# The Synthesis of Medium-Sized Cyclic Lactams by the Intramolecular Friedel-Crafts Cyclization of Isocyanates. Formation of Novel Pyrazolo[3,4-*c*]benzolactams



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A series of 4-ω-phenylalkyl substituted-1*H*-pyrazol-5-amines has been synthesized from the corresponding α-acetylphenylalkanenitriles and methylhydrazine. They were converted into the corresponding 5-isocyanates and cyclized under Friedel-Crafts conditions to medium-sized cyclic lactams. The reaction was shown to give the 7-, 8-, 9-, and 10-membered lactams but failed to yield the 11-membered lactam. Rings synthesized were: pyrazolo[3,4-*c*][2]benzazepin-2(1*H*)-one; 10*H*-pyrazolo[3,4-*c*][2]benzazocin-10-one; pyrazolo[3,4-*c*][2]benzazonin-11(1*H*)-one; 12*H*-pyrazolo[3,4-*c*][2]benzazocin-12-one.

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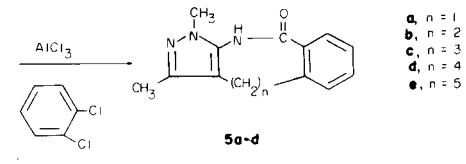
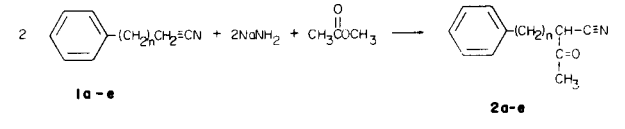
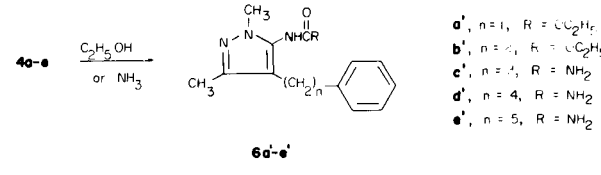
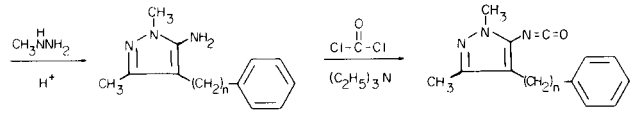
Since Butler (1) described the formation of phenanthridone by the intermolecular Friedel-Crafts cyclization of the corresponding isocyanate, a number of investigators have used the method to form 6-, 7-, and 8-membered cyclic lactams (2,3,4).




Scheme I



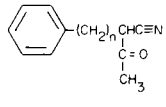




We felt that larger lactams could also be produced. Using a 1*H*-pyrazol-5-amine as part of the substrate for an investigation into even larger rings was perceived to have several advantages: 1. The necessary 1*H*-pyrazol-5-amines could be readily synthesized in good yields from readily available starting materials. 2. The 1*H*-pyrazol-5-amines

Table I

α-Acetyl-ω-phenylalkanenitriles

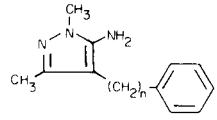


| Compound Number | n | Emperical Formula | Bp °C (mm Hg) | Yield % | IR (ν C≡N, ν C≡N, ν C≡O) cm⁻¹ (c) | Analyses % C Calcd. | C Found | H Calcd. | H Found | N Calcd. | N Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **2a** (a) | 1 | $C_{11}H_{11}NO$ | 90-92 (0.4) | 80 | 2255, 2210, 1730 | 76.27 | 75.93 | 6.40 | 6.32 | 8.09 | 7.73 |
| **2b** | 2 | $C_{12}H_{13}NO$ | 85-87 (0.15) | 83 | 2250, 2210, 1715 | 76.96 | 76.98 | 7.00 | 7.18 | 7.48 | 7.71 |
| **2c** (b) | 3 | $C_{13}H_{15}NO$ | 95-97 (0.13) | 90 | 2250, 2205, 1720 | 77.58 | 76.99 | 7.51 | 7.60 | 6.96 | 6.65 |
| **2d** | 4 | $C_{14}H_{17}NO$ | 109-110 (0.2) | 79 | 2245, 2200, 1720 | 78.08 | 77.87 | 7.96 | 7.81 | 6.51 | 6.23 |
| **2e** | 5 | $C_{15}H_{19}NO$ | 128-130 (0.25) | 72 | 2255, 2205, 1732 | 78.56 | 78.45 | 8.35 | 8.43 | 6.10 | 6.10 |

