Anal. Calcd for $C_{12}H_{23}NO_3$ (6): C, 62.85; H, 10.11; N, 6.11; mol wt, 229. Found: C, 62.82; H, 10.08; N, 6.22; mol wt, 237 (determined in benzene by vapor phase osmometry).

N-*p*-Tolyl-5-*n*-butoxymethylene-2-oxazolidone (8).—After reaction of *p*-tolyl isocyanate (26.6 g, 0.2 mol) with butyl glycidyl ether (27.3 g, 0.21 mol) and removal of the solvent as described earlier, an amber oil (54 g) remained. The oil was distilled twice to yield 38 g of **8**: bp 185.5–188° (0.2 mm); $n^{20}D$ 1.5255; ir (neat) 2965 (s), 2935 (s), 2870 (m), 1753 (vs), 1523 (s), 1425 (s), 1410 (s), 1320 (s), 1228 (s), 1135 (s), 983 (m), 810 (m), and 750 (w) cm^{-1}.

Anal. Calcd for $C_{15}H_{21}NO_3$ (8): C, 68.41; H, 8.04; N, 5.32; mol wt, 263. Found: 68.32; H, 7.99; N, 5.52; mol wt, 264 (determined in benzene by vapor phase osmometry).

Glpc of analytically pure **8** at 250° using an 8 ft × 1/8 in. column packed with 3% SE-52 on Chromosorb W indicated the presence of two components: a minor component A, thought to be the 4 isomer, (*ca.* 4% by weight), and a major component B, **8** (*ca.* 96% by weight, 70% yield).

The reaction was repeated using 0.98 mol of *p*-tolyl isocyanate and 1.03 mol of *n*-butyl glycidyl ether to provide a 78% yield of analytically pure **8**.

N-*p*-Tolyl-5-phenoxymethylene-2-oxazolidone (7).—Reaction of *p*-tolyl isocyanate (26.6 g, 0.2 mol) with phenyl glycidyl ether (31.5 g, 0.21 mol) in the presence of a catalytic amount of lithium chloride (0.08 g) gave 48.2 g (0.17 mol, 85% yield) of crude **7**, mp 153–155°, after removing the solvent (DMF) and subsequent treatment with ice-cold carbon tetrachloride. Recrystallization from boiling 95% ethyl alcohol gave analytically pure **7**: mp 153.5–155.5°; ir (KBr) 1735 (vs), 1595 (m), 1520 (s), 1500 (m), 1445 (m), 1420 (m), 1405 (s), 1340 (s), 1253 (s), 1226 (m), 1146 (s), 1095 (m), 1085 (m), 1043 (m), 988 (m), 803 (m), 753 (s), and 687 (m) cm^{-1}.

Anal. Calcd for $C_{17}H_{17}NO_3$ (7): C, 72.06; H· 6.05; N, 4.94; mol wt, 283. Found: C, 71.84; H, 5.88; N, 5.01; mol wt, 280 (determined in benzene by vapor phase osmometry).

N-*n*-Butyl-5-phenoxymethylene-2-oxazolidone (5).—The preceding reaction was repeated using 19.8 g (0.2 mol) of *n*-butyl isocyanate. Removal of solvent (DMF) *in vacuo* left 51.6 g of an oily amber solid. One recrystallization from carbon tetrachloride (35 ml)–hexane (70 ml) provided 41.7 g (168 mmol, 84% yield) of **5**, mp 35–39°. Analytically pure **5**, mp 41.5–43.5°, was obtained after recrystallization from 50% aqueous alcohol and then from cyclohexane: ir (KBr) 2950 (m), 2920 (m), 2860 (w), 1740 (s), 1580 (m), 1480 (m), 1445 (m), 1240 (m), 1055 (m, broad), 750 (w), and 685 (w) cm^{-1}.

Anal. Calcd for $C_{14}H_{19}NO_3$ (5): C, 67.45; H, 7.68; N, 5.62; mol wt, 249. Found: C, 67.70; H, 7.68; N, 5.51; mol wt, 243 (determined in benzene by vapor phase osmometry).

Registry No.—**1**, 17539-79-6; **2**, 17539-80-9; **3**, 17539-81-0; **4**, 17539-82-1; **5**, 17539-83-2; **6**, 17539-84-3; **7**, 5255-84-5; **8**, 17539-86-5; **9**, 17539-87-6; **10**, 17539-88-7; **11** (R = *p*-tolyl), 7549-96-4; **12**, 17539-90-1; **13**, 7693-76-7; **14**, 7693-82-5; **15**, 14627-60-2; **16**, 17539-94-5; **17**, 7693-77-8; **18**, 17539-96-7; **19**, 15042-67-8; **20**, 15042-69-0.

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The Thermal Rearrangement of Some Optically Active Pyrroles[1]

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At 575° (+)-N-(1-phenylethyl)pyrrole isomerizes to the corresponding 2- (42 ± 3%) and 3-(1-phenylethyl)-pyrrole (11 ± 1%), each isomer being formed with 77 ± 3% retention of configuration. Under the same conditions (+)-2-(1-phenylethyl)pyrrole is converted into the 3 isomer in 18% yield, the 2 isomer being recovered with 73 ± 3% retention of configuration. Likewise at 600° the *sec*-butyl group in N-(*sec*-butyl)pyrrole migrates to both the 2 and 3 positions with 85 ± 1 and 75 ± 2% retention of configuration, respectively. (+)-N-(1-Phenylethyl)- or N-(*sec*-butyl)-2,5-dimethylpyrrole on pyrolysis give mixtures of 2-alkyl-3,5-dimethylpyrrole and 3-alkyl-2,5-dimethylpyrrole. When the migrating group is 1-phenylethyl, migration produces both isomers with 40% retention of configuration; when the migrating group is *sec*-butyl, the 2 and 3 isomers are produced with 77 and 75% retention of configuration, respectively. The results are consistent with the formation of a 2H-pyrrole intermediate arising through a closely associated transition state.

Alkyl[2] and benzyl[3] substituents in N-substituted pyrroles migrate at high temperatures to the 2 and 3 positions in the pyrrole ring by a homogeneous unimolecular process. The large negative entropies of activation observed imply a cyclic transition state. In addition, the facts that activation energies were about 90% as large as the estimated bond dissociation energies and that all substituents (in substituted benzyl substituents) increased the reaction rate led Pine[3] to suggest that homolytic bond breaking had occurred to the extent of 90% in the transition state.

To investigate further the nature of a migration involving a radicallike species, thermal isomerizations were carried out with pyrroles in which the migrating group was asymmetric. The results of experiments in which (+)-N-(1-phenylethyl)-, (+)-2-(1-phenylethyl)-, (+)-N-(*sec*-butyl)-, and (+)-2-(*sec*-butyl)-pyrrole were pyrolyzed are reported in Table I. The precision of the data is indicated by the average deviations obtained from duplicate and triplicate experiments.

