The β-lactams 8, 11, 12, 15, 19, 21, 23, and 24 were prepared by the same general procedure using the appropriate acid chloride and Schiff base.

Preparation of α-Amido-β-lactams. 1-Benzhydryl-3-amino-4-(p-methoxyphenyl)-2-azetidinone (9). Platinum oxide (1 g) was added to a solution of 4 g of the azido-β-lactam 8 in ethyl acetate and the mixture hydrogenated at 40 psi overnight, filtered, and evaporated to give 9 (3.5 g).

1-Benzhydryl-3-phenylacetamido-4-(p-methoxyphenyl)-2-azetidinone (10). Phenylacetyl chloride (0.7 g) in dry methylene chloride (50 ml) was added dropwise over a period of 45 min to a stirred solution of 9 (1.5 g) and triethylamine (0.5 g) and stirred overnight. The resulting solution was washed with water (50 ml × 3) and dried ($MgSO_4$). Removal of the solvent gave a thick oily liquid which was chromatographed over Florisil to provide the amido-β-lactam 10.

The nitro-β-lactam 12 was reduced to the amino compound 13 using Adams catalyst and subsequently acylated to 14 with phenylacetyl chloride using similar conditions as described for the synthesis of 10.

1-(p-Carboxyphenyl)-3-phenoxy-4-furfuryl-2-acetidinone (20). A mixture of the carbomethoxy-β-lactam 19 (1.0 g) and LiI (2.5 g) in anhydrous pyridine (30 ml) was refluxed (12 hr) under nitrogen atmosphere. The golden yellow solution was cooled, diluted with $CHCl_3$ (100 ml), and poured into 150 ml of cooled (0°) concentrated HCl. The aqueous phase was extracted with $CHCl_3$ (4 × 100 ml); the combined organic phase was washed with cold water (3 × 50 ml) and dried ($MgSO_4$). Removal of the solvent under reduced pressure provided 0.85 g of the carboxy derivative 20.

Acknowledgment. The authors are thankful to Gist-Brocades N.V., The Netherlands, and Stevens Institute of Technology for financial support of this research and biological evaluation of the compounds described in this communication.

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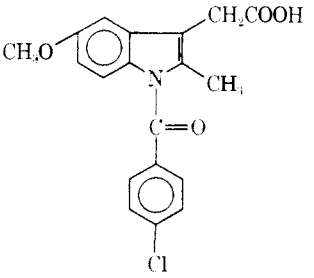
Synthesis and Antiinflammatory Activity of a Series of 2-Aroyl-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic Acids

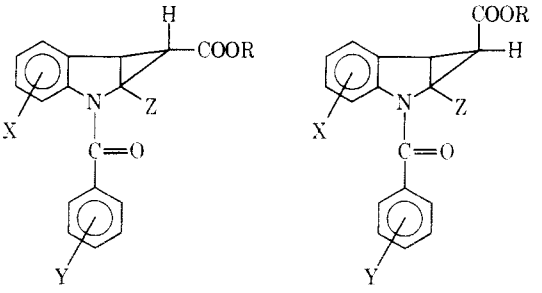
William J. Welstead, Jr.,* Harold F. Stauffer, Jr., and Lawrence F. Sancilio

A. H. Robins Research Laboratories, A. H. Robins Company, Inc., Richmond, Virginia 23220. *Received September 21, 1973*

In an attempt to prepare an effective antiinflammatory agent and, at the same time, better define the hypothetical receptor proposed by Shen for antiinflammatory compounds related to indomethacin,[1] we have prepared a series of 2-aroyl-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic acids and esters, I and II, for structure–activity studies. This chemical modification provides structural rigidity without the addition of bulky substituents and allows a pharmacological comparison of the two diastereomers. In addition, the reduction in electron density brought about by expanding the 2,3 double bond into a cyclopropyl ring was expected to shed some light on the electronic requirements of the receptor.



indomethacin



Ia, R = C_2H_5
b, R = H

IIa, R = C_2H_5
b, R = H

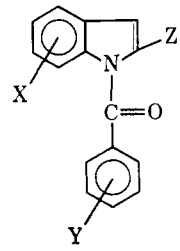
X = H, Cl, OCH_3
Y = H, Cl, OCH_3, CF_3
Z = H, CH_3

Chemistry. Previous attempts to prepare the 1,1a,2,6b-tetrahydrocycloprop[*b*]indole ring system by the addition of ethyl diazoacetate to indoles have led to rearrangement products.[2] We have found that deactivation of the indole nucleus with a 1-aroyl group allows the insertion of a carbalkoxymethylene group into the 2,3 double bond without rearrangement. In our case, ethyl diazoacetate was added to a 1-aroylindole using CuCN as a catalyst to produce the desired ring system. The reaction conditions are critical for acceptable yields.

Nmr analysis of the reaction mixtures indicated the formation of a mixture of exo and endo isomers Ia and IIa, usually in the ratio of about 5:1. After separation by column chromatography, the structures were unequivocally assigned on the basis of characteristic nmr coupling constants for *cis*- and *trans*-cyclopropyl hydrogens[3] and the marked upfield shift (*ca.* 0.3 ppm) of the ethyl group signals in IIa relative to Ia, due to the shielding influence of the aromatic ring. (See paragraph at the end of the paper regarding supplementary material.)

