The Use of a Protecting Group in the Synthesis of 9-Alkyl-9H-purine-6(1H)-thiones[1a,b]

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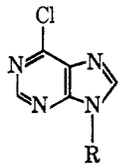
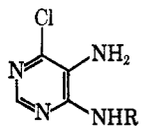
A new synthesis of 9-alkyl-9H-purine-6(1H)-thiones (I) is described which involves the direct alkylation of 6-diphenylmethylthiopurine followed by subsequent removal of the S-diphenylmethyl group.

9-Alkyl-9H-purine-6(1H)-thiones (I) have usually been prepared by treating the appropriate 6-chloro-9-alkyl-9H-purine (II) with thiourea in boiling ethanol.[2,3] The available methods for the synthesis of II are (1) synthesis of the requisite 5-amino-6-chloro-4-alkylaminopyrimidine (III) followed by subsequent ring closure to II[2,3] and (2) direct alkylation of 6-chloropurine (IV).[4,5] Method 1 gives pure 9-alkyl



II, R = alkyl group
IV, R = H

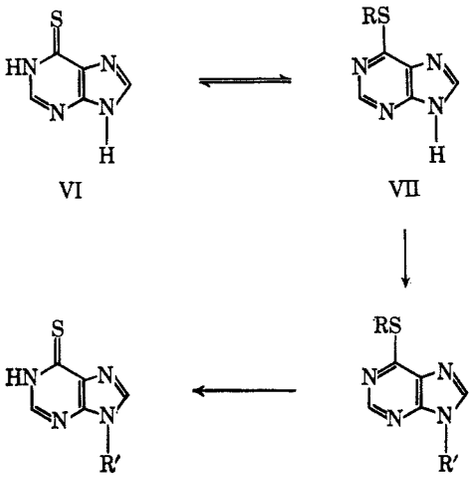


III, R = alkyl group

product and is the procedure of choice when the primary alkylamine needed to prepare III is available. Method 2 involves only one step and can be used if the necessary alkylating agent is available. However, the product obtained by method 2 is contaminated with the 6-chloro-7-alkyl-7H-purine (V) and necessitates a separation of the two similar products. Because of this difficulty, a study of alternative methods for the synthesis of pure 9-alkyl-9H-purine-6(1H)-thiones which would be applicable to the synthesis of I containing complicated 9-alkyl groups appeared desirable.

It is well established that the alkylation of purine-6-(1H)-thione (VI) under alkaline conditions normally gives 6-alkylthiopurines (VII). In addition, it has been shown that the direct alkylation of the 6-alkylthiopurines (VII) thus obtained affords mainly the 9-alkyl-6-alkylthiopurines (VIII).[6-8] Therefore, a possible alternate route to 9-alkyl-9H-purine-6(1H)-thiones (I) could involve the alkylation of a 6-alkylthiopurine (VII) containing a S-alkyl group which could subsequently be removed to regenerate the 6-thione function. Furthermore, if the S-alkyl protecting group was of sufficient steric bulk, stereoselective alkylation at the 9 position might be observed. This paper describes the results obtained when the diphenylmethyl (DPM) group was used to protect the 6-thione function of purine-6-(1H)-thione (VI).

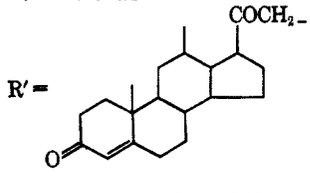
Treatment of VI with bromodiphenylmethane in N,N-dimethylformamide (DMF) catalyzed by potassium carbonate gave a 69% yield of 6-diphenylmethylthiopurine [VII, R = $(C_6H_5)_2CH$]. When VII, R = $(C_6H_5)_2CH$, was refluxed with trifluoroacetic acid containing phenol, a 96% yield of VI was obtained indicating that the DPM-protecting group could be removed without effecting the purine ring. The alkylation of VII, R = $(C_6H_5)_2CH$, with 2-bromo-4′-chloroacetophenone, iodoethane, α-bromotoluene, and desoxycortocosterone 21-*p*-bromobenzesulfonate in DMF containing potassium carbonate gave a 64–72% yield of the corresponding 9-alkyl-6-diphenylmethylthiopurine (VIII). The structural assignments were based on the elemental analysis, and uv and nmr spectral data recorded in Table I. Thin layer chromatograms of the crude reaction mixtures from which VIIIa, b, and d