While the extent of the isomerization (and decomposition) was dependent on temperature and heat exchanger (catalysis by Berl saddles) in the N-phenylethylpyrrole pyrolyses, the amount of retention of configuration was not influenced appreciably by these variables. In the N-*sec*-butylpyrrole experiments, catalysis by the Berl saddles was nil. The expected increase in product formation with higher temperatures was observed. Also the 2 isomer was formed with a greater degree of stereospecificity than the 3 isomer in the migration of the *sec*-butyl group.

The estimate of the extent of retention of configuration for the formation of 3 isomer previously reported (10%)[1] was based upon the rotation of an impure sample (3-*sec*-butylpyrrole) and upon the erroneous

(1) (a) Supported by the U. S. Army Research Office, Durham. (b) A portion of these results were communicated previously: J. M. Patterson and L. T. Burka, *J. Amer. Chem. Soc.*, **88**, 3671 (1966).

(2) (a) I. A. Jacobson, Jr., H. H. Heady, and G. V. Dinneen, *J. Phys. Chem.*, **62**, 1563 (1958); (b) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **66**, 1245 (1962); (c) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **68**, 3068 (1964).

(3) L. A. Pine, *Dissertation Abstr.*, **24**, 522 (1963).

TABLE I

YIELD AND PER CENT RETENTION OF CONFIGURATION OF PYROLYSIS PRODUCTS FROM THE N-SUBSTITUTED PYRROLES[a]

Substituent	Pyrolysis temp, °C	Yield[b] of isomer, % N	2	3	Decompn, %	Retention of isomer, % 2	3
(+)-N-Ph(Me)CH[c]	575	36 ± 8[d]	42 + 3	11 + 1	11 ± 5	77 ± 3	77 + 3
(+)-2-Ph(Me)CH[e]	575		74	18	8	73 ± 3	
(+)-N-Ph(Me)CH	550	69	24	4	3	80	
(+)-N-Ph(Me)CH[f]	550[g]	41 ± 7	40 ± 2	8 ± 1	11 ± 5	77 ± 5	80 ± 2
(+)-N-*sec*-Bu	575[g]	69	23	4	4	79	
(+)-N-*sec*-Bu	600[g]	49 ± 1[e]	34 ± 1[e]	8 ± 1[e]	9 ± 1[e]	86	78
(+)-N-*sec*-Bu[e]	600	59 ± 4[h]	30 ± 1	6 ± 2	5 ± 2	84 ± 1	74 ± 1
(+)-N-*sec*-Bu	625	36[i]	41	13	10	77	71
(+)-2-*sec*-Bu	600		64	23	11	100	56 ± 10[j]

[a] Pyrolysis over Vycor beads. [b] Reported as glpc area per cent. [c] Average of three experiments. [d] Retention of optical activity, 99.5 ± 0.2%. [e] Average of two experiments. [f] Average of four experiments. [g] Pyrolysis over Berl saddles. [h] Retention of optical activity, 99.1 ± 0.1%. [i] Retention of optical activity, 96.2%. [j] Based on average deviation of observed rotation.

TABLE II

YIELD AND PER CENT RETENTION OF CONFIGURATION OF PYROLYSIS PRODUCTS FROM THE SUBSTITUTED DIMETHYLPYRROLES[a]

Substituent	Pyrolysis temp, °C	Yield[b] of isomer, % N	2[c]	3[d]	Decompn, %	Retention of isomer, % 2[c]	3[d]
(+)-N-Ph(Me)CH[e]	525	25 ± 5[f]	15 ± 2	46 ± 9	15 ± 5	40 ± 1	39 ± 1
(+)-N-Ph(Me)CH	500	37	10	43	10	...	49
(+)-N-*sec*-Bu[e]	575	16 ± 4[g]	31 ± 5	40 ± 1	13 ± 2	77 ± 3	75 ± 1
(+)-N-*sec*-Bu	525	59	14	23	4	77	75

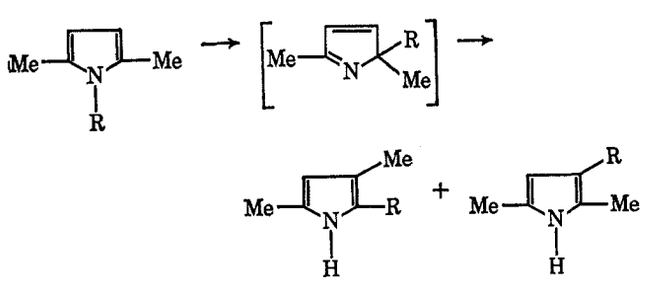
[a] Pyrolysis over Vycor beads. [b] Reported as glpc area per cent. [c] 2-Substituted 3,5-dimethylpyrrole. [d] 3-Substituted 2,5-dimethylpyrrole. [e] Average of two experiments. [f] Retention of optical activity, 97 ± 2%. [g] Retention of optical activity, 99.6 ± 0.2%.

assumption (phenylethylpyrroles) that the rotations of the 2 and 3 isomers were approximately the same.

In all experiments except those carried out at 625°, the N isomer was recovered with 99+% of its original optical activity. At the higher temperature some racemization of the N isomer was found. These results are consistent with the mechanism proposed by Jacobson and coworkers[2] in which the 2 isomer is irreversibly formed from the N isomer, while the 3 isomer is reversibly formed from the 2 isomer.

In some preliminary experiments in which the 2 isomer was pyrolyzed under the same conditions as the N isomer, the recovered starting material was obtained in 73 + 3% retention when the migrating group was 1-phenylethyl and in 100% retention when the migrating group was *sec*-butyl. The 3-(*sec*-butyl)pyrrole was obtained with 56 ± 10% retention in this experiment.

As the pyrolysis of trisubstituted pyrroles leads to rearrangement products probably arising through a 2H-pyrrole intermediate,[4] the stereochemistry of the thermal isomerization of optically active N-substituted 2,5-dimethylpyrroles was also investigated. The results of these pyrolysis studies are reported in Table II.



Both the ease of isomerization and the extent of racemization appear to be a function of the stability of the radicals or partially developed radicals making up the closely associated transition state involved in the migration. Thus the phenylethyl substituent migrates more readily and is racemized to a greater extent than the *sec*-butyl substituent. Similarly, the methyl substituents enhance the stability of the partially developed pyrryl radical, and the result is a more facile isomerization and a larger amount of racemization than that observed with the N-substituted pyrroles. Steric crowding at the migration terminus (by the methyl substituents) may also contribute to the higher degree of racemization observed with the dimethylpyrroles and to increased radical dissociation. The isolation of *meso*-2,3-diphenylbutane as a minor product from the N-(1-phenylethyl)-2,5-dimethylpyrrole pyrolysate and of 2,4- and 2,5-dimethylpyrrole from the N-(*sec*-butyl)-2,5-dimethylpyrrole pyrolysate is evidence for the radical dissociation. No special effort was made to detect the presence of *dl*-2,3-diphenylbutane in the pyrolysate.