(a) These are stable, clear, colorless liquids that can be stored indefinitely. (b) Calcd. for C = 77.58; Found = 76.99. (c) The double absorption for the ν C≡N is presumable due to the enolized tautomer of the above β-ketonitriles.

Table II

1,3-Dimethyl-4(ω-phenylalkyl)-1*H*-pyrazol-5-amines



| Compound Number | n | Emperical Formula | Mp °C | Yield % | IR ($\nu$ $NH_2$) $cm^{-1}$ | Analyses % C Calcd. | C Found | H Calcd. | H Found | N Calcd. | N Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **3a** (a,b,c) | 1 | $C_{12}H_{15}N_3$ | 104-106 | 85 | 3340, 3300, 3190, 1640 (d) | 71.61 | 71.63 | 7.52 | 7.61 | 20.87 | 20.96 |
| **3b** | 2 | $C_{13}H_{17}N_3$ | 144-146 | 60 | 3380, 3320, 3160, 1640 | 72.54 | 72.79 | 7.96 | 7.89 | 19.50 | 19.46 |
| **3c** | 3 | $C_{14}H_{19}N_3$ | 85-86 | 76 | 3370, 3190, 3160, 1635 | 73.32 | 73.48 | 8.35 | 8.28 | 18.33 | 18.34 |
| **3d** | 4 | $C_{15}H_{21}N_3$ | 106-108 | 82 | 3380, 3305, 3200, 1635 | 74.04 | 73.91 | 8.70 | 8.51 | 17.26 | 17.20 |
| **3e** | 5 | $C_{16}H_{23}N_3$ | 43-45 | 95 | 3380, 3305, 3190, 1640 | 74.66 | 74.31 | 9.01 | 8.99 | 16.33 | 16.11 |

(a) These are stable white solids if stored under nitrogen in a bottle. The surface will turn yellow if exposed for days to light and air. (b) This compound was isolated as a degradation product from 1,3-dimethyl-4-phenyl-1*H*-pyrazolo[3,4-*e*][1,4]thiazepin-7-one by Swett, *et al.* (c), with reported mp 102-105° and had essentially identical $^1H$ nmr assignments (the position of the absorption of the hydrogen atoms on nitrogen ($NH_2$) was not reported by these investigators. (c) L. R. Swett, J. D. Ratajczyk, C. W. Nordeen and G. H. Aynilian, *J. Heterocyclic Chem.*, **12**, 1137 (1975). (d) The 1635-1640 $cm^{-1}$ band was also assigned to the $NH_2$ because it shifted position in chloroform solution.

should be convertible into the necessary isocyanates. 3. The completely substituted pyrazole nucleus would be unreactive under the Friedel-Crafts conditions and thus remove one source of intermolecular condensation.

These large ring lactams would be new heterocyclic systems. In addition success with the pyrazole examples would indicate that the corresponding larger benzo analogs could be synthesized using the intramolecular Friedel-Crafts Cyclization.

The synthetic pathway is outlined in Scheme I.

