(9) (a) E. H. W. Bohme, H. E. Applegate, B. Toeplitz, and J. E. Dolfini, *J. Amer. Chem. Soc.*, **93**, 4324 (1971); (b) R. A. Firestone, N. Schelechow, D. B. R. Johnston, and B. G. Christensen, *Tetrahedron Lett.*, 375 (1972); (c) R. A. Firestone, N. Schelechow, and B. G. Christensen, *J. Chem. Soc., Chem. Commun.*, 1106 (1972); (d) W. A. Spitzer, T. Goodson, R. J. Smithey, and I. G. Wright, *ibid.*, 1138 (1972); (e) G. H. Rasmusson, G. F. Reynolds, and G. E. Arth, *Tetrahedron Lett.*, 145 (1973); (f) W. A. Spitzer and T. Goodson, *ibid.*, 273 (1973); (g) W. A. Slusarchyk, H. E. Applegate, P. Funke, W. Koster, M. S. Puar, M. Young, and J. E. Dolfini, *J. Org. Chem.*, **38**, 943 (1973); (h) E. H. W. Bohme, H. E. Applegate, J. B. Ewing, P. T. Funke, M. S. Puar, and J. E. Dolfini, *ibid.*, **38**, 230 (1973).

(10) R. H. Wiley and N. R. Smith, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 731.
(11) J. E. Herz, V. M. Rodriguez, and P. Joseph-Nathan, *Tetrahedron Lett.*, 2949 (1971).
(12) S. Wolfe and S. K. Hasan, *Chem. Commun.*, 833 (1970).
(13) A. K. Bose, B. Dayal, H. P. S. Chawla, and M. S. Manhas, *Tetrahedron Lett.*, 2823 (1972).
(14) D. B. Denney and N. Sherman, *J. Org. Chem.*, **30**, 3760 (1965).
(15) D. M. Brunwin, G. Lowe and J. Parker, *Chem. Commun.*, 865 (1971).
(16) G. Lowe and M. V. J. Ramsay, *J. Chem. Soc., Perkin Trans. 1*, 479 (1973).

Acylation of Selected Pyrroles and Tertiary Amides

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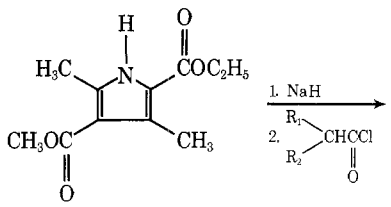
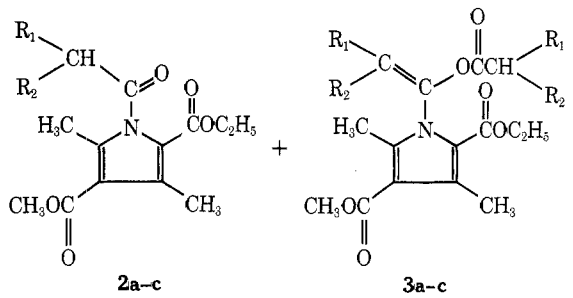
Acylation of 2-ethyl 4-methyl-3,5-dimethylpyrrole-2,4-dicarboxylate (**1**) with acetyl, propionyl, and isobutyryl chlorides gave 1-acylpyrroles **2a–c** and the 1-(1-hydroxyvinyl)pyrrole esters **3a–c** formed by further O-acylation of **2a–c**. Acetylation of *N*-methylacetanilide gave the C-acylation product *N*-methylacetoacetanilide (**7a**), which reacted further to form 3-acetoxy-*N*-methyl-*N*-phenyl-2-butenamide (**8a**); similar C-acetylation products were formed from 9-acetylcarbazole. While C- and O-acetylation products were formed from 1-acetyl-2,5-dimethylpyrrole, the related compounds 1-isobutyryl-2,5-dimethylpyrrole and diethyl 1-acetyl-2,5-dimethylpyrrole-3,4-dicarboxylate afforded only O-acylation products.

A recent report described the preparation of bis acyl derivatives from tetraalkylpyrroles.[1] Our pyrrole work has afforded a second type of bis acylation product, prepared from **1**,[2] and formed by O-acylation of the anion derived from the initially formed monoacyl products **2a–c**.