VI VII

I

VIIIa, R = $(C_6H_5)_2CH$; R′ = *p*-$ClC_6H_4COCH_2$
b, R = $(C_6H_5)_2CH$; R′ = C_2H_5
c, R = $(C_6H_5)_2CH$; R′ = $C_6H_5CH_2$
d, R = $(C_6H_5)_2CH$;



e, R = $C_6H_5CH_2$; R′ = $(C_6H_5)_3C$

(1) (a) This research was carried out under Contract SA-43-ph-4531 of the Cancer Chemotherapy Service Center, National Cancer Institute, National Institute of Health. (b) Part of this work was presented at the 19th Southeastern Regional Meeting of the American Chemical Society, Atlanta, Ga., Nov 1967, Abstract No. 326.

(2) J. A. Montgomery and C. Temple, Jr., *J. Amer. Chem. Soc.*, **79**, 5238 (1957).

(3) R. K. Robins and H. H. Lin, *ibid.*, **79**, 490 (1957).

(4) J. A. Montgomery and C. Temple, Jr., *ibid.*, **83**, 630 (1961).

(5) The chloromercuri-6-chloropurine could also be subjected to direct alkylation. However, chloromercuri-6-chloropurine is contaminated by a variable amount of bis(6-chloropurinyl)mercury. In addition the alkylation of 6-chloromercuri-6-chloropurine has generally been successful only when very active alkyl halides such as halo sugars have been used.

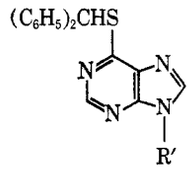
(6) T. P. Johnston, L. B. Holum, and J. A. Montgomery, *J. Amer. Chem. Soc.*, **80**, 6265 (1958).

(7) D. E. O'Brien, J. D. Westover, R. K. Robins, and C. C. Cheng, *J. Med. Chem.*, **8**, 182 (1965).

(8) O'Brien and coworkers reported that the alkylation of 6-benzylthiopurine with ethylene bromohydrin in DMSO catalyzed by potassium carbonate gave a 57% yield of 6-benzylthio-9-(β-hydroxyethyl)purine.[7] Johnston and coworkers reported that the treatment of purine-6(1H)-thione with 2 equiv of α-chlorotoluene in DMF containing 2.2 mol of potassium carbonate gave a 82% yield of dibenzylated product from which both 9-benzyl-6-benzylthiopurine and 7-benzyl-6-benzylthiopurine were isolated.[6]

TABLE I

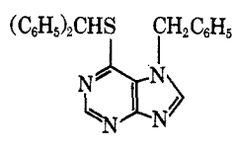
9-ALKYL-6-DIPHENYLMETHYLTHIOPURINES (VIII)



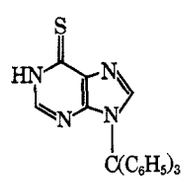
Compound[a]	Yield, %[b]	Mp, °C	Uv $\lambda_{max}^{CH_3OH}$, mμ	Uv ε × 10⁻³	Nmr resonances $CDCl_3$,[c] δ Purine-2-H	Purine-8-H	Other resonances	Molecular formula	Calcd (found), % C	H	N	S
VIIIa[d]	72	168–169	292	18.2	8.65	7.97	5.51 (NCH_2CO)	$C_{26}H_{19}N_4ClOS$	66.31	4.04	11.90	6.80
			286	18.4	(8.79)	(8.58)	6.87 [$SCH(Ar)_2$]		(66.23)	(4.23)	(12.19)	(6.77)
			254	15.6								
VIIIb[d]	64	184–186	292	21.1	8.75	7.95	6.88 [$SCH(Ar)_2$]	$C_{20}H_{18}N_4S$	69.33	5.24	16.17	9.26
			286	21.5					(69.43)	(5.31)	(16.35)	(9.13)
VIIIc[d]	64	138–139	293	16.6	8.71	7.87	5.29 (NCH_2Ar)	$C_{25}H_{20}N_4S$	73.50	4.94	13.71	7.85
			286	16.3			6.88 [$SCH(Ar)_2$]		(73.34)	(4.89)	(13.63)	(7.81)
IX[d]	12[e]	149–151	302	15.2	8.85	8.03	5.67 (NCH_2Ar)	$C_{25}H_{20}N_4S$	73.50	4.94	13.71	7.85
			296	15.5			6.87 [$SCH(Ar)_2$]		(73.46)	(4.98)	(13.65)	(7.59)
VIIId[f]	66	146–149	293	20.1	8.65	7.95	0.68 (18-CH_3)	$C_{39}H_{42}N_4O_3S$[g]	72.22	6.79	8.64	4.93
			286	20.2	(8.76)	(8.62)	1.15 (19-CH_3)		(72.23)	(6.66)	(8.66)	(4.66)
							4.98 (NCH_2CO)					
							5.73 (Δ-4 H)					
							6.87 [$SCH(Ar)_2$]					

