—A 0.6-g. sample of IV, 6 g. of ethanol, 1 g. of water, and 1 g. of potassium

hydroxide were heated in a Parr bomb at 200° for 16 hr. The cleavage product was isolated by preparative v.p.c. after diluting with pentane and extraction with water. Isomers IVA and IVB gave 0.290 (78%) and 0.340 g. (92%), respectively, of 2,5-diphenylhexane, n_D^{25} 1.5392. The infrared and H^1 n.m.r. spectra were identical with those of an authentic mixture of *dl* and *meso* isomers.¹¹ The H^1 n.m.r. spectrum shows a doublet for CH_3 at τ 8.86, a multiplet for CH_2 at 8.55, a multiplet for CH at 7.46, and $C_{ar}-H$ at 2.95 in a ratio of 3:2:1:5.

Heating the above samples for 16 hr. at 150° gave partial desilylation of IV to a mixture of V and 2,5-diphenylhexane.

1,1-Dimethyl-2,5-diphenyl-1-silacyclopentane (X).—Heating 2.0 g. of X, 6 g. of ethanol, 1 g. of water, and 2 g. of potassium hydroxide in a Parr bomb at 100° for 24 hr., dilution with water, and recrystallization from methanol gave 1.38 g. (88%) of 1,4-diphenylbutane.

1,1-Dimethyl-3,4-diphenyl-1-silacyclopentane (XI).—Treatment of 2 g. of XI by the above procedure gave 1.7 g. of recovered XI. A v.p.c. analysis prior to work-up showed no trace of cleavage products.

Acknowledgment.—We wish to thank Dr. A. Lee Smith, Dr. Paul Lauterbur, and Miss Wanda Ratsek for their aid in obtaining and interpreting the H^1 n.m.r. spectra.

(25) J. W. Ryan and J. L. Speier, *J. Org. Chem.*, **24**, 2052 (1959).

(26) K. T. Serijam and P. H. Wise, *J. Am. Chem. Soc.*, **74**, 365 (1952).

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Synthesis of Substituted β - and γ -Lactams

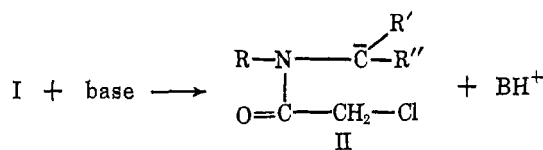
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The cyclization of N-substituted diethyl chloroacetamidomalonates, ethyl α -chloroacetamidophenylacetates, and diethyl ω -bromopropionamidomalonates to the corresponding substituted β - and γ -lactams has been achieved in high yields using a quaternary ammonium hydroxide type of anion-exchange resin, Amberlite IRA-400 (OH⁻), as catalyst.

Interest in the synthesis and chemistry of β -lactams has been greatly accelerated since the discovery of penicillin in 1929. Several¹ special and unique methods were developed to build up this cyclic amide which is very susceptible to reactions involving the carbonyl group. Among these, the Sheehan and Bose² synthesis appears to be most general in nature, as the yields reported were very high in all the cases. The method depends on a base-catalyzed ring closure of N-substituted diethyl chloroacetamidomalonates. It was shown that this intramolecular alkylation could be carried out in presence of such a weak base as triethylamine. The method, though novel, suffers from the fact that all the β -lactams possess one or two carbethoxy groups in position 4. The work carried out in this laboratory (to be published later) has shown the effectiveness of alcoholic potassium hydroxide in the intramolecular alkylation of compounds (I) in which the methine hydrogen is activated by groups other than two carbethoxy functions. A carbanion (II) is formed as an intermediate in all the cases, which undergoes cyclization with the elimination of halide ion.