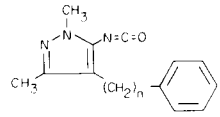
The ω-phenylalkanenitriles were obtained as described in the Experimental. The α-acetylphenylalkanenitriles (Table I) were synthesized by a slight variation of the method of Levine and Hauser (5) and were distilled or used crude. The acid catalysed condensation of methylhydrazine with the α-acetylphenylalkanenitriles, modeled on the methods of Jucker, *et al.* (6), and Aspart-Pascot, *et al.* (7) gave good yields of the 1*H*-pyrazol-5-amines, (Table II). General methods for the synthesis of arylisocyanates (8,9) (Table III) had to be modified extensively before the reaction conditions described in the Experimental section were obtained. The isocyanates were distilled before use in the Friedel-Crafts reaction. They were converted to the cyclic lactams (Table IV) and to additional crystalline derivatives (Table V). The Friedel-Crafts cyclization was essentially the method originated by Butler (1).

Results.

The intramolecular Friedel-Crafts reaction worked well for the 7-, 8-, and 9-membered rings giving over 80% isolated yields of the desired products. The 10-membered

Table III

1,3-Dimethyl-4-(ω-phenylalkyl)-5-isocyanato-1*H*-pyrazoles (a)

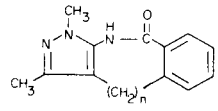


| Compound Number | n | Emperical Formula | Bp °C (mm Hg) | Yield % | IR ($\nu$ N≡C≡O) $cm^{-1}$ (b) | Analyses % C Calcd. | C Found | H Calcd. | H Found | N Calcd. | N Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **4a** | 1 | $C_{13}H_{13}N_3O$ | 79-80 (0.2) | 82 | 2250 | 68.70 | 68.71 | 5.76 | 5.58 | 18.48 | 18.54 |
| **4b** | 2 | $C_{14}H_{15}N_3O$ | 108-110 (0.15) | 64 | 2250 | 69.68 | 69.37 | 6.26 | 6.45 | 17.42 | 17.31 |
| **4c** | 3 | $C_{15}H_{17}N_3O$ | 110-115 (0.1) | 64 | 2250 | 70.55 | 70.55 | 6.71 | 6.91 | 16.46 | 16.46 |
| **4d** | 4 | $C_{16}H_{19}N_3O$ | 119-120 (0.15) | 89 | 2275 | 71.35 | 71.35 | 7.11 | 7.37 | 15.60 | 15.59 |
| **4e** | 5 | $C_{17}H_{21}N_3O$ | 130-132 (0.27) | 62 | 2280 | 72.06 | 71.79 | 7.47 | 7.67 | 14.83 | 14.51 |

(a) These compounds can be stored under nitrogen in the refrigerator for days. (b) The ir spectra were run as liquid films and sometimes if run slowly would show apparent reaction with atmospheric water.

Table IV

Products of Friedel-Crafts Cyclization of the Compounds of Table III

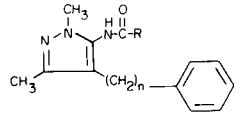


| Compound Number | n | Emperical Formula | Yield % | Mp °C | IR(χ NH-C=O) $cm^{-1}$ | Recrystallization Solvent | Analyses % C, Calcd. (Found) | H, Calcd. (Found) | N, Calcd. (Found) |
|---|---|---|---|---|---|---|---|---|---|
| **5a** (a) | 1 | $C_{13}H_{13}N_3O$ | 83 | 237.5-240 (b) | 1650 and 1670 (potassium bromide) 1658 in chloroform | THF-hexane | 68.70 (68.47) | 5.76 (5.85) | 18.49 (18.14) |
| **5b** | 2 | $C_{14}H_{15}N_3O$ | 85 | 205-207 | 1660 | chloroform-petroleum ether | 69.68 (69.53) | 6.27 (6.33) | 17.42 (17.58) |
| **5c** | 3 | $C_{15}H_{17}N_3O$ | 84 | 222-225 | 1670 | chloroform | 70.59 (70.42) | 6.71 (6.69) | 16.46 (16.53) |
| **5d** | 4 | $C_{16}H_{19}N_3O$ | 47 | 215-217 | 1680 | (c) | 71.34 (71.04) | 7.11 (6.98) | 15.60 (15.48) |
| **5e** | 5 | $C_{17}H_{21}N_3O$ | 0 | | | | | | |

(a) See references (10) and (11). (b) Mp reported in reference (11) is 238-240°, ir (nujol): λ (NH-C=O) = 1655 $cm^{-1}$. (c) Sublimed at 150° and 0.1 mm Hg pressure, crystals could be grown in acetone.