1

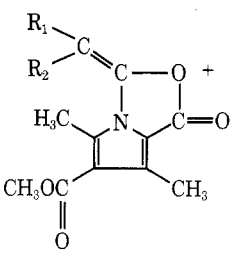


2a–c **3a–c**

a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$
c, $R_1 = R_2 = CH_3$

The mixture of **2a**, **3a**, and **1** obtained when acetyl chloride or acetic anhydride was added to a solution of the sodium salt of **1** in THF was separated into its components by silica gel chromatography. Similar three-component mixtures were formed in the reaction of **1** with propionyl chloride (**2b**, **3b**, and **1**) and isobutyryl chloride (**2c**, **3c**, and **1**), while pivaloyl chloride and benzoyl chloride gave only monoacylation products.[3]

The structures of products **3a–c** were evident from spectral and chemical properties. The nmr spectra showed the absorptions characteristic of the olefinic proton or methyl substituents R_1 and R_2.[4] As expected,[5] the chemical shifts for the remaining substituents in the pyrrole ring were little changed from those in **1** and **2a–c**. The major ions in the mass spectra of **3a–c** were those characteristic of the acyl group and ion **4**.[6] Compound **3a** showed an absorption at 1770 cm^{-1} characteristic for a vinyl ester,[7] with the ring ester groups absorbing at 1680 cm^{-1} as in **1**;[8] compounds **3b** and **3c** showed similar ir carbonyl bands. The uv maxima of **3a–c** in ethanol were at 268 mμ. The absorption is at lower wavelength than in **1** (273 mμ) and has a reduced intensity; both effects have previously been noted for 1-substituted pyrroles.[9,10] Alkaline hydrolysis of **3a–c** regenerated **1**, while refluxing **3c** with excess morpholine gave 4-isobutyrylmorpholine and **1** as the only products.

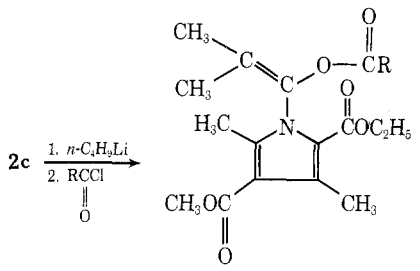


4

Formation of **3** from **2** apparently involves hydrogen abstraction from **2** by the sodium salt of **1**, followed by reaction of the acyl chloride with the resulting anion. Attempts to complete conversion of **1** to **3a** by varying the proportions of reagents in the reaction, or by repeated addition of sodium hydride followed by acetyl chloride to the reaction mixture, were unsuccessful. This appeared to result in part from surface deactivation of the sodium hydride by the acylating reagent. Thus, no hydrogen was evolved when **1** was added to a stirred suspension of sodium hydride in THF containing acetyl chloride; in absence of acetyl chloride, hydrogen evolution was rapid at room temperature.

While compound **2c** did not react with sodium hydride at room temperature,[11] it was converted to the anion using *n*-butyllithium and this was acylated to give **3c**, **5**, and **6**.

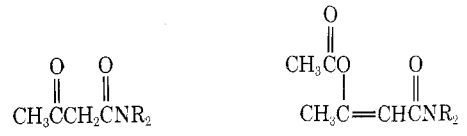
Our findings with **1** prompted us to study the acylation



3c, R = $CH(CH_3)_2$
5, R = CH_3
6, R = $C(CH_3)_3$

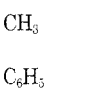
of other tertiary amides. C-Alkylation of anions derived from tertiary amides has been reported,[12] and we have found that the anion of *N*-methylacetanilide, formed in THF using *n*-butyllithium, similarly undergoes initial C-acetylation with no detectable O-acetylation. The major product isolated was not *N*-methylacetoacetanilide (**7a**), but **8a**, formed by further O-acetylation of **7a**; no attempt was made to suppress this further acetylation by addition of the anion to an excess of acetyl chloride, or by otherwise modifying the reaction conditions. Higher yields of **8a** were obtained by acetylation of **7a**. Acetylation of 9-acetylcarbazole under similar conditions gave the related products **7b** and **8b**, resulting from initial C-acylation.

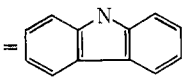
Exclusive O-acylation is not a characteristic of all enolizable 1-acylpyrroles. Acetylation of the anion of 2,5-dimethylpyrrole in THF gave 1-acetyl-2,5-dimethylpyrrole, which reacted further to give C- and O-acylation products **8c** and **9a** in about equal amount. Introduction of electron-withdrawing carboethoxy substituents in the pyrrole ring or increasing the steric hindrance at the α carbon in the acyl group essentially eliminated C-acylation in closely related pyrroles. Acetylation of diethyl 2,5-dimethylpyrrole-3,4-dicarboxylate gave diethyl 1-acetyl-2,5-dimethylpyrrole-3,4-dicarboxylate (39%) and **9b** (26%) as the only significant acylation products. Similarly, the only side-chain acylation product obtained on reaction of 1-isobutyryl-2,5-dimethylpyrrole with isobutyryl chloride was **10**. Analysis of the acylation products, usually made difficult by incomplete acylation or the formation of more than one, somewhat unstable product, may be further complicated in pyrroles having unsubstituted ring positions, as these are known to undergo C-acylation[13] or *N*- to *C*-acyl group migration.[14]