Ion-exchange resins are finding increasing importance in a wide variety of organic reactions.³ Resins have been shown to be excellent catalysts in reactions such as cyanohydrin formation; aldol, Knoevenagel, and Michael condensations^{4,5}; the preparation of heterocyclic ketols⁶; the synthesis of nitriles⁷ from appropriate benzylhalides; and C-acylation of phenols.⁸

Shimo and Wakamatsu⁹ have reported the alkylation of various active methylene group containing compounds like ethyl malonate, cyanoacetic ester, and cyanoacetamide with various alkyl halides in the presence of an anion-exchange resin, Amberlite IRA-400 (OH⁻). However, utilization of an anion-exchange resin for the intramolecular alkylation leading to a ring closure has not been reported so far. The success achieved with anion-exchange resin in various alkylations encouraged us to synthesize β -lactams and γ -lactams according to Scheme I.

(3) R. Kunian, "Ion Exchange Resins," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958.

(4) R. W. Hein, M. J. Astle, and J. R. Shelton, *J. Org. Chem.*, **26**, 4874 (1961).

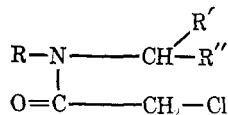
(5) E. D. Bergmann and R. Corett, *ibid.*, **23**, 1507 (1958).

(6) W. R. Boehme and J. Koo, *ibid.*, **26**, 3589 (1961).

(7) M. Gordon, M. L. Depamphilis, and C. E. Griffin, *ibid.*, **26**, 698 (1963).

(8) J. Price and S. S. Israelstam, *ibid.*, **29**, 2800 (1964).

(9) K. Shimo and S. Wakamatsu, *ibid.*, **23**, 504 (1963).

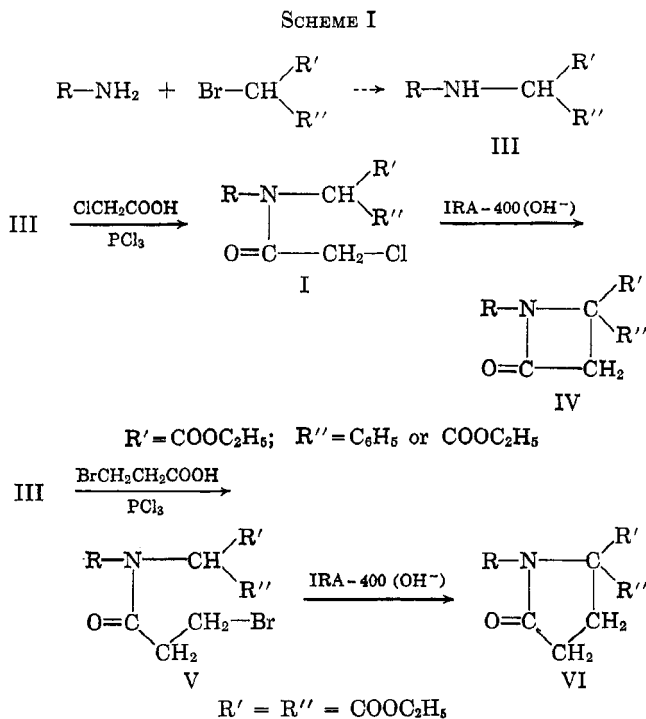


Ia, R' = H; R'' = COC₆H₅
b, R' = C₆H₅; R'' = COOC₂H₅

(1) J. C. Sheehan and E. J. Corey, *Org. Reactions*, **9**, 388 (1957).

(2) J. C. Sheehan and A. K. Bose, *J. Am. Chem. Soc.*, **72**, 5158 (1950).

SCHEME I



A quaternary ammonium hydroxide type of anion-exchange resin, Amberlite IRA-400 (OH⁻), was found to be an excellent catalyst for the cyclization of compounds I and V. The reaction was carried out in absolute ethanolic solution using molar equivalents of the reactants at room temperature with agitation for about 2 hr. with a magnetic stirrer. The cyclized product was obtained by simple filtration of the solution from the resin and evaporating the filtrate *in vacuo*. The yields with few exceptions were about 90–95%. This method therefore seems to be a rather general method for making lactams. The isolation of the products is less time consuming and involves fewer operations as compared to earlier methods of β -lactam synthesis.^{2,10} The resin can be readily regenerated and repeatedly used by washing with dilute sodium hydroxide solution. Solvents other than ethanol can also be used; *e.g.*, in one operation the reactants were stirred for 12 hr. in dry benzene and gave the product in 93–95% yield.