The N-substituted pyrroles were synthesized from the appropriate amine and 2,5-dimethoxytetrahydrofuran[5] or from the appropriate amine and 2,5-hexanedione.[4] The (+)-N-substituted pyrroles were obtained from the (+)-amine in all synthesis experiments except for (+)-N-(1-phenylethyl)pyrrole which was obtained from (−)-amine.

The ir and nmr spectra of the (+)-2-*sec*-butyl- and (+)-3-*sec*-butylpyrroles (obtained from the pyrolyses) were consistent with the structures assigned, and the properties of these isomeric pyrroles corresponded to

(4) J. M. Patterson and S. Soedigdo, *J. Org. Chem.*, **33**, 2057 (1968).

(5) Procedure adapted from N. Elming and N. Clauson-Kaas, *Acta Chem. Scand.*, **5**, 867 (1952).

those previously reported.[6] The relationship of rotation to optical purity as well as the relationship of the configurations of (+)-2-*sec*-butyl- and (+)-3-*sec*-butylpyrroles to (+)-*sec*-butyl bromide has been established previously.[6] Since (+)-*sec*-butyl bromide has the same configuration as (+)-*sec*-butylamine,[7] migration of the substituent occurred with retention of configuration.

The structures assigned to the pyrolysis products of N-(1-phenylethyl)pyrrole were verified by synthesis from pyrrylmagnesium bromide and 1-phenylethyl bromide. The ir and nmr spectra of each of the isomers were consistent with the assigned structures.

The configuration and optical purity of the (+)-2 and (+)-3 isomers, obtained from the pyrolysis of (+)-N isomer and in turn synthesized from (−)-phenylethylamine, were established by permanganate oxidation[6] to (+)-hydratropic acid. The acid was converted into methyl hydrotropate for purification by glpc. The two isomers had the same configuration and exhibited very similar optical rotatory dispersion curves. As it has been shown by Bernstein and Whitmore[8] that (+)-hydratropic acid and (−)-phenylethylamine have the same configuration, the 1-(phenylethyl) group migrates to both the 2 and 3 positions with retention of configuration.

The ir and nmr spectra obtained from the (+)-N-(*sec*-butyl)-2,5-dimethylpyrrole pyrolysis products were identical with those obtained from the reaction products of 2,5-dimethylpyrrylmagnesium bromide and of 2,4-dimethylpyrrylmagnesium bromide with *sec*-butyl bromide. The configuration and optical purity of the isomeric pyrroles were established by permanganate oxidation;[6] both the (+)-2-(*sec*-butyl)- and (+)-3-(*sec*-butyl)dimethylpyrroles were converted into (+)-2-methylbutyric acid. The isomerization occurs with retention of configuration.

Likewise the structures of the pyrolysis products of (+)-N-(1-phenylethyl-2,5-dimethylpyrrole were verified by synthesis from 2,5-dimethylpyrryl- and 2,4-dimethylpyrrylmagnesium bromides and 1-phenylethyl bromide.

Pyrolysis of (+)-N-(1-phenylethyl)-2,5-dimethylpyrrole, synthesized from (+)-1-phenylethylamine produced (+)-2-(1-phenylethyl)- and (−)-3-(1-phenylethyl)dimethylpyrroles. Since oxidation of each isomer followed by esterification produced methyl (−)-hydratropate, the N substituent migrates to the 2 and 3 position with retention of configuration.

Experimental Section

Boiling points are uncorrected. Gas chromatographic analyses and separations were made on an F & M Model 810-R-12 gas chromatograph using the columns and temperatures specified. Infrared spectra were measured on a Beckman IR-8 spectrophotometer; ultraviolet spectra were measured on a Perkin-Elmer Model 202 spectrophotometer; and nmr spectra (δ) were measured on a Varian HA-60 IL spectrometer in carbon tetrachloride solutions (*ca.* 10%) using tetramethylsilane (TMS) as an internal standard (δ 0). Optical rotatory dispersion curves were measured on a Jasco recording spectropolarimeter. Rotations were obtained on neat liquids in 1-dm tubes, unless otherwise specified, using a Rudolph Model 63 polarimeter. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

N-(1-Phenylethyl)pyrrole.[5]—To a solution of 60.6 g (0.5 mol) of 1-phenylethylamine in 100 ml of glacial acetic acid (exothermic reaction) was added 66.0 g (0.5 mol) of 2,5-dimethoxytetrahydrofuran, and the mixture was refluxed 1.5 hr. After removal of the acetic acid by distillation, the reaction mixture was cooled and dissolved in 150 ml of ether. The ether solution was washed with two 100-ml portions of water, two 100-ml portions of 0.1 *N* sodium hydroxide, and two 100-ml portions of 0.05 *N* hydrochloric acid and then dried over magnesium sulfate. After removal of the drying agent by filtration and the ether by distillation, the residue was distilled at reduced pressure. There was obtained 58 g (68%) of colorless liquid: bp 116–117° (7 mm); n^{25}D 1.5581; λ_{max}^{MeOH} 206 mμ (ϵ 17,000), 258 (280), 262 (250), 268 (170); nmr spectrum, 1.71 (doublet, 3 H), 5.08 (quartet, 1 H), 5.97 (triplet, 2 H), 6.51 (triplet, 2 H), and 7.05 ppm (multiplet, 5 H).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.31; H, 7.86; N, 7.96.

(+)-N-(1-Phenylethyl)pyrrole.—1-Phenylethylamine was resolved by the method of Theilacker and Winkler[9] using (+)-tartaric acid: bp 69.5–70.5° (12 mm); n^{25}D 1.5244; $[\alpha]^{25}$D −37.97 ± 0.02°. Rotations reported are $[\alpha]^{22}$D −40.3°,[9] $[\alpha]^{15}$D +40.7°,[10] $[\alpha]^{23}$D +39.9°.[11] Using the rotation of Leithe,[10] the optical purity was 93.3%. Reaction of the amine with 2,5-dimethoxytetrahydrofuran produced 73.7 g (67%) of colorless liquid: bp 112–112.5° (6 mm); n^{25}D 1.5588; d^{25} 1.018 g/ml; $[\alpha]^{25}$D +47.65 ± 0.02° (neat). The nmr and ir spectra were identical with those obtained with the racemic N-(1-phenylethyl)pyrrole. Gas chromatographic analysis on a 6 ft × 0.125 in. 10% SE-30 column at 150° showed one peak.