Table V

Solid Derivatives of the Compounds of Table III



| Compound Number | n | R | Emperical Formula | Yield % | Mp °C | Recrystallization Solvent | Analyses % C Calcd. | C Found | H Calcd. | H Found | N Calcd. | N Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **6a** | 1 | $OC_2H_5$ | $C_{15}H_{19}N_3O_2$ | 83 | 58.5-62 | ethanol | 65.91 | 65.78 | 7.01 | 7.06 | 15.37 | 15.61 |
| **6b** | 2 | $OC_2H_5$ | $C_{16}H_{21}N_3O_2 \cdot HCl$ | 89 | 182.5-185 | 2-propanol-ether | 59.34 | 59.57 | 6.85 | 6.87 | 12.98 | 12.84 |
| **6c** | 3 | $NH_2$ | $C_{15}H_{20}N_4O$ | 90 | 220-222 | ethanol | 66.15 | 66.23 | 7.40 | 7.45 | 20.57 | 20.55 |
| **6d** | 4 | $NH_2$ | $C_{16}H_{22}N_4O$ | 57 | 206-208 | ethanol | 67.11 | 66.98 | 7.75 | 7.73 | 19.57 | 19.79 |
| **6e** | 5 | $NH_2$ | $C_{17}H_{24}N_4O$ | 94 | 212-214 | ethanol | 67.97 | 67.66 | 8.05 | 8.01 | 18.65 | 18.53 |

ring was isolated in 47% yield and the synthesis failed in the 11-membered case (Table IV). The following cyclic lactams were obtained: 1,3-Dimethyl-4,10-dihydropyrazolo-[3,4-*c*][2]benzazepin-9(1*H*)-one (**5a**); 1,4,5,11-tetrahydro-1,3-dimethyl-10*H*-pyrazolo[3,4-*c*][2]benzazocin-10-one (**5b**); 4,5,6,12-tetrahydro-1,3-dimethylpyrazolo[3,4-*c*][2]benzazonin-11(1*H*)-one (**5c**); 1,4,5,6,7,13-hexahydro-1,3-dimethyl-12*H*-pyrazolo[3,4-*c*][2]benzazecin-12-one (**5d**).

## EXEPERIMENTAL

General.

The melting points were determined in open capillary tubes in a Thomas-Hoover apparatus and are uncorrected. The ir spectra were determined with a Beckman IR-9 spectrophotometer. The nmr spectra were determined with a Varian A-60 instrument with TMS as the internal standard. Concentration was carried out under reduced pressure. The ir (liquids were run as liquid films, solids as potassium bromide disks) and $^1H$ nmr spectra were obtained for all compounds and were consistent with the assigned structures and are compiled in Table VI. The C, H, and N analyses checked to within ± 0.4% unless otherwise noted. All reactions were run in dry apparatus consisting of a three necked round bottom flask equipped with a mechanical stirrer, a side arm equipped with a thermometer and a reflux condenser with a bubbler exit and a dropping funnel or gas inlet tube. All solvents were used as obtained from commercial suppliers. 3-Phenylpropanenitrile (hydrocinnamonitrile) (**1a**) was purchased from Eastman Organic Chemicals. 4-Phenylbutanenitrile (**1b**), 5-phenylpentanenitrile (**1c**), and 6-phenylhexanenitrile (**1d**) were prepared as described by Butler (12). Methyl 6-phenyl-5-oxohexanoate-[methyl-ω-benzoylvalerate] was synthesized by the method of Grateau (13).