Substituted anilinomalونات and ethyl α -anilino-phenylacetates were prepared according to the method developed by Chatterjee, *et al.*,¹⁰ from the appropriate bromo esters. The products were characterized by elemental analyses and infrared spectra. The infrared spectra of these condensed products had two distinct peaks, one at 2.85 to 2.88 μ owing to the N–H stretching bond and the other at 5.72 to 5.78 μ owing to the carbonyl group of the carbethoxy function. Table I summarizes the properties of these products.

The chloroacetylated derivatives were prepared by heating a mixture of the condensed product III, monochloroacetic acid, and phosphorus trichloride in refluxing benzene for a period of 3–4 hr. according to the method of Bose.¹¹ The products (V) were obtained in a similar manner by treating the condensed products (III) with β -bromopropionic acid and phosphorus trichloride. In most cases, the products were colorless

(10) B. G. Chatterjee, P. N. Moza, and S. K. Roy, *J. Org. Chem.*, **28**, 1418 (1963).

(11) A. K. Bose, *J. Indian Chem. Soc.*, **31**, 108 (1954).

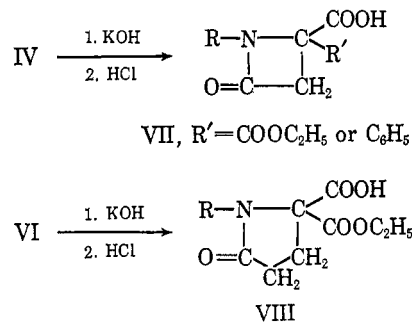
TABLE I
SUBSTITUTED DIETHYL ANILINOMALONATES AND
ETHYL α -ANILINOPHENYLACETATES

| Sl. no. | R | R' | R'' | M.p., °C. | Recrystn. solvent ^a | % yield |
|---------|---|----------------------------------|----------------------------------|-----------|--------------------------------|---------|
| 1 | C ₆ H ₅ | C ₆ H ₅ | COOC ₂ H ₅ | 81–82 | A | 86 |
| 2 | <i>p</i> -ClC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 82–83 | A–B | 95 |
| 3 | <i>p</i> -CH ₃ C ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 84–85 | A | 86 |
| 4 | <i>p</i> -BrC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 98–99 | A–B | 90 |
| 5 | C ₆ H ₅ | COOC ₂ H ₅ | COOC ₂ H ₅ | 44–45 | C | 100 |
| 6 | <i>p</i> -ClC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 91–92 | A | 100 |
| 7 | <i>p</i> -CH ₃ C ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 55–56 | D | 96 |
| 8 | <i>p</i> -BrC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 92–93 | A | 95 |
| 9 | β -C ₁₀ H ₇ | COOC ₂ H ₅ | COOC ₂ H ₅ | 86–87 | A–C | 95 |

^a A, petroleum ether (b.p. 60–80°); B, benzene; C, ether; and D, petroleum ether (b.p. 90–120°).

crystalline solids having a sharp melting point. They were characterized by elemental analyses as well as by infrared spectra. The infrared spectra of these compounds showed a peak at 5.95–6.0 μ owing to the carbonyl of the amide function and the usual peak at about 5.75 μ owing to the carbonyl of the ester functions. The absence of the peak at 2.82–2.88 μ showed that acylation had taken place. Table II summarizes the products prepared and their properties.