N-(*sec*-Butyl)pyrrole.[5]—2,5-Dimethoxytetrahydrofuran (40.8 g, 0.31 mol) was added to a solution of 23.0 g (0.32 mol) of *sec*-butylamine in 75 ml of glacial acetic acid, and the mixture was refluxed 3.5 hr. The reaction mixture was cooled, poured into 900 ml of water, and extracted with four 500-ml portions of ether. The ether extract was washed four times with water and once with saturated sodium bicarbonate solution and dried over magnesium sulfate. After removal of the drying agent by filtration and the ether by distillation, the residue was distilled at atmospheric pressure yielding 17 g (45%) of colorless liquid: bp 156–157.5°; n^{25}D 1.4687; λ_{max}^{MeOH} 215 mμ (ϵ 7030); nmr spectrum, 0.74 (triplet, 3 H), 1.34 (doublet, 3 H), 1.63 (triplet, 2 H), 3.77 (quartet, 1 H), 5.90 (triplet, 2 H), and 6.45 ppm (triplet, 2 H).

Anal. Calcd for $C_8H_{13}N$: C, 77.99; H, 10.63; N, 11.37. Found: C, 78.34; H, 10.57; N, 11.30.

(+)-N-(*sec*-Butyl)pyrrole.—*sec*-Butylamine was resolved by the method of Leithe[12] using (+)-tartaric acid: bp 62.5–63°; n^{25}D 1.3912; $[\alpha]^{25}$D +8.12 ± 0.04° (neat). Based upon the reported rotation of $[\alpha]^{25}$D +8.1° (neat),[11] optical purity was 100%. Treatment of 36.5 g (0.50 mol) of the amine with 66.0 g (0.50 mol) of 2,5-dimethoxytetrahydrofuran in 100 ml of glacial acetic acid yielded 31.3 g (51%) of colorless liquid: bp 156.5–157.5°; n^{25}D 1.4683; d^{25} 0.871 g/ml; $[\alpha]^{25}$D +34.8 ± 0.1°. The ir spectrum was identical with the one obtained from the racemic N-(*sec*-butyl)pyrrole. Gas chromatographic analysis using a 6 ft × 0.125 in. 10% SE-30 column showed only one peak.

In another experiment, N-(*sec*-butyl)pyrrole of 30.8% optical purity, $[\alpha]^{25}$D +10.2° (neat), was prepared from *sec*-butylamine, $[\alpha]^{25}$D +2.5° (neat).

(+)-N-(1-Phenylethyl)-2,5-dimethylpyrrole.—(+)-1-Phenylethylamine was recovered from the mother liquor of the resolution of 1-phenylethylamine with (+)-tartaric acid by the procedure described by Ault:[13] bp 71–71.5° (12 mm); n^{25}D 1.5245; $[\alpha]^{25}$D +39.72 ± 0.02°; 97.6% optical purity.[10] The procedure reported for the synthesis of N-benzyl-2,5-dimethylpyrrole was employed.[4] From 85.9 g (0.75 mol) of 2,5-hexanedione, 90.8 g (0.75 mol) of (+)-1-phenylethylamine, and 15 ml of acetic acid in benzene, there was obtained 125.8 g (86%) of colorless liquid

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(10) W. Leithe, *Monatsh. Chem.*, **51**, 381 (1929).
(11) H. E. Smith, S. L. Cook, and M. E. Warren, Jr., *J. Org. Chem.*, **29**, 2263 (1964).
(12) W. Leithe, *Ber.*, **63**, 800 (1930).
(13) A. Ault, *J. Chem. Educ.*, **42**, 269 (1965).

boiling at 133–134° (7 mm): $n^{25}D$ 1.5554; d^{25} 1.006 g/ml; $[\alpha]^{25}D$ +26.97 ± 0.02° (neat), +35.6 ± 0.4° (*c* 6.29, CCl_4); λ_{max}^{MeOH} 213 mμ (ε 4880); nmr spectrum, 1.72 (doublet, 3 H), 1.96 (singlet, 6 H), 5.30 (quartet, 1 H), 5.57 (singlet, 2 H), and 7.07 ppm (multiplet, 5 H).

Anal. Calcd for $C_{14}H_{17}N$: C, 84.36; H, 8.60; N, 7.03. Found: C, 84.58; H, 8.86; N, 7.15.

(+)-N-(*sec*-Butyl)-2,5-dimethylpyrrole.—A solution of 59.4 g (0.81 mol) of (+)-*sec*-butylamine {$[\alpha]^{25}D$ +7.91 ± 0.02° (neat); 97.6% optical purity[11]} and 92.5 g (0.81 mol) of 2,5-hexanedione was refluxed for 4 hr during which time the water formed in the reaction was removed by azeotropic distillation. After removal of the benzene, the residue was distilled through a 10-cm Vigreux column to give 98.5 g (81%) of colorless liquid: bp 199°; $n^{25}D$ 1.4834; d^{25} 0.8952 g/ml; $[\alpha]^{25}D$ +25.40 ± 0.01° (neat), 27.0 ± 0.1 (*c* 8.12, CCl_4); λ_{max}^{MeOH} 214 mμ (ε 7564); nmr spectrum, 0.76 (triplet, 3 H), 1.39 (doublet, 3 H), 1.75 (multiplet, 2 H), 2.16 (singlet, 6 H), 4.0 (multiplet, 1 H), 5.47 ppm (singlet, 2 H).

Anal. Calcd for $C_{10}H_{17}N$: C, 79.41; H, 11.33; N, 9.26. Found: C, 79.06; H, 11.10; N, 9.10.

Pyrolysis of the Substituted Pyrroles—The following procedures are representative of the pyrolysis experiments. The pyrolyses were carried out in a vertically arranged 95 × 2.5 cm Vycor reactor tube which contained 50 ml of Vycor beads or Berl saddles used as a heat exchanger. The tube was heated in a Lindberg Hevi-Duty three-zone tube furnace; the temperature was regulated to ±5° of the indicated value over the volume containing the heat exchanger. The sample was introduced at a constant rate from a syringe mounted on a syringe drive (driven by a Troemner monodrum unit) and swept through the reactor by a stream of dry nitrogen at a flow of 100 ml/min. The liquid products were collected in a trap cooled by an ice–water mixture, weighed, and analyzed by gas chromatography. A 6 ft × 0.125 in. 10% SE-30 column was used for the analysis of the phenylethylpyrroles (150°), the *sec*-butylpyrroles (80°), and the phenylethyldimethylpyrroles (160°); a 6 ft × 0.125 in. 10% UC-W98 column was used for the analysis of the *sec*-butyldimethylpyrroles (130°).

Pyrolysis of (+)-N-(1-Phenylethyl)pyrrole.—The pyrrole (28.8 g) was added at a constant rate over 6.5 hr to the reactor tube, containing Vycor beads, at 575°. The crude pyrolysate weighed 27.3 g (94% recovery) and contained (glpc analysis) 28.5% N isomer, 41.3% 2-(1-phenylethyl)pyrrole, 12.0% 3-(1-phenylethyl)pyrrole, and 18.2% decomposition products. Unrearranged N isomer was removed from the pyrolysate by distillation through a 30 × 1 cm column packed with glass helices. The fraction boiling at 110–113° (7 mm) was 100% pure (glpc analysis) and had a rotation of $[\alpha]^{25}D$ +47.37 ± 0.05° (neat), which corresponds to 99.4% retention of its optical activity.