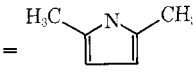


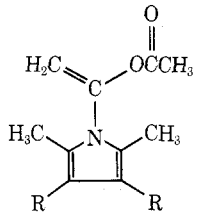
7a,b

8a-c

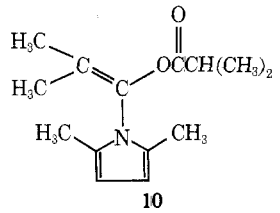
a, NR_2 = 

b, NR_2 = 

c, NR_2 = 



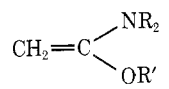
9a, R = H
b, R = $COOC_2H_5$



10

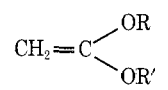
The 1-acylpyrroles are not typical tertiary amides. This is a consequence of attachment of the acyl group to an electron-deficient heterocyclic nitrogen atom. Atypical properties already reported for these compounds are the high-frequency ir amide absorption (>1700 cm^{-1})[15] and the reductive cleavage of 1-benzoylpyrroles with formation of toluene.[3] Further examples are the susceptibility to hydrolysis and ready ionization found in our studies. Acylated pyrroles with electron-withdrawing carboalkoxy substituents which further enhance the positive character of the nitrogen atom show both the highest frequency ir amide absorption (*ca.* 1750 cm^{-1}) and the greatest amount of O-acylation. In these cases the anion once formed should be more stabilized by the adjacent ring system than in compounds lacking the carboalkoxy substituents. This may facilitate existence of these ions in solution as solvent-separated ion pairs, and afford an explanation for their O-acylation; kinetic acylation of such species has been shown, in the case of ketones, to lead predominantly to O-acylated products.[16]

Acylation products **3a-c** may be considered as new ketene derivatives **11**. While some compounds of this structure type are known[17] or have been proposed as reaction intermediates,[18] the simplest examples are not reported;[19] better known are the related vinyl esters **12**,[20,21] ketene aminals **13**,[22,23] and ketene acetals **14**.[23]



11, R′ = CR

13, R = R′ = alkyl



12, R = alkyl; R′ = CR

14, R = R′ = alkyl

Experimental Section[24]

Compound 1 was prepared as described by Küster[25] and had the following spectral properties: nmr δ 1.37 (t, 3, CH_3), 2.53 (s, 3, CH_3), 2.57 (s, 3, CH_3), 3.84 (s, 3, OCH_3), 4.35 (q, 2, CH_2), and 10.10 (s, 1, NH); λ_{max} (EtOH) 222 mμ (ϵ 27,300) and 275 (16,450).

General Procedure for Acylation of 1 Using Sodium Hydride. Sodium hydride (5.05 g, 57% in oil, 0.12 mol) was added to a stirred solution of 1 (22.5 g, 0.10 mol) in THF (200 ml) at 10°. After 1 hr, the appropriate acid chloride (0.2 mol) was added, and after a further 1 hr at room temperature methanol (20 ml) was added to destroy excess NaH. The product was partitioned between benzene and water and the benzene layer was washed with water, dried, and evaporated. Where more than one product was formed, the residual oil was chromatographed on silica gel using benzene–ethyl acetate (40:1) as solvent. Analytical samples were recrystallized from Skellysolve B. Using this procedure the following eight compounds were prepared.

2-Ethyl 4-methyl-3,5-dimethyl-1-pivaloylpyrrole-2,4-dicarboxylate had mp 80.5–81.5° from methanol (75% yield); nmr δ 1.25 [s, 9, $C(CH_3)_3$], 1.35 (t, 3, CH_3), 2.46 (s, 3, CH_3), 2.56 (s, 3, CH_3), 3.83 (s, 3, OCH_3), and 4.32 (q, 2, OCH_2); mass spectrum *m/e* (rel intensity) 309 (18), 225 (57), and 71 (100); ir 1680 (vs) and 1740 cm^{-1} (s); λ_{max} (EtOH) 225 mμ (ϵ 23,350) and 273 (11,050).

Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.04; H, 7.49; N, 4.60.

2-Ethyl 4-methyl-1-benzoyl-3,5-dimethylpyrrole-2,4-dicarboxylate had mp 92–94° from methanol (80% yield); nmr δ 1.05 (t, 3, CH_3), 2.48 (s, 3, CH_3), 2.53 (s, 3, CH_3), 3.87 (s, 3, OCH_3), 4.03 (q, 2, OCH_2), and 7.55 (m, 5, ArH); ir 1690 cm^{-1} (C=O).

Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.87; H, 5.73; N, 3.86.

Reaction of 1 with Acetyl Chloride. This gave a mixture containing 1 (43%), **2a** (23%), and **3a** (34%) as estimated by gc anal-

ysis. Silica gel chromatography gave, in order of elution from the column, **2a**, **3a**, and **1**; chromatography was accompanied by partial deacetylation.

Compound 2a had mp 72–74°; nmr δ 1.30 (t, 3, CH_3), 2.40 (s, 3, CH_3), 2.47 (s, 6, CH_3), 3.84 (s, 3, OCH_3), and 4.35 (q, 2, OCH_2); mass spectrum m/e (rel intensity) 267 (67), 225 (100), 148 (42), and 43 (41); ir 1680 (vs) and 1745 cm^{-1} (s).

Anal. Calcd for $C_{13}H_{17}NO_5$: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.45; H, 6.47; N, 4.70.

Compound 3a had mp 39–42°; nmr δ 1.35 (t, 3, CH_3), 2.12 (s, 3, CH_3CO), 2.54 (s, 3, CH_3), 2.58 (s, 3, CH_3), 3.84 (s, 3, OCH_3), 4.32 (q, 2, OCH_2), 4.98 (d, 1, J = 2 Hz, =CH), and 5.47 (d, 1, J = 2 Hz, =CH); mass spectrum m/e (rel intensity) 309 (39), 266 (28), 225 (70), 221 (99), and 43 (86); ir 1680 (vs) and 1770 cm^{-1} (s); λ_{max} (EtOH) 225 mμ (ϵ 27,350) and 268 (12,400).

Anal. Calcd for $C_{15}H_{19}NO_6$: C, 58.24; H, 6.19; N, 4.53. Found: C, 58.40; H, 6.15; N, 4.66.

Reaction of 1 with Propionyl Chloride. This gave, in order of elution from the column, **2b** (7%), **3b** (28%), and unchanged **1**.

Compound 2b had mp 72.5–73.5°; nmr δ 1.24 (t, 3, CH_3), 1.35 (t, 3, CH_3), 2.48 (s, 3, CH_3), 2.54 (s, 3, CH_3), 2.68 (q, 2, CH_2), 3.83 (s, 3, OCH_3), and 4.34 (q, 2, CH_2); mass spectrum m/e (rel intensity) 281 (5), 225 (100), 57 (22), and 29 (26); ir 1680 (vs) and 1750 cm^{-1} (s); λ_{max} (EtOH) 230 mμ (ϵ 24,700) and 273 (10,700).

Anal. Calcd for $C_{14}H_{19}NO_5$: C, 59.77; H, 6.81; N, 4.98. Found: C, 60.13; H, 6.67; N, 4.81.

Compound 3b had nmr δ 1.12 (t, 3, CH_3), 1.35 (t, 3, CH_3), 1.76 (d, 3, J = 7 Hz, $=CHCH_3$), 2.42 (q, 2, CH_2), 2.53 (s, 3, CH_3), 2.60 (s, 3, CH_3), 3.84 (s, 3, OCH_3), 4.32 (q, 2, OCH_2), and 5.36 (q, 1, J = 7 Hz, $=CHCH_3$); mass spectrum m/e (rel intensity) 337 (19), 281 (24), 235 (85), 225 (55), 57 (100), and 29 (57).

Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.53; H, 6.87; N, 4.02.

Reaction of 1 with Isobutyryl Chloride. This gave, in order of elution from the column, **2c** (45%), **3c** (14%), and unchanged **1**.

Compound 2c had mp 56–57°; nmr δ 1.15 [d, 6, $CH(CH_3)_2$], 1.35, (t, 3, CH_3), 2.48 (s, 3, CH_3), 2.55 (s, 3, CH_3), 2.90 [m, 1, $CH(CH_3)_2$], 3.83 (s, 3, OCH_3), and 4.32 (q, 2, OCH_2); mass spectrum m/e (rel intensity) 295 (5), 225 (100), 71 (12), and 43 (42); ir 1680 (vs) and 1750 cm^{-1} (s); λ_{max} (EtOH) 230 mμ (ϵ 26,950) and 272 (10,100).

Anal. Calcd for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.81; H, 7.15; N, 4.72.