Synthesis of 7-Phenylheptanenitrile (**1e**).

Methyl 6-phenyl-5-oxohexanoate (13), (588 g, 2.67 moles) was hydrogenated at 50 psi using 20% Pd/C catalyst and concentrated sulfuric acid (6

Table VI

$^1$H NMR Results (a)

| Compound Number | $^1$H NMR (ppm) |
|---|---|
| **2a** | δ 2.05 (s (b), 3H), 2.8-3.1 (m (c), 2H), 3.4-3.7 (m, 1H), 7.15 (s, 5H) |
| **2b** | δ 1.9-2.5 (m, ss (d) 2.3, 5H), 2.6-3.05 (m, 2H), 3.25-3.5 (m, 1H), 7.25 (s, 5H) |
| **2c** | δ 1.4-1.9 (m, 4H), 2.15 (s, 3H), 2.4-2.75 (m, 2H), 3.15-3.4 (m, 1H), 7.15 (s, 5H) |
| **2d** | δ 1.2-2.0 (m, 6H), 2.05 (s, 3H), 2.35-2.85 (m, 2H), 3.25-3.5 (m, 1H), 7.15 (s, 5H) |
| **2e** | δ 1.15-2.1 (m, 8H), 2.25 (s, 3H), 2.65-2.85 (m, 2H), 3.1-3.45 (m, 1H), 7.15 (s, 5H) |
| **3a** | δ 2.05 (s, 3H), 3.0-3.4 (br s (e), 2H), 3.5 (s, 3H), 3.6 (s, 2H), 7.13 (br s, 5H) |
| **3b** | δ 2.05 (s, 3H), 2.3-2.7 (m, 4H), 2.7-3.1 (br s, 2H), 3.5 (s, 3H), 7.15 (br s, 5H) |
| **3c** | δ 1.5-2.8 (m, ss 2.05, 9H), 3.0-3.4 (br s, 2H), 3.5 (s, 3H), 7.15 (br s, 5H) |
| **3d** | δ 1.3-2.0 (m, 4H), 2.05-2.45 (m, ss 2.05, 5H), 2.5-2.9 (m, 2H), 3.05-3.45 (br s, 2H), 3.55 (s, 3H), 7.15 (br s, 5H) |
| **3e** | δ 1.15-1.9 (m, 6H), 2.0-2.4 (m, ss 2.05, 5h), 2.45-2.8 (m, 2H), 3.05-3.40 (br s, 2H), 3.55 (s, 3H), 7.10 (br s, 5H) |
| **4c** | δ 1.65-2.0 (m, 2H), 2.05-2.8 (m, ss 2.12 7H), 3.65 (s, 3H), 7.15 (br s, 5H) |
| **4d** | δ 1.25-1.9 (m, 4H), 2.0-2.8 (m, ss 2.09, 7H), 3.60 (s, 3H), 7.15 (s, 5H) |
| **4e** | δ 1.15-1.9 (m, 6H), 2.1-2.8 (m, ss 2.13, 7H), 3.63 (s, 3H), 7.15 (s, 5H) |
| **5a** | δ 2.2 (s, 3H), 3.67 (s, 2H), 3.75 (s, 3H), 7.0-7.45 (m, 3H), 7.7-8.5 (m, 1H), 10.67 (s, 1H) |
| **5b** | δ 2.1 (s, 3H), 2.3-3.4 (m, 4H), 3.68 (s, 3H), 6.95-7.7 (m, 4H), 9.4-9.6 (br s 1H) |
| **5c** | δ 1.95 (s, 3H), 2.3-3.1 (m, 6H), 3.5 (s, 3H), 6.9-7.2 (m, 4H), 8.35-8.58 (br s, 1H) |
| **5d** | δ 1.0-2.25 (m, ss 1.9, 7H), 2.25-3.1 (2 br t (f), 4H), 3.57 (s, 3H), 6.9-7.2 (m, 4H), 7.5-7.7 (br s, 1H) |