The residue was distilled through a short-path distillation apparatus, and the distillate was separated into the 2 and 3 isomers by preparative glpc using a 12 ft × 0.375 in. 20% Carbowax 20M column at 225°.

(+)-2-(1-Phenylethyl)pyrrole was further purified by glpc using a 12 ft × 0.375 in. 20% SE-30 column at 225° (99.9% pure, glpc analysis): bp 138–140° (10 mm); $n^{25}D$ 1.5708; d^{25} 1.043 g/ml; $[\alpha]^{25}D$ +60.19 ± 0.03°, +66.2 ± 0.7° (*c* 10.07, CCl_4), $[\alpha]_{546}^{25}$ +71.84 ± 0.03° (neat); $\nu_{max}^{CCl_4}$ 3490 cm^{-1} (N–H); λ_{max}^{MeOH} 209 mμ (ε 13,800), 262 (610), 269 (343); nmr spectrum, 1.48 (doublet, 3 H), 3.83 (quartet, 1 H), 5.84 (multiplet, 2 H), 6.23 (multiplet, 1 H), and 7.03 ppm (multiplet, 5 H).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 83.82; H, 7.41; N, 8.10.

(+)-3-(1-Phenylethyl)pyrrole was further purified by glpc using an 8 ft × 0.375 in. 24% Apiezon L column at 175° (99.1% pure, glpc analysis): bp 153° (10 mm); $n^{25}D$ 1.5728; d^{25} 1.047 g/ml; $[\alpha]^{25}D$ +8.58 ± 0.04° (neat), +24.0 ± 0.7° (*c* 4.62, CCl_4), $[\alpha]_{546}^{25}$ +10.10 ± 0.04°; $\nu_{max}^{CCl_4}$ 3490 cm^{-1} (N–H); λ_{max}^{MeOH} 210.5 mμ (ε 12,800), 262.5 (383), 269 (290); nmr spectrum, 1.48 (doublet, 3 H), 3.88 (quartet, 1 H), 5.85 (multiplet, 1 H), 6.10 (multiplet, 1 H), 6.30 (multiplet, 1 H), and 7.10 ppm (multiplet, 5 H).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.29; H, 7.67; N, 8.06.

Synthesis of 2- and 3-(1-Phenylethyl)pyrrole.—To pyrrylmagnesium bromide, prepared from ethylmagnesium bromide (0.5 mol, 12 g of magnesium and 54 g of ethyl bromide) and 33.5 g (0.5 mol) of pyrrole was added slowly 92.5 g (0.5 mol) of 1-phenylethyl bromide. The mixture was heated on a steam bath for 30 min and allowed to stand overnight. After the complex was decomposed with 200 ml of 15% ammonium chloride solution, the ether layer was separated, washed with water, and dried over magnesium sulfate. After removal of the drying agent and the ether, the residue was distilled under reduced pressure, bp 137–142° (9 mm). The 2 and 3 isomers were separated on an 8 ft × 0.375 in. Carbowax 20M column at 250° giving refractive indices of $n^{25}D$ 1.5709 and 1.5724, respectively. The gas chromatography retention times, the ir spectra, and the nmr spectra were identical with those obtained from the 2 and 3 isomers produced on pyrolysis.

Oxidation of (+)-2-(Phenylethyl)pyrrole.—The method of Skell and Bean[6] was adapted. To a solution of 44 g (0.28 mol) of potassium permanganate in 500 ml of water cooled to 10°, 4.0 g (0.023 mol) of (+)-2-(1-phenylethyl)pyrrole ($[\alpha]^{25}D$ +60.19°) was added portionwise while maintaining the temperature at 10°. After stirring at 5–10° for an additional 2 hr, the manganese dioxide and excess permanganate were decomposed with sulfur dioxide. The reaction mixture was made acidic to congo red with concentrated hydrochloric acid. The acidic material, obtained by extraction of the reaction mixture with five 50-ml portions of ether, was extracted into 125 ml of 25% sodium hydroxide solution which, in turn, was extracted twice with 50 ml of ether. The acid was recovered from the alkaline solution by acidification with 50% sulfuric acid and by extraction with three 100-ml portions of ether. After drying over anhydrous magnesium sulfate, the drying agent was removed by filtration, and the ether was removed by distillation. The crude acid residue was converted into the acid chloride by the method of Smejkal and Farkas[14] in which the acid was refluxed for 30 min with a mixture of 3 ml of thionyl chloride and 10 ml of hexane. After removal of the hexane and thionyl chloride on a rotary evaporator, the crude acid halide was treated with an excess of anhydrous methanol (*ca.* 5 ml). The unreacted methanol was removed by distillation; the residue was dissolved in ether; and the ether solution was washed twice with 25 ml of saturated sodium bicarbonate solution. After drying (magnesium sulfate), the ether was distilled and the crude methyl hydratropate purified by preparative glpc using an 8 ft × 0.375 in. 24% Apiezon L column at 125°: $n^{25}D$ 1.4933; $[\alpha]^{25}D$ +79.4° (*c* 3.59, ethanol) (authentic sample, $n^{25}D$ 1.5000). The ester showed only one peak on glpc analysis (retention time identical with that obtained on an authentic sample), and the ir spectrum was identical with one obtained from authentic material. Based upon the reported[15] rotation of $[\alpha]^{23}D$ + 108.7° (*c* 5.5 ethanol) for ester prepared from 96% optically pure hydratropic acid, the methyl hydratropate obtained from the oxidation of the 2 isomer is 70% optically pure. The isomerization of the substituent from the N to the 2 position occurred with 75% retention of configuration.

Oxidation of (+)-3-(Phenylethyl)pyrrole.—Using the procedure described for the oxidation of the 2 isomer, there was obtained insufficient methyl hydratropate for an accurate rotation. Oxidation of a larger sample of the 3 isomer (obtained in another experiment from the isomerization of the N isomer of 83.7% optical purity), $[\alpha]^{25}D$ +7.55 ± 0.03° (neat), +20.4 ± 0.1° (*c* 3.77, CCl_4), gave methyl hydratropate (99.3% pure, glpc analysis) with a rotation of $[\alpha]^{25}D$ +73 ± 1° (*c* 3.91, ethanol) and optical purity of 65%. Using these values, the optical purity of the 3 isomer initially oxidized was 74%. The ir spectrum and the glpc retention time of the ester were identical with those obtained from an authentic sample. The isomerization to the 3 position occurred with 79% retention of configuration.