[a] A typical procedure is given in the Experimental Section. [b] Based on pure compound isolated. [c] Values in parentheses were obtained in $(CD_3)_2SO$. [d] Recrystallized from ethanol. [e] 7-Benzyl-6-diphenylmethylthiopurine. [f] Recrystallized from a chloroform and petroleum ether (bp 30–60°) mixture. [g] Calculated as the monohydrate.

were obtained indicated that trace amounts of other products were present; however, none were present in sufficient amount to be isolated.[9] In contrast the alkylation of VII, R = $(C_6H_5)_2CH$, with α-bromotoluene gave, in addition to a 64% yield of 9 benzyl-6-diphenylmethylthiopurine (VIIIc), a 12% yield of 7-benzyl-6-diphenylmethylthiopurine (IX).[10] In a study of the alkylation of 6-chloropurine with a number of alkyl halides, Montgomery and Temple[4] found that α-chlorotoluene gave the highest yield of 7 isomer. The ratio of 9 isomer–7 isomer obtained in the alkylation of 6-chloropurine with α-chlorotoluene was 2.53. The alkylation of VII, R = $(C_6H_5)_2CH$, with α-chlorotoluene in dimethyl sulfoxide[11] gave a ratio of 4.93 for VIII/IX. Therefore, the alkylation of VII, R = $(C_6H_5)_2CH$, with α-chlorotoluene is approximately twice as selective for alkylation at the 9 position as in 6-chloropurine. If



IX



X

this selectivity is due in part to the large steric bulk of the DPM group, the perference for 9 alkylation could be enhanced by using the larger triphenylmethyl (TPM) protecting group in place of the DPM group. However, we were unable to test this possibility since attempts to prepare VII, R = $(C_6H_5)_3C$, by the alkylation of VI with bromotriphenylmethane or by the reaction of triphenylmercaptan with IV were unsuccessful. When VI was treated with bromotriphenylmethane, an unknown product was obtained which showed one spot on thin layer chromatograms. The elemental analysis and mass spectrum showed that the product was a monotriphenylmethyl derivative of VI. The uv spectrum, $\lambda_{max}^{CH_3OH}$ 324 mμ (ε 22,300) and λ_{max}^{pH11} 312 (24,700), indicated that substitution was not occurring at the thione group of VI. The fact that the product gave a high yield of triphenylcarbinol and VI when treated with aqueous acetic acid showed that the substitution had occurred at one of the heterocyclic nitrogens. 9-Triphenylmethyl-6-benzylthiopurine (VIIIc) was obtained when 6-benzylthiopurine (VII, R = $C_6H_5CH_2$) in DMF was treated with bromotriphenylmethane. The uv spectrum showed $\lambda_{max}^{CH_3OH}$ 286 mμ (ε 24,200) and 292 (23,200) typical of a 9-alkyl-6-alkylthiopurine. Compound VIIIe is identical with the product obtained by treating the unknown product with α-bromotoluene. On the basis of this evidence, along with the uv spectrum, the unknown compound has been assigned the structure 9-triphenylmethyl-9H-purine-6(1H)-thione (X). This anomalous alkylation apparently results from the instability of the expected 6-triphenylmethylthiopurine under the reaction conditions thus allowing VI to undergo the normally less favorable alkylation of the 9 position.

Treatment of the 9-alkyl-6-diphenylmethylthiopurines (VIII) with refluxing trifluoroacetic acid containing a small amount of phenol gave 85–95% yield of the corresponding 9-alkyl-9H-purine-6(1H)-thiones (I). The structure proof was based on the elemental analysis and uv spectral data recorded in Table II.