(a) All spectra were run in deuteriochloroform with the exception of that of **5d** which was run in DMSO-$d_6$ for solubility reasons. (b) s = singlet. (c) m = multiplet. (d) ss = superimposed singlet. (e) br s = broad singlet. (f) br t = broad triplet.

ml) in methanol (1 ℓ) to yield methyl 6-phenylhexaneoate (**7**), 521 g (95%); bp 85-87° (0.35 mm); ir (liquid film): ν (C=O) 1742 cm$^{-1}$; $^1$H nmr (deuteriochloroform): δ 1.5-2.1 (m, 6H), 2.2-2.6 (m, 2H), 2.8-3.2 (m, 2H), 3.7 (s, 3H), 7.1-7.7 (m, 3H), 7.8-8.2 (m, 2H).

A solution of **7** (418 g, 2.03 moles) in dry diethyl ether (500 ml) was added dropwise with stirring to a suspension of lithium aluminum hydride, (76 g, 2.0 moles) in dry diethyl ether (3 ℓ). The mixture was refluxed 16 hours. After cooling, water (180 ml) was added dropwise with caution. This was followed with 10% sulfuric acid (2 ℓ). The layers were separated and the organic layer was dried (magnesium sulfate), filtered, concentrated, and distilled to yield 6-phenyl-1-hexanol (**8**), 358 g (98.6%); bp 90-92° (0.2 mm); $^1$H nmr (deuteriochloroform): δ 1.1-1.9 (m, 8H), 2.0 (s, 1H), 2.4-2.8 (m, 2H), 3.4-3.8 (m, 2H), 7-7.4 (br s, 5H).

*Anal.* Calcd. for $C_{12}H_{16}O$: C, 80.85; H, 10.18. Found: C, 80.95; H, 10.09.

A solution of **8** (356 g, 2.0 moles) in chloroform (500 ml) was added dropwise with stirring to a solution of thionyl chloride (300 g, 2.5 moles) in chloroform) (2 ℓ) and the mixture was refluxed 1 hour. The mixture was concentrated to yield 1-chloro-6-phenylhexane (**9**), 391 g (99%) and was used without further purification; $^1$H nmr (deuteriochloroform): δ 1.1-2.0 (m, 8H), 2.4-2.8 (m, 2H), 3.38-3.7 (m, 2H), 7.2 (s, 5H).

A solution of sodium cyanide (53 g, 1.08 moles) and potassium iodide (2 g, 12 mmoles) in dimethyl sulfoxide (400 ml) was heated to 45° and with stirring, **9** (197 g, 1.0 mole) was added dropwise over 3 hours. The mixture was heated during the addition to 80°. The mixture was stirred 16 hours and heated at 140° for 8 hours, cooled and poured into ice water. The aqueous mixture was extracted with diethyl ether. The combined extracts were dried (magnesium sulfate), filtered, concentrated and distilled to yield 7-phenylheptanenitrile (**1e**) (14), 185 g (98.5%); bp 93-95° (0.1 mm); ir (liquid film): ν C≡N 2320 cm$^{-1}$; $^1$H nmr: δ 1.1-2 (m, 8H), 2.1-2.8 (2 overlapping m, 4H), 7.18 (br s, 5H).

*Anal.* Calcd. for $C_{13}H_{17}N$: C, 83.38; H, 9.15; N, 7.47. Found: C, 83.21; H, 9.11; N, 7.35.

General Procedure for the Synthesis of α-Acetyl-ω-phenylalkanenitriles (**2a-e**) (5).