Pyrolysis of (+)-2-(1-Phenylethyl)pyrrole.—When 5 g of the 2-substituted pyrrole {bp 136–138° (10 mm); $n^{25}D$ 1.5723; 99.9% pure, glpc analysis; $[\alpha]^{25}D$ +63.11 ± 0.03° (neat); 70.7% optical purity} was pyrolyzed under the conditions used for the N isomer, there was obtained 4.7 g (94% recovery) of of pyrolysate which contained (by glpc analysis) 74.1% 2 isomer, 18.6% 3 isomer, and 6.6% decomposition products. In addition, there was produced material (0.7%) which had the same glpc retention as the N isomer but which was not characterized further. Separation and purification of the pyrolysate by the procedures previously described for the N-(1-phenylethyl)pyrrole pyrolysis gave recovered 2-(1-phenylethyl)-

(14) J. Smejkal and J. Farkas, *Coll. Czech. Chem. Commun.*, **28**, 481 (1963).
(15) W. A. Bonner and J. A. Zderic, *J. Amer. Chem. Soc.*, **78**, 3218 (1956).

pyrrole (99.5% pure, glpc analysis; $n^{25}D$ 1.5716; $[\alpha]^{25}D$ +48.09 ± 0.04°) with 76% retention of optical activity.

In another experiment, the 2 isomer was obtained in 74.3% yield (70% retention of optical activity), and the 3 isomer was obtained in 18.1% yield.

The ir spectra of all the isomers were identical with those obtained from authentic samples.

Pyrolysis of (+)-N-(*sec*-Butyl)pyrrole.—The pyrrole (24.6 g, $[\alpha]^{25}D$ +34.8 ± 0.1°, optical purity 100%) was added at a constant rate over 6 hr to the reactor tube (containing Vycor beads) at 600°. The pyrolysate (21.7 g, 88% recovery) contained (glpc analysis) 54.9% N isomer, 31.1% 2-(*sec*-butyl)-pyrrole, 7.5% 3-(*sec*-butyl)pyrrole, and 6.5% decomposition products. Most of the unreacted N isomer was removed from the pyrolysate by distillation through a 30 × 1 cm column packed with glass helices. The fraction boiling at 65–69° (40 mm) was collected and further purified by preparative glpc using an 8 ft × 0.375 in. 30% SE-30 column at 70°: 99.7% pure (glpc analysis); $n^{25}D$ 1.4685; $[\alpha]^{25}D$ +34.5 ± 0.1° (neat), 99.1% optical purity. This represents 99.1% retention of the optical activity. The residue, consisting of 2 and 3 isomers, was separated by preparative glpc using an 8 ft × 0.375 in. 30% Carbowax 20M column at 150°.

The (+)-2-(*sec*-butyl)pyrrole after further purification using glpc (8 ft × 0.375 in. 30% SE-30 column at 85°) was 99.7% pure: $n^{25}D$ 1.4910; d^{25} 0.904 g/ml; $[\alpha]^{25}D$ +22.00 ± 0.05°, 84% optical purity; ν_{CCl_4} 3390, 3480 cm^{-1} (N–H); nmr spectrum, 0.90 (multiplet, 3 H), 1.22 (multiplet, 3 H), 1.50 (multiplet 2 H), 2.57 (multiplet, 1 H), 5.79 (multiplet, 1 H), 5.97 (multiplet, 1 H), 6.43 (multiplet, 1 H), and 7.55 ppm (broad) {lit.[6] $n^{25}D$ 1.4900; $[\alpha]^{25}D$ +11.24 (43% optical purity)}. The isomerization to the 2 isomer occurred with 84% retention of configuration.

The (+)-3-(*sec*-butyl)pyrrole was purified by preparative glpc using an 8 ft × 0.375 in. 30% SE-30 column at 100°: 99.9% pure, glpc analysis; $n^{25}D$ 1.4873; d^{25} 0.910 g/ml; $[\alpha]^{25}D$ +20.4 ± 0.1° (neat, 0.5 dm), +22.0 ±0.8° (*c* 2.50, ethanol), 22.3 ± 0.4° (*c* 5.16, ethanol); ν_{CCl_4} 3390, 3490 cm^{-1} (N–H); nmr spectrum, 0.80 (triplet, 3 H), 1.12 (doublet, 3 H), 1.40 (multiplet, 2 H), 2.43 (multiplet, 1 H), 5.90 (multiplet, 1 H), 6.30 (multiplet, 1 H), and 6.40 ppm (multiplet, 1 H) {lit.[6] $n^{25}D$ 1.4878; $[\alpha]^{25}D$ +11.98° (43% optical purity)}. The isomerization to the 3 isomer occurred with 73% retention of configuration.

In another experiment in which pyrrole (9.73 g) of 30.8% optical purity {$[\alpha]^{25}D$ 10.2° (neat)} was pyrolyzed in a tube containing Berl saddles at 575°, there was obtained 8.68 g (90% recovery) of pyrolysate containing (glpc analysis) 69% N isomer, 23% 2 isomer, and 4% 3 isomer. The (+)-2-(*sec*-butyl)pyrrole obtained on isolation was 24% optically pure ($[\alpha]^{25}D$ +26.1°). The 2 isomer was obtained with 79% retention of configuration during the isomerization.

Pyrolysis of (+)-2-(*sec*-Butyl)pyrrole.—Pyrolysis of 1.35 g of the pyrrole {$[\alpha]^{25}D$ +23.4 ± 0.4° (*c* 5.26, CCl_4); 99.9% pure, glpc analysis} at 600° in a tube containing Vycor beads produced 63.5% 2 isomer, 23.0% 3 isomer, and 10.5% decomposition products. The 2 and 3 isomers were separated by preparative glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 120°. The 2 isomer, thus recovered (100% pure, glpc analysis), had the same optical purity {$[\alpha]^{25}D$ +24.3 ± 1.5° (*c* 2.63, CCl_4)} as starting material. The 3 isomer (99.7% pure, glpc analysis was formed with 56 ± 10% retention of configuration during the pyrolysis.

Pyrolysis of (+)-N-(1-Phenylethyl)-2,5-dimethylpyrrole.—The pyrrole (38.5 g) was added at a constant rate over 9.75 hr to the reactor tube at 525°. The crude pyrolysate weighed 34.5 g (90% recovery) and contained (glpc analysis) 30% N isomer, 13% 2-(1-phenylethyl)-3,5-dimethylpyrrole, 37% 3-(1-phenylethyl)-2,5-dimethylpyrrole, and 20% decomposition products. The pyrolysate was separated by preparative glpc using a 10 ft × 0.375 in. 30% Carbowax 20M column at 200–250°.

Meso-2,3-Diphenylbutane was obtained from the decomposition products, mp 128° after two recrystallizations from hexane (lit. mp 128°,[16] 125.5°[17]). Calculations of the molecular weight and empirical formula from the mass spectrum gave 210 and $C_{16}H_{18}$, respectively.