Compound 3c had mp 69.5–70.5°; nmr δ 1.10 (d, 3, $CHCH_3$), 1.14 (d, 3, $CHCH_3$), 1.33 (t, 3, CH_3), 1.53 (s, 3, $=CCH_3$), 1.87 (s, 3, $=CCH_3$), 2.52 (s, 3, CH_3), 2.54 (s, 3, CH_3), 3.82 (s, 3, OCH_3), 4.28 (s, 2, OCH_2); mass spectrum m/e (rel intensity) 365 (12), 249 (69), 225 (19), 71 (69), and 43 (100); ir 1680 (vs) and 1745 cm^{-1} (s); λ_{max} (EtOH) 225 mμ (ϵ 26,000), 260 (shoulder, 12,000), and 268 (12,150).

Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.33; H, 7.34; N, 3.67.

Reaction of 3c with Morpholine. A mixture of **3c** (1.6 g) and morpholine (3 ml) was heated under reflux for 30 min. The excess morpholine was removed by evaporation at 10 mm and the residual oil was distilled to give 4-isobutyrylmorpholine (0.85 g, 62%), bp 70–80° (0.5 mm). Recrystallization of the residue in the distillation flask from Skellysolve B gave **1** (0.78 g, mp 130–132°).

General Procedure for Acylation (0.01–0.05-Mol Scale) Using *n*-Butyllithium.[26] *n*-Butyllithium[26] in hexane (1.2 equiv) was added at 0° to a stirred solution of the substrate (1 equiv) in THF (150 ml). The solution was stirred for 10 min and the appropriate acid chloride (1.5 equiv) was added. After 1 hr the THF was evaporated and the residue was partitioned between benzene and water. The oil obtained on evaporation of the benzene was purified by silica gel chromatography and recrystallization from Skellysolve B, or as otherwise indicated below. Using this procedure the following 11 reactions were carried out.

Reaction of 2c with Isobutyryl Chloride. This afforded 1.7 g (39%) of **3c**, mp 69–70°, identical by ir, nmr, and tlc with the sample previously prepared.

Reaction of 2c with Acetyl Chloride. This gave 1.3 g (32%) of **5**: mp 71–73°; nmr δ 1.35 (t, 3, CH_3), 1.54 (s, 3, $=CCH_3$), 1.80 (s, 3, $=CCH_3$), 2.10 (s, 3, CH_3CO), 2.53 (s, 3, CH_3), 2.56 (s, 3, CH_3), 3.84 (s, 3, OCH_3), and 4.31 (q, 2, OCH_2); ir 1680 (vs) and 1755 cm^{-1} (s); λ_{max} (EtOH) 225 mμ (ϵ 26,000), 258 (11,800), and 268 (12,200).

Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.40: H, 6.71; N, 4.03.

Reaction of 2c with Pivaloyl Chloride. This gave 1.5 g of **6**, a liquid, which was characterized by nmr and mass spectral analysis: nmr δ 1.17 [s, 9, $C(CH_3)_3$], 1.32 (t, 3, CH_3), 1.55 (s, 3, $=CCH_3$), 1.78 (s, 3, $=CCH_3$), 2.54 (s, 6, CH_3), 3.80 (s, 3, OCH_3), and 4.28 (q, 2, OCH_2); mass spectrum m/e (rel intensity) 379 (13), 295 (18), 249 (100), 225 (22), 85 (12), and 57 (96).

Reaction of *N*-Methylacetoacetanilide[27] with Acetyl Chloride. This gave an oil containing 60% of 3-acetoxy-*N*-methyl-*N*-phenyl-2-butenamide (**8a**), which was purified by chromatography and recrystallized from cyclohexane: mp 74–76°; nmr δ 1.82 (d, 3, J = 1 Hz, $=CCH_3$), 2.25 (s, 3, CH_3), 3.27 (s, 3, NCH_3), 5.38 (q, 1, J = 1 Hz, =CH), and 7.33 (m, 5, ArH); ir 1755, 1675, 1630, and 1595 cm^{-1}; mass spectrum m/e (rel intensity) 234 (1), 192 (22), 108 (100), 86 (46), and 78 (47).

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01. Found: C, 66.80; H, 6.22; N, 5.82.

Reaction of *N*-Methylacetanilide with Acetyl Chloride. The crude acetylation product (0.1-mol scale) was analyzed by gc (75° initial temperature, programmed at 5°/min to 150°) and contained *N*-methylacetanilide (1.7 min, 53% of product), **8a** (7.7 min, 34% of product), and an unknown (10.2 min, 13% of product). Column chromatography of the crude gave 1.2 g of **8a** which was crystallized from cyclohexane to give 0.9 g, mp 74–76°; this was identical with the previously prepared sample by nmr and tlc analysis.