The cyclized products were easily identified and distinguished from the starting materials by means of their infrared spectra. The infrared spectra of the cyclized products show a shift of the band at 6.0 μ , present in the spectra of the starting material, to 5.65–5.75 μ . This band is assigned to the lactam carbonyl. The products were further characterized by comparison with authentic samples obtained by conventional methods or with the derivatives of authentic samples obtained by usual methods; for example, the liquid lactams IV or VI could be easily hydrolyzed by alcoholic potassium hydroxide to the corresponding mono acids VII and VIII which were crystalline



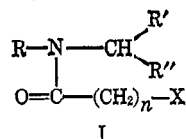
solids with sharp melting points. A change in the time of reaction or in the ratio of the reactants in the above cyclizations did not improve the yields. Table III summarizes the results of these cyclizations.

Experimental Section¹²

Typical procedures are described for the synthesis of β - and γ -lactams.

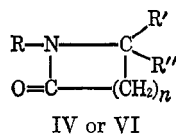
Synthesis of 1-*p*-Tolyl-4-carbethoxy-4'-phenylazetid-2-one.
A. Ethyl α -*p*-Toluidinophenylacetate (III).—A mixture of 10.7 g. of *p*-toluidine and 12.0 g. of ethyl α -bromophenylacetate

(12) All melting points are uncorrected.

TABLE II
HALOACYLATED DERIVATIVES

| Sl. no. | R | R' | R'' | n | X | M.p., °C. (n_D^{20}) | % yield | % C | | % H | | % N | |
|---------|---|----------------------------------|----------------------------------|---|----|--------------------------|---------|--------|-------|--------|-------|--------|-------|
| | | | | | | | | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| 1 | C ₆ H ₅ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | Cl | 93-94 ^a | 80 | 65.16 | 65.00 | 5.43 | 5.43 | 4.22 | 4.40 |
| 2 | <i>p</i> -ClC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | Cl | 76-77 ^b | 70 | 57.44 | 57.43 | 4.52 | 4.61 | 3.72 | 3.76 |
| 3 | <i>p</i> -BrC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | Cl | 175-177 ^b | 80 | 52.61 | 52.67 | 4.14 | 4.32 | 3.41 | 3.56 |
| 4 | <i>p</i> -CH ₃ C ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | Cl | 74-75 ^b | 85 | 65.80 | 66.01 | 5.77 | 5.82 | 4.04 | 4.14 |
| 5 | C ₆ H ₅ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | Cl | 93-94 ^c | 84 | | | | | | |
| 6 | <i>p</i> -ClC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | Cl | (1.5187) ^d | 82 | 49.72 | 49.95 | 4.69 | 4.91 | 3.86 | 4.01 |
| 7 | <i>p</i> -CH ₃ C ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | Cl | (1.4755) ^c | 75 | | | | | | |
| 8 | <i>p</i> -BrC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | Cl | (1.5323) ^d | 80 | 44.28 | 44.41 | 4.18 | 4.32 | 3.44 | 3.51 |
| 9 | β -C ₁₀ H ₇ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | Cl | (1.5605) ^e | 78 | | | | | | |
| 10 | C ₆ H ₅ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | Br | 51-52 ^c | 85 | | | | | | |
| 11 | <i>p</i> -ClC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | Br | 72-73 ^b | 80 | | | | | 3.32 | 3.19 |
| 12 | <i>p</i> -CH ₃ C ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | Br | 49-50 ^c | 70 | | | | | | |
| 13 | <i>p</i> -BrC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | Br | 94-95 ^a | 70 | | | | | 3.04 | 2.94 |

^a Crystallized from benzene-petroleum ether (b.p. 40-60°). ^b Crystallized from petroleum ether (b.p. 60-80°). ^c A. K. Bose, B. N. G. Mazumdar, and B. G. Chatterjee, *J. Am. Chem. Soc.*, **82**, 2382 (1960). ^d Known compounds. P. N. Moza, Ph.D. Thesis, Indian Institute of Technology, Kharagpur, 1962. ^e Final product characterized.