The good yields of easily crystallizable 9-alkyl-6-diphenylmethylthiopurines (VIII) obtained in the alkylation of VII, R = $(C_6H_5)_2CH$, and the ease of

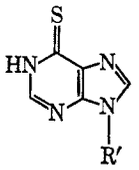
(9) Thin layer plates were prepared using silica gel HF. The plates were eluted with hexane–chloroform–methanol (4:4:1) and developed by spraying with a 5% solution of phosphomolybdic acid in ethanol followed by heating to 100°.

(10) When the benzylation of VII, R = $(C_6H_5)_2CH$, was carried out with α-chlorotoluene in dimethyl sulfoxide, a 64% yield of VIIIc and a 13% yield of IX was obtained (see the Experimental Section).

(11) These are the conditions that Montgomery and Temple[4] used in the benzylation of 6-chloropurine.

TABLE II

9-ALKYL-9H-PURINE-6(1H)-THIONES



Compound[a]	R′	Yield, %[b]	Mp,[c] °C	Uv $\lambda_{max}^{pH\ 11}$, mμ	Uv ε × 10^{-3}	Molecular formula	Calcd (found), % C	H	N	S
Ia[d]	p-$ClC_6H_4COCH_2$	95	295–297	312	26.0	$C_{13}H_9ClN_4OS$	51.23	2.95	18.39	10.52
				258	18.8		(50.98)	(3.06)	(18.24)	(10.26)
				235	19.0					
Ib[e]	C_2H_5	92	340–342[f,g]	309	21.9					
				231	14.1					
Ic[d]	$C_6H_5CH_2$	93	293–296[h]	312	27.6					
				234	17.6					
Id[d]	$C_{21}H_{29}O_2$	85	325–328	312	17.8	$C_{26}H_{32}N_4O_2S$	67.24	6.89	12.07	6.89
				247	16.7		(66.87)	(7.05)	(11.56)	(6.56)
				236	24.4					
VI	H	96	310–315[i]							

[a] A typical procedure is given in the Experimental Section. [b] Based on pure compound isolated. [c] All these compounds decomposed on melting. [d] Recrystallized from N,N-dimethylformamide. [e] Purified by dissolving in 1 N sodium hydroxide solution and precipitation by neutralization with acetic acid. [f] This melting point was obtained in an oil bath. [g] J. A. Montgomery and C. Temple, Jr., reported mp 333–337°. [h] Lit.[g] mp >260°. [i] G. B. Elion, E. Burgi, and G. H. Hitchings, *J. Amer. Chem. Soc.*, **74**, 411 (1952), reported mp 313–314°.

removal of the DPM-protecting group from VIII makes this procedure an attractive route to 9-alkyl-9H-purine-6(1H)-thiones.

Experimental Section[12]

6-Diphenylmethylthiopurine [VII, R = $(C_6H_5)_2CH$].—A mixture of 0.151 g (1.0 mmol) of purine-6(1H)-thione,[13] 0.138 g (1.0 mmol) of anhydrous potassium carbonate and 1 ml of N,N-dimethylformamide (DMF) under a nitrogen atmosphere was stirred for 15 min. To this mixture was added 0.247 g (1.0 mmol) of bromodiphenylmethane, and the contents were stirred at room temperature for 3 hr. The mixture was diluted with 20 ml of water and acidified with acetic acid. The mixture was stirred vigorously for 30 min, filtered, and dried to give an amorphous solid. Recrystallization from methanol gave 0.22 g (69%) of 6-diphenylmethylthiopurine, mp 224–229°. The analytical sample prepared by further recrystallization from methanol had mp 229–231°; uv max (CH_3OH), 290 mμ (ε 19,900) with a shoulder at 286 (19,100); ν_{max}^{KBr} 1575 and 1495 cm^{-1} (C=C and C=N); nmr [$(CD_3)_2SO$], δ 6.92 (-S-CH), 8.62 and 8.83 ppm (purine 8 H and 2 H). *Anal.* Calcd for $C_{18}H_{14}N_4S$: C, 67.92; H, 4.40; N, 17.61; S, 10.06. Found: C, 67.79; H, 4.46; N, 17.61; S, 10.04.