Reaction of 9-Acetoacetylcarbazole[28] with Acetyl Chloride. The crude product contained 60% of 9-(3-acetoxy-1-oxo-2-butenyl)carbazole (**8b**), which was purified by chromatography and recrystallized from cyclohexane: mp 79–81°; nmr δ 2.15 (d, 3, J = 1 Hz, $=CCH_3$), 2.21 (s, 3, CH_3), 6.27 (m, 1, =CH), 7.35 (m, 4, ArH), 7.90 (m, 2, ArH), and 8.13 (m, 2, ArH).

Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.91; H, 5.29; N, 4.73.

Reaction of 9-Acetylcarbazole[29] with Acetyl Chloride. The crude acylation product was analyzed by gc (125° initial temperature, programmed to 200° at 5°/min) and showed peaks for carbazole and 9-acetoacetylcarbazole[30] (3.3 min, 30% of product), 9-acetylcarbazole (6.2 min, 50%), and **8b** (12.0 min, 20%). Chromatography (6.0 g crude) on silica gel using benzene as eluent gave, in order of elution, carbazole (0.4 g), a mixture of 9-acetylcarbazole and 9-acetoacetylcarbazole (2.9 g), and **8b** (1.2 g). Compound **8b** was recrystallized from cyclohexane and was identical by melting point, ir, nmr, and tlc with the previously prepared sample.

Reaction of 2,5-Dimethylpyrrole with Acetyl Chloride. The crude product from the acetylation was analyzed by gc (60° initial temperature, programmed to 100° at 5°/min) and showed, in addition to starting material, peaks for 1-acetyl-2,5-dimethylpyrrole (1.5 min, *ca.* 10% of product), **9a** (2.5 min, *ca.* 10% of product), and **8c** (8.0 min, *ca.* 20% of product). Distillation of the product under reduced pressure gave starting pyrrole (4.5 g), a mixture of 1-acetyl-2,5-dimethylpyrrole and **9a** (1.5 g), and **8c** (2.3 g). Chromatography of the second distillation fraction (1.5 g) on silica gel in benzene gave **9a** (0.35 g) as the first fraction eluted from the column followed by 1-acetyl-2,5-dimethylpyrrole (0.25 g).

Compound **9a** was distilled before analysis: nmr δ 2.09 (s, 3, CH_3), 2.22 (s, 6, CH_3), 4.88 (d, 1, J = 2 Hz, =CH), 5.18 (d, 1, J = 2 Hz, =CH), and 5.77 (s, 2, ArH); ir 1770 (vs) and 1675 cm^{-1} (s); mass spectrum m/e (rel intensity) 179 (100), 137 (100), 120 (63), 95 (100), and 94 (100).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.69; H, 7.92; N, 7.67.

Chromatography of the last distillation fraction (2.3 g) gave 1.2 g of **8c** that was purified by distillation before analysis: nmr δ 2.07 (d, 3, J = 1 Hz, $=CCH_3$), 2.13 (s, 3, CH_3), 2.31 (s, 6, CH_3), 5.78 (s, 2, ArH), and 5.98 (m, 1, =CH); ir 1760 (vs), 1690 (vs), and 1650 cm^{-1} (s); mass spectrum m/e (rel intensity) 221 (16), 95 (100), 94 (50), and 85 (59).

Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 64.10; H, 7.19; N, 6.00.

Reaction of 2,5-Dimethylpyrrole with Isobutyryl Chloride. The crude oil obtained from the acylation reaction (0.1-mol scale) was chromatographed on silica gel and gave, as the first product eluted from the column, 13.1 g of 1-isobutyryl-2,5-dimethylpyrrole: bp 43° (0.5 mm); nmr δ 1.22 (d, 6, CH_3), 2.32 (s, 6, CH_3), 3.23 [m, 1, $CH(CH_3)_2$], and 5.80 (s, 2, ArH); ir 1705 cm^{-1} (vs).

Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.97; H, 9.30; N, 8.30.

Further elution of the column gave 2.1 g of material, a mixture containing two major components (one spot on tlc in benzene with an R_f 0.30 that of 1-isobutyryl-2,5-dimethylpyrrole). While these compounds have not been fully characterized, they are believed to arise by isobutyrylation at the 3 position in the pyrrole

ring as well as the ring nitrogen; nmr of the crude product showed in single pyrrole ring hydrogen at δ 6.25. Gc–mass spectrum at 130° showed two major bands at 1.8 and 3.4 min with molecular ions at 236 and 306, respectively.