(16) F. Wesseley and H. Welleba, *Ber.*, **74**, 777 (1941).

(17) H. H. Richmond, E. J. Underhill, A. G. Brook, and G. F. Wright, *J. Amer. Chem. Soc.*, **69**, 937 (1947).

The N isomer recovered from the pyrolysate was further purified by glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 225°: 100% pure (glpc analysis); $[\alpha]^{25}D$ +34.6 ± 0.4° (*c* 6.74, CCl_4). This corresponds to 97 ± 2% retention of its optical activity.

(+)-2-(1-Phenylethyl)-3,5-dimethylpyrrole was further purified by glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 190°: 99.5% pure (glpc analysis); $n^{25}D$ 1.5623; bp 226–228°; $[\alpha]^{25}D$ +12.5 ± 0.4 (*c* 4.57, CCl_4); $\nu_{max}^{CCl_4}$ 3460 cm^{-1} (N–H); λ_{max}^{MeOH} 211 mμ (ε 5800); nmr spectrum, 1.50 (doublet, 3 H), 1.89 (singlet, 3 H), 2.08 (singlet, 3 H), 4.07 (quartet, 1 H), 5.39 (singlet, 1 H), and 7.10 ppm (singlet 5 H).

Anal. Calcd for $C_{14}H_{17}N$: C, 84.36; H, 8.60; N, 7.03. Found: C, 84.43; H, 8.72; N, 7.02.

Oxidation of the 2 isomer followed by esterification of the acid produced gave methyl hydratropate: 100% pure (glpc analysis); $[\alpha]^{25}D$ −45.2 ± 0.5° (*c* 4.20, ethanol); optical purity, 39.9 ± 0.4%. The ir spectrum was identical with that obtained from an authentic sample. The isomerization from the N to the 2 position occurred with 40.9 ± 0.4% retention of configuration.

The structure of the 2 isomer was verified by synthesis from 3,5-dimethylpyrrylmagnesium bromide and 1-phenylethyl bromide. The ir and nmr spectra obtained from the Grignard reaction product were identical with those obtained from the pyrolysis product.

(−)-3-(1-Phenylethyl)-2,5-dimethylpyrrole was further purified by glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 225°: 100% pure (glpc analysis); mp 73–75°; $[\alpha]^{25}D$ −6.6 ± 0.7° (*c* 4.57, CCl_4); $\nu_{max}^{CCl_4}$ 3465, 3420 cm^{-1} (N–H); λ_{max}^{MeOH} 210.7 mμ (ε 4480); nmr spectrum, 1.40 (doublet, 3 H), 1.85 (singlet, 3 H), 2.03 (singlet, 3 H), 3.78 (quartet, 1 H), 5.54 (singlet, 1 H), and 7.03 ppm (singlet, 5 H).

Anal. Calcd for $C_{14}H_{17}N$: C, 84.36; H, 8.60; N, 7.03. Found: C, 84.21; H, 8.74; N, 7.12.

Oxidation of the 3 isomer followed by esterification gave methyl hydratropate: $[\alpha]^{25}D$ −43.4 ± 0.5° (*c* 2.07, ethanol); 100% pure (glpc analysis); optical purity 38.3%. The ir spectrum and glpc retention time of the ester were identical with those obtained from an authentic sample. The isomerization to the 3 position occurred with 39.2 ± 0.5% retention of configuration.

The structure of the 3 isomer was verified by synthesis from 2,5-dimethylpyrrylmagnesium bromide and 1-phenylethyl bromide. The ir and nmr spectra obtained from the Grignard reaction product were identical with those obtained from the pyrolysis product.

Pyrolysis of (+)-N-(*sec*-Butyl)-2,5-dimethylpyrrole.—The pyrolysis temperature producing the maximum isomerization was determined by pyrolyzing samples of the pyrrole at various temperatures. From 50 g (0.33 mol) of the pyrrole added to the reactor tube (575°) at a rate of 3.9 g/hr, there was obtained 41 g (82% recovery) of pyrolysate, which contained (glpc analysis) 12% N isomer, 36% 2-(*sec*-butyl)-3,5-dimethylpyrrole, 41% 3-(*sec*-butyl)-2,5-dimethylpyrrole, and 11% decomposition products. Distillation of the crude pyrolysate through a 30 × 1 cm column packed with glass helices gave the following fractions: decomposition product, bp 60–63° (14 mm); N isomer, bp 63–75° (12 mm); 2 isomer, bp 75–78° (10 mm); and residue (3 isomer).

The first fraction, bp 60–63° (14 mm), was purified by preparative glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 160°. The fraction, a mixture of 2,4-dimethylpyrrole and 2,5-dimethylpyrrole, showed a glpc retention time and ir and nmr spectra which were identical with those obtained from a mixture of authentic samples of the two pyrroles.

Purification of the recovered N isomer was accomplished by glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 130°: purity 99.9%; $[\alpha]^{25}D$ +25.37 ± 0.01° (neat); 99.8% retention of optical activity.

(+)-2-(*sec*-Butyl)-3,5-dimethylpyrrole was purified further (glpc) using a 10 ft × 0.375 in. 30% Carbowax 20M column at 200°: purity, 98.7%; bp 210°; $n^{25}D$ 1.4915; d^{25} 0.8968 g/ml; $[\alpha]^{25}D$ +36.9 ± 0.1° (*c* 8.02, CCl_4); $\nu_{max}^{CCl_4}$ 3480 cm^{-1} (N–H); λ_{max}^{MeOH} 222 mμ (ε 8284); nmr spectrum, 0.80 (triplet, 3 H), 1.12 (doublet, 3 H), 1.37 (multiplet, 2 H), 1.88 (singlet, 3 H), 2.10 (singlet, 3 H), 2.63 (multiplet, 1 H), 5.39 (doublet, 1 H), 7.04 ppm (singlet, 1 H).

Anal. Calcd for $C_{10}H_{17}N$: C, 79.41; H, 11.33; N, 9.26. Found: C, 79.40; H, 11.46; N, 9.30.

Oxidation of the 2-*sec*-butyl isomer by the procedure used for the oxidation of 2-(1-phenylethyl)pyrrole gave on distillation 2-methylbutyric acid: bp 165–175°; $n^{25}D$ 1.4048; $[\alpha]^{25}D$ +15.31 ± 0.01° (neat) (lit.[18] bp 176–177.5°; $n^{25}D$ 1.4042). The ir spectrum of the acid was identical with that obtained from an authentic sample. Assuming that the value of $[\alpha]^{25}D$ +20.5° [6,17] represents the rotation of 100% optically pure acid, the 2-methylbutyric acid obtained on oxidation was 75% optically pure. The isomerization from the N to the 2 position occurred with 77% retention of configuration.