TABLE III
SUBSTITUTED β - AND γ -LACTAMS

| Sl. no. | R | R' | R'' | n | M.p., °C. (n_D^{20}) | Recrystn. solvent ^a | % yield |
|---------|---|----------------------------------|----------------------------------|---|--------------------------|--------------------------------|---------|
| 1 | C ₆ H ₅ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | 75-76 ^b | A-B | 95 |
| 2 | <i>p</i> -ClC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | (1.5773) ^c | ... | 89 |
| 3 | <i>p</i> -CH ₃ C ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | 49-50 ^d | A | 90 |
| 4 | <i>p</i> -BrC ₆ H ₄ | C ₆ H ₅ | COOC ₂ H ₅ | 1 | (1.5850) ^c | ... | 91 |
| 5 | C ₆ H ₅ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | (1.5162) ^c | ... | 90 |
| 6 | <i>p</i> -ClC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | (1.5260) ^c | ... | 83 |
| 7 | <i>p</i> -CH ₃ C ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | 85-87 ^b | C | 92 |
| 8 | <i>p</i> -BrC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | (1.5395) ^c | ... | 95 |
| 9 | β -C ₁₀ H ₇ | COOC ₂ H ₅ | COOC ₂ H ₅ | 1 | 76-77 ^e | A | 92 |
| 10 | <i>p</i> -BrC ₆ H ₄ | COOCH ₃ | COOCH ₃ | 1 | 143-144 ^f | B | 95 |
| 11 | C ₆ H ₅ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | (1.5135) ^c | ... | 85 |
| 12 | <i>p</i> -ClC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | (1.5220) ^c | ... | 85 |
| 13 | <i>p</i> -CH ₃ C ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | (1.5245) ^c | ... | 89 |
| 14 | <i>p</i> -BrC ₆ H ₄ | COOC ₂ H ₅ | COOC ₂ H ₅ | 2 | (1.5410) ^c | ... | 83 |

^a A, Petroleum ether (b.p. 60-80°); B, benzene; and C, cyclohexane. ^b Identified by comparison with an authentic sample. ^c These compounds were hydrolyzed to their monoacids and characterized. ^d *Anal.* Calcd. for C₁₉H₁₉NO₅: C, 73.54; H, 6.12; N, 4.51. Found: C, 73.48; H, 6.13; N, 4.45. ^e Known compound: P. N. Moza, Ph.D. Thesis, Indian Institute of Technology, Kharagpur, 1962. ^f *Anal.* Calcd. for C₁₃H₁₂BrNO₅: C, 45.90; H, 3.50; N, 4.09. Found: C, 45.76; H, 3.54; N, 3.85.

(prepared by brominating phenylacetyl chloride and treating the product with absolute ethanol) was placed in a round-bottomed flask fitted with a two-way stopcock and evacuated to 40-mm. pressure. It was kept in an oven maintained at 65-70° for 8 hr. by which time the reaction mixture became a solid cake. This was extracted with benzene and filtered. The residue, *p*-toluidine hydrobromide, weighed 8.5 g. (90.0%). The filtrate was washed with 2 *N* hydrochloric acid and then with distilled water. The benzene solution was dried over anhydrous sodium sulfate and the solvent was removed under slightly reduced pressure whereupon pale yellow needles crystallized from the residue. Recrystallization from a mixture of benzene-petroleum ether (b.p. 40-60°) afforded a pale yellow needlelike crystalline material, m.p. 84-85°. The infrared spectrum showed peaks at 2.82 μ owing to the N-H stretching bond and 5.78 μ owing to the carbonyl of the carboxylic function: yield 10.8 g. (80%).

Anal. Calcd. for C₁₇H₁₉NO₅: C, 75.83; H, 7.06; N, 5.20. Found: C, 75.45; H, 7.04; N, 5.35.