9-p-Chlorophenacyl-6-diphenylmethylthiopurine (VIIIa).—To a stirred mixture of 0.318 g (1.0 mmol) of 6-diphenylmethylthiopurine, 0.138 g (1.0 mmol) of anhydrous potassium carbonate and 1 ml of DMF was added 0.234 g (1.0 mmol) of 2-bromo-4′-chloroacetophenone. The mixture was stirred at room temperature for 2 hr. The mixture was diluted with 50 ml of water, and the resulting precipitate was separated by filtration.[14] Recrystallization of the product from ethanol gave 0.34 g (72%) of 9-p-chlorophenacyl-6-diphenylmethylthiopurine (VIIIa), mp 168–169°. The elemental analysis and spectral data are recorded in Table I. The 9-alkyl-6-diphenylmethylthiopurines VIIIa–d listed in Table I were obtained in a similar manner. The reaction times were reduced if the reactions were conducted at 50°.

The Preparation of 9-Benzyl-6-diphenylmethylthiopurine (VIIIc) and 7-Benzyl-6-diphenylmethylthiopurine (IX) Using DMSO as Solvent.—A mixture of 0.318 g (1.0 mmol) of 6-diphenylmethylthiopurine, 0.138 g (1.0 mmol) of anhydrous potassium carbonate, and 0.127 g (1.0 mmol) of α-chlorotoluene in 1 ml of dimethyl sulfoxide was stirred at room temperature for 4 hr. The reaction mixture was diluted with 20 ml of water and extracted with ether. The ethereal extract was dried (Na_2SO_4) and concentrated to give 0.42 g of solid which showed two spots on thin layer chromatograms.[9] The solid was dissolved in 7 ml of hot ethanol. On cooling, 0.21 g (52%) of 9-benzyl-6-diphenylmethylthiopurine (VIIIc), mp 135–137°, was obtained. The product showed one spot by tlc. The filtrate was concentrated to dryness under reduced pressure. The remaining residue was subjected to tlc on silica gel HF using hexane–chloroform–methanol (4:4:1) solvent. Two distinct bands were detected by uv quenching. The two bands were separated and extracted with ethyl acetate. Concentration of the extracts followed by trituration of the product obtained from the top band gave an additional 0.050 g (12%) of VIIIc, mp 135–137°. Concentration of the extracts of the lower band followed by trituration of the residue with ethanol and cooling to 0° gave 0.054 g (13%) of 7-benzyl-6-diphenylmethylthiopurine (IX), mp 149–151°. A thin layer chromatogram showed one spot.[9] Similar results were obtained if the reaction was carried out in N,N-dimethylformamide (Table I). The analysis and spectral data for VIIIc and IX are recorded in Table I.

The Preparation of 9-p-Chlorophenacyl-9H-purine-6(1H)-thione (Ia) from 9-p-Chlorophenacyl-6-diphenylmethylthiopurine (VIIIa).—A mixture of 1.2 g (2.56 mmol) of 9-p-chlorophenacyl-6-diphenylmethylthiopurine, 1.2 g of phenol, and 3 ml of trifluoroacetic acid was refluxed for 0.5 hr. The trifluoroacetic acid was removed under reduced pressure, and the remaining residue was treated with ether. The resulting solid was washed well with ether and acetone and recrystallized from hot DMF to give 0.75 g (95%) of 9-p-chlorophenacyl-9H-purine-6(1H)-thione, mp 295–300°. Compounds Ia–d and VI were obtained in a similar manner. The results obtained with individual compound along with the analytical and spectral data are listed in Table II.

9-Triphenylmethyl-9H-purine-6(1H)-thione (X).—A mixture of 0.34 g (2.2 mmol) of purine-6(1H)-thione, 0.276 g (2.0 mmol) of anhydrous potassium carbonate, and 5 ml of N,N-dimethylformamide under a nitrogen atmosphere was stirred for 15 min.

(12) Melting points were determined on a Kofler hot stage microscope using a calibrated thermometer. Uv and visible spectra were measured on a Cary Model 14 spectrophotometer. Nmr spectra were recorded on a Varian Model A-60, using tetramethylsilane as an internal standard. Ir spectra were measured with a Perkin–Elmer 221 spectrophotometer; samples were prepared in the form of pressed KBr disks. Mass spectra were determined on an AEI MS-902 spectrometer. Microanalyses were carried out by Micro-Tech Laboratories, Skokie, Ill.