Sodium amide (2 moles) was prepared in liquid ammonia (2 ℓ) using ferric nitrate catalysis. To the resulting suspension was added a solution of the ω-phenylalkanenitrile (**1a-e**) (2 moles) in anhydrous diethyl ether (200 ml). The mixture was stirred for 10 minutes and a solution of methyl acetate (1 mole) in anhydrous diethyl ether (100 ml) was added. The mixture was stirred for 10 minutes and diluted with anhydrous diethyl ether (2 ℓ) and the ammonia was allowed to evaporate overnight. The ether suspension was poured into a mixture of ice and water and the layers were separated. Unreacted ω-phenylalkanenitrile could be recovered from the ether layer. The aqueous layer was acidified with excess dilute hydrochloric acid and was extracted with diethyl ether. The extracts were dried (magnesium sulfate), concentrated and distilled to yield the α-acetylphenylalkanenitriles **2a-e** (Table I).

General Procedure for the Synthesis of 1,3-Dimethyl-4-(ω-phenylalkyl)-1*H*-pyrazol-5-amines (**3a-e**) (6,7).

A solution of the α-acetyl-ω-phenylalkanenitrile (**2a-e**) (0.77 mole) in 95% ethanol (500 ml) was treated with concentrated hydrochloric acid (10 ml) and with stirring methyl hydrazine (0.77 mole) was added dropwise. The mixture was refluxed 2 hours and concentrated hydrochloric acid (110 ml) was added dropwise and refluxing was continued 16 hours. The mixture was concentrated to dryness at reduced pressure. The resulting solid was added to a mixture of an excess of sodium hydroxide solution and diethyl ether. The organic extracts were dried (magnesium sulfate), filtered, concentrated, and yielded the crystalline 1*H*-pyrazol-5-amines **3a-e** (Table II). These were routinely recrystallized from anhydrous diethyl ether.

General Procedure for the Synthesis of 1,3-Dimethyl-4-(ω-phenylalkyl)-1*H*-pyrazol-5-isocyanates (**4a-e**) (8,9).

Phosgene (2 moles) was bubbled into toluene (500 ml) at -5°. The temperature of the reaction mixture was maintained between -7 and +9° by cooling in an ice-acetone bath during the addition of the reactants over a 10 minute period. Alternate additions of the 1*H*-pyrazol-5-amine (1 mole) and triethylamine (2 moles) were made with stirring. The resulting mixture was stirred and allowed to warm to 25° over 16 hours. Phosgene was slowly bubbled into the stirred mixture as the reaction mixture was heated slowly to the reflux point. Rapid gas evolution usually took place between 50-100°. The phosgene addition was stopped at the reflux point and the mixture was refluxed 6 hours. The mixture was cooled by blowing a stream of nitrogen through the solution. The mixture was filtered rapidly through filter aid to remove triethylamine hydrochloride. The filtrate was concentrated at reduced pressure and the resulting oil was distilled at vacuum pump pressures to obtain the 1*H*-pyrazol-5-isocyanates **4a-e** (Table III). The isocyanates were reacted either with ethanol or ammonia to produce solid derivatives (Table V) other than cyclic lactams (Table IV).

General Procedure for the Intramolecular Friedel-Crafts Cyclization (1).

A mixture of powdered aluminum chloride (0.21 mole) in *o*-dichlorobenzene (300 ml for 0.1 mole of starting isocyanate) was heated to 90°. A solution of the 1*H*-pyrazol-5-isocyanate (**4a-e**) (0.1 mole in 30 ml of *o*-dichlorobenzene) was added dropwise with stirring over 10-15 minutes.

The mixture was heated for 1 hour at 115° and then briefly to 145°. The mixture was allowed to cool slowly to 25° and crushed ice and water was added with rapid stirring. The mixture was allowed to stir and the product crystallized and was recovered by filtration. After the products were dried in a vacuum oven, they were purified by recrystallization or sublimation (Table IV).

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(10) This compound (**5a**) has been prepared by Swett and Aynilian (11) by dehydration of 5-amino-4-(*o*-carboxybenzyl)-1,3-dimethylpyrazole and had the same mp, mixed mp, and spectral characteristics. We are indebted to Dr. H. A. DeWald for a sample of **5a** prepared by this method.

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