Reaction of 1-Isobutyryl-2,5-dimethylpyrrole with Isobutyryl Chloride. Chromatography of the crude product on silica gel gave a mixture of starting pyrrole (30%) and **10** (70%) (gc retention time 1.0 and 3.3 min, respectively, at 80°). Nmr of this product showed, in addition to the signals for 1-isobutyryl-2,5-dimethylpyrrole, the following peaks for **10**: δ 1.17 [d, 6, $(CH_3)_2CH$], 1.48 (s, 3, $=CCH_3$), 1.72 (s, 3, $=CCH_3$), 2.18 (s, 6, CH_3), 2.60 [m, 1, $CH(CH_3)_2$], and 5.75 (s, 2, ArH). Mass spectrum *m/e* (rel intensity) for compound **10** was 235 (73), 165 (26), 147 (21), 96 (37), and 71 (100).

Reaction of Diethyl 2,5-Dimethylpyrrole-3,4-dicarboxylate with Acetyl Chloride. The crude product (2.6 g) was analyzed by gc at 140° and showed peaks for starting material (2.5 min, 34% of product), diethyl 1-acetyl-2,5-dimethylpyrrole-3,4-dicarboxylate (3.4 min, 39% of product), and **9b** (6.4 min, 26% of product). Chromatography of the product on silica gel using benzene–ethyl acetate (4:1) as eluent gave 1.35 g of acetylated material (58% of 1-acetyl derivative, 42% of **9b**). Three crystallizations from Skellysolve B gave 0.55 g of diethyl 1-acetyl-2,5-dimethylpyrrole-3,4-dicarboxylate, mp 85–88°. The analytical sample was further recrystallized from methanol and finally Skellysolve B: mp 86–88°; nmr δ 1.32 (t, 3, CH_3), 2.49 (s, 6, $ArCH_3$), 2.59 (s, 3, CH_3CO), and 4.29 (q, 2, OCH_2); mass spectrum *m/e* (rel intensity) 281 (37), 239 (23), 236 (37), 235 (41), 194 (67), 199 (100), 166 (69), 165 (79), and 164 (52); ir 1730 and 1700 cm^{-1}.

Anal. Calcd for $C_{14}H_{19}NO_5$: C, 59.77; H, 6.81; N, 4.98. Found: C, 60.07; H, 6.92; N, 5.07.

The mother liquors from the first Skellysolve B crystallization contained 0.35 g of **9b** which was distilled and recrystallized twice from benzene and Skellysolve B for analysis: mp 45–47°; nmr δ 1.31 (t, 3, CH_3), 2.14 (s, 3, CH_3CO), 2.40 (s, 6, CH_3), 4.28 (q, 2, OCH_2), 5.04 (d, 1, J = 2 Hz, =CH), and 5.41 (d, 1, J = 2 Hz, =CH); mass spectrum *m/e* (rel intensity) 323 (23), 278 (29), 277 (34), 235 (27), 234 (46), and 193 (100); ir 1770 (s) and 1690 cm^{-1} (vs).

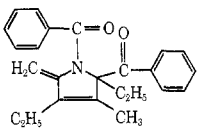
Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.56; H, 6.32; N, 4.32.

Continued elution of the column afforded diethyl 2,5-dimethylpyrrole-3,4-dicarboxylate (0.65 g).

Registry No. 1, 21898-57-7; **2a**, 49558-97-6; **2b**, 49558-98-7; **2c**, 49558-99-8; **3a**, 49559-00-4; **3b**, 49559-01-5; **3c**, 49559-02-6; **5**, 49559-03-7; **6**, 49559-04-8; **7a**, 2584-48-7; **7b**, 49559-05-9; **8a**, 49559-06-0; **8b**, 49559-07-1; **8c**, 49559-08-2; **9a**, 49559-09-3; **9b**, 49559-10-6; **10**, 49559-11-7; 2-ethyl 4-methyl-3,5-dimethyl-1-pivaloylpyrrole-2,4-dicarboxylate, 49559-12-8; 2-ethyl 4-methyl-1-benzoyl-3,5-dimethylpyrrole-2,4-dicarboxylate, 49559-13-9; acetyl chloride, 75-36-5; propionyl chloride, 79-03-8; isobutyryl chloride, 79-30-1; morpholine, 110-91-8; 4-isobutyrylmorpholine, 18071-39-1; pivaloyl chloride, 3282-30-2; *N*-methylacetanilide, 579-10-2; 9-acetylcarbazole, 574-39-0; 2,5-dimethylpyrrole, 625-84-3; 1-isobutyryl-2,5-dimethylpyrrole, 49559-14-0; diethyl 2,5-dimethylpyrrole-3,4-dicarboxylate 2199-56-6; diethyl 1-acetyl-2,5-dimethylpyrrole-3,4-dicarboxylate, 49559-16-2.