(13) Lower yields were obtained if purine-6(1H)-thione monohydrate was used.

(14) In the case of iodoethane and α-bromotoluene an oil was obtained which was extracted into ether. The extracts were dried (Na_2SO_4), concentrated, and recrystallized from ethanol to give VIIIb and VIIIc, respectively. 7-Benzyl-6-diphenylmethylthiopurine (IX) was obtained from the filtrate of VIIIc as described in the preparation of VIIIc and IX using DMSO as reaction medium.

To this mixture was added 0.67 g (2.0 mmol) of bromotriphenylmethane, and the contents were stirred at room temperature for 3 hr. The mixture was diluted with water and extracted with chloroform. The extracts were dried (Na_2SO_4), concentrated, and recrystallized from methanol to give 0.12 g (20%) of 9-triphenylmethyl-9H-purine-6(1H)-thione (X), mp 213–216°. The mass spectrum showed M^+ at *m/e* 394.1292 (Calcd for $C_{24}H_{18}N_4S$: 394.1252). The analytical sample prepared by further recrystallization from methanol had mp 214–216°. *Anal.* Calcd for $C_{24}H_{18}N_4S \cdot 0.25H_2O$: C, 72.24; H, 4.67; N, 14.04; S, 8.04. Found: C, 72.11; H, 4.59; N, 13.97; S, 7.95.

Removal of the Triphenylmethyl Group from 9-Triphenylmethyl-9H-purine-6(1H)-thione (X).—A mixture of 0.0103 g (0.02 mmol) of X in 0.5 ml of 50% aqueous acetic acid was heated on a steam bath for 5 min. The cooled mixture was filtered to give 0.0061 g (90%) of triphenylcarbinol, mp 165–166°. The filtrate was concentrated by freeze-drying to give a yellow solid. Recrystallization from water gave 0.0044 g (98%) of purine-6(1H)-thione monohydrate, mp 308–312° dec (lit.[15] mp 313–314°). The infrared spectrum of this sample was identical with the spectrum of an authentic sample.

Preparation of 9-Triphenylmethyl-6-benzylthiopurine (VIIIe) from 6-Benzylthiopurine.—The alkylation of 6-benzylthiopurine with bromotriphenylmethane under conditions similar to those used for the preparation of VIIIa gave a 60% yield of VIIIe, mp 248–249°. The analytical sample prepared by further recrystallization from a N,N-dimethylformamide and methanol mixture had mp 249–250°. *Anal.* Calcd for $C_{31}H_{24}N_4S$: C, 76.83; H, 4.99; N, 11.56; S, 6.62. Found: C, 76.71; H, 5.12; N, 11.59; S, 6.56.

Preparation of 9-Triphenylmethyl-6-benzylthiopurine (VIIIe) from 9-Triphenylmethyl-9H-purine-6(1H)-thione (X).—A mixture of 0.085 g (0.218 mmol) of X, 0.02 g (0.218 mmol) of an anhydrous potassium carbonate, and 0.0373 g (0.218 mmol) of α-bromotoluene was stirred for 16 hr at 25°. The mixture was diluted with cold water and filtered. The precipitate was washed with ethanol and recrystallized from a N,N-dimethylformamide–methanol mixture to give 0.062 g (62%) of X, mp 248–251°. The ir spectra of this product was identical with VIIIe obtained by the alkylation of 6-benzylthiopurine with bromotriphenylmethane.

(15) See Table II, footnote *i*.

Registry No.—Ia, 17416-84-1; Ib, 17416-85-2; Ic, 17447-84-6; Id, 17392-79-9; VI, 5759-99-9; VII, 17416-87-4; VIIIa, 17416-88-5; VIIIb, 17449-06-8; VIIIc, 17449-07-9; VIIId, 17392-78-8; VIIIe, 17449-08-0; IX, 17477-83-7; X, 17449-09-1.

Acknowledgment.—We take pleasure in thanking Dr. M. E. Wall, director of this laboratory, for his kind encouragement and support of this work.