The structure of the 2-(*sec*-butyl)-3,5-dimethylpyrrole was confirmed by synthesis from 2,4-dimethylpyrrylmagnesium bromide and *sec*-butyl bromide. The glpc retention times and nmr and ir spectra were identical with those of authentic samples.

(+)-3-(*sec*-Butyl)-2,5-dimethylpyrrole was purified by glpc (12 ft × 0.375 in. 20% Apiezon L column at 170°): purity, 99.4%; mp 28°; d^{28} 0.8859 g/ml; $[\alpha]^{25}D$ +30.1 ± 0.2° (*c* 8.46, CCl_4); $\nu_{max}^{CCl_4}$ 3840 cm^{-1} (N–H); λ_{max}^{MeOH} 211 mμ (ε 6900); nmr spectrum, 0.75 (triplet, 3 H), 1.05 (doublet, 3 H), 1.34 (multiplet, 2 H), 2.00 (singlet, 3 H), 2.03 (singlet, 3 H), 2.31 (multiplet, 1 H), 5.46 (doublet, 1 H), 6.95 ppm (singlet, 1 H).

Anal. Calcd for $C_{10}H_{17}N$: C, 79.41; H, 11.33; N, 9.26. Found: C, 79.25; H, 11.06; N, 9.21.

(18) K. B. Wiberg and T. W. Hutton, *J. Amer. Chem. Soc.*, **78**, 1640 (1956).

Oxidation produced 2-methylbutyric acid: $n^{25}D$ 1.4056; $[\alpha]^{25}D$ +15.11 ± 0.01° (neat); 74% optical purity. The isomerization to the 3 position occurred with 76% retention of configuration.

The glpc retention time and the ir and nmr spectra of the product obtained from reaction of 2,5-dimethylpyrrylmagnesium bromide with *sec*-butyl bromide were identical with those obtained from the 3-*sec*-butyl isomer produced on pyrolysis.

Registry No.—N-(1-Phenethyl)pyrrole, 17289-34-8; (+)-N-(1-phenethyl)pyrrole, 13245-05-1; N-(*sec*-butyl)-pyrrole, 17289-36-0; (+)-N-(*sec*-butyl)pyrrole, 13245-04-0; (+)-N-(1-phenylethyl)-2,5-dimethylpyrrole, 17289-38-2; (+)-N-(*sec*-butyl)-2,5-dimethylpyrrole, 17289-39-3; (+)-2-(1-phenylethyl)pyrrole, 13245-06-2; (+)-3-(1-phenylethyl)pyrrole, 13245-07-3; (+)-2-(*sec*-butyl)pyrrole, 17289-42-8; (+)-3-(*sec*-butyl)pyrrole, 17289-43-9; (+)-2-(1-phenylethyl)-3,5-dimethylpyrrole, 17289-44-0; (−)-3-(1-phenylethyl)-2,5-dimethylpyrrole, 17289-45-1; (+)-2-(*sec*-butyl)-3,5-dimethylpyrrole, 17289-46-2; (+)-3-(*sec*-butyl)-2,5-dimethylpyrrole, 17289-47-3.

Studies on Pyrimidine Derivatives and Related Compounds. LVIII.[1] Reaction of Dialkyl Acylphosphonates with 3-Benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium Halides (Takamizawa Reaction 7)

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The novel reactions of 3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium salts (**9a–c**) with diethyl benzoyl- or diethyl acetylphosphonate (**3a** or **b**) producing 2-phenyl-3-oxo-4-benzyl-5-methyl-6-(2-benzoyloxy)ethyl-2,3-dihydro-4H-1,4-thiazine (**8**) and 2-methyl-3-oxo-4-benzyl-5-methyl-6-(2-benzoyloxy)ethyl-2,3-dihydro-4H-1,4-thiazine (**17**) afforded 2-(1-diethylphosphoroyl)benzyl-3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium salts (**10a–c**) or 2-(1-diethylphosphoroyl)ethyl-3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium bromide (**16**) as the intermediates. 3-Alkylimino-2,3-dihydro-4H-1,4-thiazine derivatives (**20–22** and **24**) were also obtained by the reaction of **10b** or **16** with ammonia or primary amines. The reaction of **10b** with dimethylamine gave 2-phenyl-3-dimethylamino-4-benzyl-5-methyl-6-(2-benzoyloxy)ethyl-4H-1,4-thiazine (**23**). The reaction of **16** with dimethylamine gave **17** unexpectedly. The rearrangement of **10b** to **8** was kinetically studied by measuring the successive changes in the ultraviolet absorption spectra. The mechanism of this novel reaction involving ring conversion was discussed. The reaction mechanism of thiamine with dialkyl acylphosphonates producing 1-alkyl-3-(2-hydroxy)ethyl-4,9-dimethyl-1,6-dihydropyrimido[4′,5′:4,5]pyrimido[2,3-*d*][1,4]thiazine (**4**) was also discussed briefly.

In previous papers,[2–4] we reported that the reaction of thiamine (B_1) with dialkyl acylphosphonate involving a novel conversion of thiazolium moiety into thiazine afforded tricyclic 1-alkyl-3-(2-hydroxy)ethyl-4,9-dimethyl-1,6-dihydropyrimido[4′,5′:4,5]pyrimido-[2,3-*d*][1,4]thiazine (**4**), which was quite easily hydrolyzed to give 2-alkyl-3-oxo-4-(2-methyl-4-aminopyrimidin-5-yl)methyl-5-methyl-6-(2-hydroxy)-ethyl-2,3-dihydro-4H-1,4-thiazine (**5**). 1,4-Thiazine derivatives (**7** and **8**) were directly obtained in fairly good yields in the case of thiazolium salts containing no functional groups such as the pyrimidine C-4 amino group (Scheme I). This is new reaction for dialkyl acylphosphonate. The present paper is aimed to elucidate the reaction mechanism of thiazolium salts with acylphosphonates using 3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium halides and diethyl benzoyl- and diethyl acetylphosphonates. The information obtained here offers data useful for the elucidation of the Perkow reaction mechanism.

Reaction of Thiazolium Salts with Diethyl Benzoyl- and Diethyl Acetylphosphonate.—We already reported[5] that the reaction of the so-called "neutral form" of benzyl thiazolium salt (**6**) with diethyl benzoylphosphonate (**3a**) gave 2-phenyl-3-oxo-4-benzyl-5-methyl-6-(2-hydroxy)ethyl-2,3-dihydro-4H-1,4-thiazine (**7**) and its benzoate (**8**). In this paper the reactions of 3-benzyl-4-methyl-5-(2-benzoyloxy)ethylthiazolium halides (**9a–c**) with **3a** and diethyl acetylphosphonate (**3b**) in the presence of triethylamine in N,N-dimethylformamide are described.

The 1:1 adducts (**10a–c**) of **9a–c** and **3a** were obtained in approximately 80% yields by the reactions of **9a–c** with **3a**; each gave the nitrate (**10d**) on treat-

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