B. Ethyl *N*-(*p*-Tolyl)- α -chloroacetamidophenylacetate (I).—

Ethyl α -*p*-toluidinophenylacetate (5.0 g.) and monochloroacetic acid (5.0 g.) were dissolved in dry benzene (75 ml.) and refluxed with phosphorus trichloride (2.5 ml.) for a period of 4 hr. The reaction mixture was cooled and the benzene solution was decanted and washed several times (five and six times) with distilled water. The solution was dried over anhydrous sodium sulfate and the solvent was stripped off under slightly reduced pressure. The residue obtained soon solidified, and it was recrystallized from petroleum ether (b.p. 60-80°) as a colorless crystalline substance, m.p. 74-75°, yield 5.5 g. (85%). The infrared spectrum shows peaks at 5.70 μ owing to the carbonyl of the ester group and 5.95 μ owing to the carbonyl of the open-chain amide function.

Anal. Calcd. for C₁₉H₂₀ClNO₅: C, 65.80; H, 5.77; N, 4.04. Found: C, 66.01; H, 5.82; N, 4.14.

Conversion of the Resin to the Hydroxyl Form.—The anion-exchange resin Amberlite IRA-400 was obtained as the chloride salt. The conversion of the resin to the hydroxyl form was accomplished by washing the resin with 1 *N* sodium hydroxide

until the eluate gave a negative silver nitrate test for chloride ion. The resin was then thoroughly washed with distilled water until the washings were neutral. It was then dried in an oven for several hours at about 40° and kept in a vacuum desiccator for 24 hr. before use.

C. 1-*p*-Tolyl-4-carbethoxy-4'-phenylazetid-2-one (IV).—Ethyl *N*-(*p*-tolyl)- α -chloroacetamidophenylacetate (0.69 g.) was dissolved in absolute ethanol (10 ml.) and the resin (0.88 g.) was added to it and the contents were stirred by means of a magnetic stirrer for 2 hr. at room temperature. The reaction mixture was then filtered and the resin was washed once with a little absolute alcohol. The resin gave a positive test for chloride ion. The filtrate was evaporated in a vacuum desiccator leaving behind a colorless viscous liquid. Maceration of this liquid with petroleum ether (b.p. 90–120°) afforded a colorless crystalline material (0.56 g., 90%). Recrystallization from petroleum ether afforded colorless crystals, m.p. 49–50°. The infrared spectrum had peaks at 5.65 μ owing to the β -lactam carbonyl and 5.72 μ owing to the carbonyl of the ester group.

Anal. Calcd. for C₁₉H₁₉NO₃: C, 73.54; H, 6.12; N, 4.51. Found: C, 73.48; H, 6.13; N, 4.45.

Synthesis of 1-Phenyl-5,5'-dicarbethoxypyrrolidin-2-one (VI). **A. Diethyl Anilinomalonate (III).**—A mixture of 9.3 g. of freshly distilled aniline and 11.95 g. of diethyl bromomalonate was placed in a round-bottomed flask fitted with a two-way stopcock and evacuated to 40-mm. pressure. The reaction mixture was then allowed to stand at 70° in an oven for 8 hr. Extraction of the solid cake with ether afforded a residue of 8.6 g. of aniline hydrobromide which corresponded to 100% conversion. The ethereal solution was washed with 2 *N* hydrochloric acid and then with distilled water. Removal of the solvent after drying the solution over anhydrous magnesium sulfate afforded the anilinomalonate as colorless crystalline solid, m.p. 44–45°, yield 11.9 g. (95%).

B. Diethyl ω -Bromopropionilidomalonate (V).—A mixture of

diethyl anilinomalonate (5.0 g.), β -bromopropionic acid (5.0 g.), and phosphorus trichloride (2.5 ml.) was refluxed in dry benzene solution for about 4 hr. The cooled reaction mixture was decanted and the benzene solution was thoroughly washed with distilled water. The dried solution was distilled to remove as much solvent as possible. The residue obtained was a pale yellow viscous liquid which soon solidified. Recrystallization from petroleum ether (b.p. 60–80°) afforded colorless plates, m.p. 51–52°, yield 85%. The infrared spectrum shows peaks at 5.75 μ owing to the carbonyl of the ester groups and at 6.0 μ owing to the carbonyl of the open-chain amide function. A flame test indicated the presence of halogen.