References and Notes

(1) A. Triebs, K. Jacob, and R. Tribollett, *Justus Liebigs Ann. Chem.*, **739**, 27 (1970); the structure of the product formed was



(2) The herbicidal activity of **1** has recently been described; see A. R. Church, G. A. Hüppi, M. W. Moon, A. Steinhards, and H. J. Vostral, *J. Agr. Food Chem.*, **21**, 763 (1973).
(3) Related monoacylation products have been reported by J. L. Rainey and H. Adkins, *J. Amer. Chem. Soc.*, **61**, 1104 (1939).
(4) M. Saunders, J. Plostnieks, P. S. Wharton, and H. H. Wasserman, *J. Chem. Phys.*, **32**, 317 (1960).
(5) R. A. Jones, T. McL. Spotswood, and P. Cheuychit, *Tetrahedron*, **23**, 4469 (1967).
(6) The spectra for **2a–c** are similar to those of **1**, whose fragmentation mode has been described by H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman, and J. M. Wilson, *J. Chem. Soc.*, 1949 (1964).
(7) L. J. Bellamy "Infra-Red Spectra of Complex Molecules," Methuen, London, 1959, p 179.
(8) U. Eisnet and R. L. Erskine, *J. Chem. Soc.*, 971 (1958).
(9) G. Korshun and C. Roll, *Bull. Soc. Chim. Fr.*, **43**, 1075 (1928).
(10) U. Eisner and P. H. Gore, *J. Chem. Soc.*, 922 (1958).
(11) Probably a result of the insolubility of sodium hydride in THF.
(12) H. L. Needles and R. E. Whitfield, *J. Org. Chem.*, **31**, 989 (1966), and references cited therein.
(13) R. W. Guy and R. A. Jones, *Aust. J. Chem.*, **19**, 107 (1966).
(14) C. Ciamician and P. Magnaghi, *Chem. Ber.*, **18**, 1828 (1888).
(15) R. A. Jones, *Aust. J. Chem.*, **19**, 289 (1966).
(16) H. O. House, R. A. Auerback, M. Gall, and N. P. Peet, *J. Org. Chem.*, **38**, 514 (1973).
(17) A. M. Shkrob, Yu. I. Krylova, V. K. Antonov, and M. M. Shemyakin, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 774 (1964).
(18) R. Buyle and H. G. Viehe, *Tetrahedron*, **24**, 4217 (1967).
(19) Related phosphate esters, prepared from diethyltrichloracetamide and triethyl phosphate, are also known; see *Chem. Abstr.*, **52**, P8194*i* (1958).
(20) H. H. Wasserman and P. S. Wharton, *J. Amer. Chem. Soc.*, **82**, 661 (1960).
(21) I. F. Lutsenko, V. L. Foss, and A. N. Nesmeyanov, *Dokl. Akad. Nauk SSSR*, **169**, 117 (1966).
(22) H. Bredereck, F. Effenberger, and H. P. Beyerlin, *Chem. Ber.*, **97**, 3081 (1964).
(23) S. M. McElvain, *Chem. Rev.*, **45**, 453 (1949).
(24) Melting points were taken in open capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra ($CHCl_3$) were recorded on a Perkin-Elmer Model 137 spectrophotometer and the uv spectra on a Cary Model 15 spectrophotometer. The nmr spectra were recorded on a Varian A-60A spectrometer, and chemical shifts are reported in δ units using $CDCl_3$ as solvent and tetramethylsilane as the internal standard. (In nmr descriptions s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.) Vpc data were obtained using a Micro-Tek gas chromatograph Model 220, a column (35 cm × 3 mm i.d.) of 1% OV-1 on 100–120 mesh Gas-Chrom Q, a helium carrier gas (flow rate 40 ml/min), and a hydrogen flame ionization detector. The mass spectra were recorded at 70 eV on an LKB 9000A gas chromatograph–mass spectrometer using a column of 1% OV-1 (2 ft × 3 mm i.d.) at between 90 and 130°. Elemental analyses were obtained through the Physical and Analytical Chemistry Department of The Upjohn Co.
(25) W. Küster, *Z. Phys. Chem. (Leipzig)*, **121**, 135 (1922).
(26) A 1.6 M solution of *n*-butyllithium in hexane, obtained from Foote Mineral Co., was used.
(27) C. E. Kaslow and D. J. Cook, *J. Amer. Chem. Soc.*, **67**, 1969 (1945).
(28) V. V. Perekalin and O. M. Lerner, *Zh. Obshch. Khim.*, **21**, 1995 (1951).
(29) J. Boeseken, *Recl. Trav. Chim. Pays-Bas*, **31**, 350 (1912).
(30) Under the gc conditions used 9-acetoacetylcarbazole decomposed, and had the same retention time as carbazole.