Intramolecular Amidoalkylations at Carbon. Synthesis of Heterocyclic Amines

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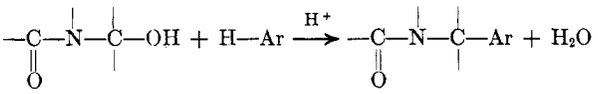
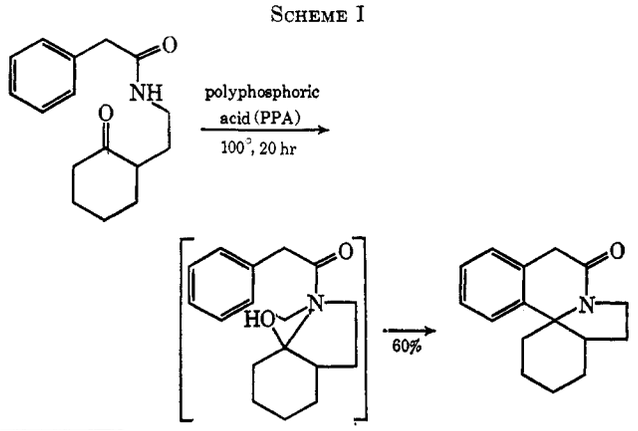
Amides of levulinic, 3-benzoylpropionic, *o*-benzoylbenzoic and phthalaldehydic acids with arylethylamines and benzylamines underwent double cyclization in strong acids, forming benzo-, dibenzo-, and thienoindolizines, and dibenzopyrrolizidines. Quaternary salts of benzoindolizines cleaved with lithium to give benzazonines.

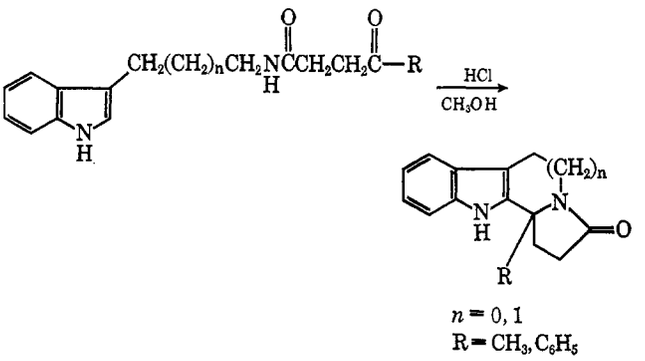
The Friedel–Crafts-type reaction of α-amido alcohols with aromatic rings has been extensively reviewed.[1] However, only a few examples of cyclizations using this method have been reported.



The first example of such a cyclization was reported by Belleau[2] in his synthesis of erythrina-like alkaloids (Scheme I). Mondon[3] synthesized the same ring system in a slightly different manner, using the dehydrated keto amide as an intermediate. These workers were able to prepare methoxy derivatives using milder conditions. With dimethoxyphenyl and indole derivatives, Boekelheide[4] and Winterfeldt[5] found that dilute hydrogen chloride in alcohol sufficed to give excellent yields of cyclized products. Recently, Brown[6] cyclized derivatives of isoquinolone to tetracyclic amides. After this work was completed, Wawzonek[7] reported intramolecular amidoalkylations of indole derivatives.

SCHEME I





n = 0, 1
R = CH_3, C_6H_5

These cyclizations are similar to our work except that we alkylated benzene and thiophene nuclei in-

(1) H. E. Zaugg and W. B. Martin, "Organic Reactions," Vol. 14, John Wiley and Sons, Inc., New York, N. Y., 1965, pp 52–270.

(2) B. Belleau, *J. Amer. Chem. Soc.*, **75**, 5765 (1953); *Can. J. Chem.*, **35**, 651, 663 (1967).

(3) A. Mondon, *Chem. Ber.*, **92**, 1461, 1472, 2543 (1959).

(4) V. Boekelheide, M. Muller, J. Jack, and T. Grossnickle, *J. Amer. Chem. Soc.*, **81**, 3955 (1959).

(5) E. Winterfeldt, *Chem. Ber.*, **97**, 2463 (1964).

(6) D. W. Brown and S. F. Dyke, *Tetrahedron*, **22**, 2429 (1966).

(7) S. Wawzonek and M. M. Maynard, *J. Org. Chem.*, **32**, 3618 (1967).