C. 1-Phenyl-5,5'-dicarbethoxypyrrolidin-2-one (VI).—An absolute ethanolic solution of diethyl ω -bromopropionilidomalonate (0.78 g.) was treated with the resin (0.88 g.) and stirred magnetically at room temperature for a period of 2 hr. The resin was filtered off and washed with little absolute alcohol. The resin gave a positive test for bromide ion. The alcoholic solution was carefully evaporated in a vacuum desiccator, leaving a pale yellow liquid. It had a refractive index of 1.5135 at 30° and was halogen free (yield 85%). The refractive index agreed well with that of an authentic sample. A small portion of the liquid was hydrolyzed with potassium hydroxide giving the monoacid, 1-phenyl-5-carboxy-5'-carbethoxypyrrolidin-2-one, m.p. 150–151°. There was no depression in a mixture melting point with a sample prepared by the conventional method. The infrared spectrum had peaks at 5.75 and 5.70 μ .

Acknowledgment.—The authors wish to express their sincere thanks to Professor Ajay K. Bose of Stevens Institute of Technology, Hoboken, New Jersey, for kindly supplying the infrared spectra of all the compounds sent to him and for his valuable suggestions.

Aromatic Fluorine Compounds. III.¹ Introduction of a Fluorine Atom into Substituted Aromatic Rings

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The gas phase decarboxylation of aromatic fluoroformates was successfully applied to substituted aromatic fluoroformates, containing substituents of sufficiently high thermal stability, such as bromine, fluorine, methyl, or trifluoromethyl. The method was also successful in the case of the polycyclic α -naphthyl fluoroformate. A polar reaction mechanism (S_Ni) is suggested. In the case of *p*-methoxyphenyl fluoroformate the corresponding fluoride could not be obtained.

In the preceding paper¹ a novel method has been described for introducing a fluorine atom into an aromatic ring by gas phase decarboxylation of phenyl fluoroformate or thiol fluoroformate. Yields of fluorobenzene as high as 90% have been achieved. In this paper the application of this method to nuclear-substituted aromatic compounds will be reported.

Eight different substituted aromatic fluoroformates were prepared and their decarboxylation was investigated. Table I gives the results of their preparation from the corresponding phenols and COFCl. When small amounts of a tertiary amine were used as a catalyst a nearly quantitative conversion of the starting material to the fluoroformate was obtained. The use of an organic solvent such as toluene or benzene in these reactions was advantageous. All reactions were carried out in stainless steel cylinders at over atmospheric pressures; however, a continuous process at atmospheric pressure should be applicable too.

(1) For part II of this series, see K. O. Christe and A. E. Pavlath, *J. Org. Chem.*, **30**, 3170 (1965).

The purity of the COFCl was not critical. Impurities as high as 10% of COCl₂ and COF₂ did not influence the yield of fluoroformate so long as COFCl was used in excess. Table II shows the physical and spectral properties of these compounds. All of them are colorless lachrymatory liquids with a strong fluoroformate odor. Their thermal stability is higher than that of comparable chloroformates.

The high-temperature gas phase decarboxylation was investigated only in quartz tubes with Pt-gauze filling, since this system had previously given the best results for phenyl fluoroformate.¹ Table III shows the results of these reactions; however, no attempts were made to maximize the yields. Therefore, the yields of the corresponding substituted aryl fluorides, listed in Table III (ranging from 25 to 57%), could probably be increased by investigating the most favorable reaction conditions.

The new method is limited to substituents that exhibit a higher thermal stability than the fluoroformate group. In the case of *p*-methoxyphenyl fluoroformate,