Saponification of the esters Ia and IIa gave the corresponding acids Ib and IIb in good yields. The nmr spectra of the crude reaction mixtures showed that little or no rearrangement to an indoleacetic acid had taken place. The larger coupling constants (7–9 Hz) confirm the all-cis arrangement for the cyclopropyl protons in IIb. In the spectra of Ib, the smaller coupling constants (2–4 Hz) for *trans*-cyclopropyl protons are visible, in addition to the dramatic upfield shift (0.2–0.5 ppm), relative to IIb, of the proton α to the carboxyl group, due to shielding by the aromatic ring.

Table I



Compd	X	Y	Z	Yield, %	Crystn solvent	Mp or bp (mm), °C	Formula
1	H	H	H	36	MeOH	59–60[a]	$C_{15}H_{11}NO$[b]
2	5-OCH_3	*p*-Cl	H	73	EtOH	125–127	$C_{16}H_{12}ClNO_2$
3	H	*p*-Cl	CH_3	82		154–158 (12)	$C_{16}H_{12}ClNO$[c]
4	5-OCH_3	*p*-Cl	CH_3	78	Et_2O–pet. ether	57–59	$C_{17}H_{14}ClNO_2$
5	5-OCH_3	*m*-CF_3	H	71	MeOH–H_2O	71–74	$C_{17}H_{12}F_3NO_2$
6	5-OCH_3	*o*-Cl	CH_3	58	EtOH–H_2O	70–73	$C_{17}H_{14}ClNO_2$
7	5-OCH_3 6-OCH_3	*p*-Cl	CH_3	48	Et_2O–pet. ether	93–95	$C_{18}H_{16}ClNO_3$
8	5-OCH_3	H	H	72	MeOH	109–111	$C_{16}H_{13}NO_2$
9	H	o-Cl	H	73	MeOH–H_2O	68–70	$C_{15}H_{10}ClNO$[d]
10	H	*p*-OCH_3	H	75	Me_2CO	137–139	$C_{16}H_{13}NO_2$
11	H	*p*-Cl	H	70	PhH–isooctane	101–103	$C_{15}H_{10}ClNO$[e]

[a] R. Weissberger, *Ber.*, **42**, 3520 (1910), reports mp 67–68°. [b] No analysis. [c] C: calcd, 71.25; found, 71.73. [d] C: calcd, 70.46; found, 71.00. [e] C: calcd, 70.46; found, 69.11.

The acids which were prepared appeared to be stable up to their melting points, at which temperature several of the compounds, **14**, **18**, **20**, **30**, and **34**, were shown to rearrange to the corresponding indole-3-acetic acids.

Compounds **35** and **36** were formed by direct chlorination of compounds **13** and **32**, respectively, with SO_2Cl_2.

Pharmacology. Compounds were evaluated in rats for antiinflammatory activity by sequential analysis using the Evans Blue carrageenan-induced pleural effusion model as described by Sancilio and Fishman.[4] They were tested, initially, at 316 mg/kg orally and in parallel with the same dose of acetylsalicylic acid (ASA). The compounds were dissolved or suspended in water containing Aquet (a nonionic surfactant, 0.05 ml/10 ml) and administered by gavage (10 ml/kg). The most active compound was **12**, which was equivalent to ASA and approximately 1/70 as potent as indomethacin in reducing the response to pleural irritation. The remaining compounds tested were inferior to ASA. None of the compounds prepared was of further interest as an antiinflammatory agent. The results show that expansion of the 2,3 double bond of indomethacin into a cyclopropane ring markedly reduces antiinflammatory activity and eliminates the possibility of meaningful structure–activity correlations within the series prepared.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Microanalyses were performed by Mr. Malcolm Stone, Analytical Research Department, A. H. Robins Co. All compounds were analyzed for C, H, and N and the results were within ±0.4% of the theoretical values except where noted. Nmr spectra were run on a Varian A-60 instrument by Mr. Ashby Johnson.

Preparation of 1-Aroylindoles (Compounds 1–11, Table I). The sodium salt of the appropriate indole was prepared by adding 1 equiv of NaH portionwise to a stirred solution of the indole in DMF at 10°. After the salt had formed, 1.1 equiv of the appropriate aroyl halide was added dropwise and the mixture was allowed to warm to room temperature. The mixture was poured into H_2O whereupon the product crystallized or was extracted into PhH or $CHCl_3$, which was then dried ($MgSO_4$) and concentrated. THe crude product was purified by recrystallization or distillation.

Preparation of Esters Ia and IIa (Tables II and III). In a typical experiment, equimolar amounts of a 1-aroylindole and CuCN were suspended in CH_2Cl_2 to make a thick slurry. The slurry was stirred rapidly, warmed to 50°, and then maintained between 50 and 70° while ethyl diazoacetate was added dropwise. The course of the reaction was followed by vpc, using a Varian Aerograph instrument, with a 10-ft 3% SE-30 on Chromosorb W column at 260–275°. Several comparative runs indicated that the best yields were obtained when 2–3 equiv of ethyl diazoacetate were used.

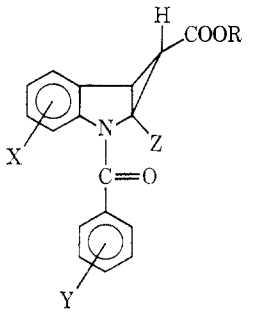
***endo*- and *exo*-2-(*p*-Chlorobenzoyl)-5-methoxy-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic Acid Ethyl Ester (40 and 15).** A stirred slurry of 24 g (0.08 mol) of **2** and 7.6 g (0.08 mol) of CuCN in 15 ml of CH_2Cl_2 at 50° was treated dropwise with 10 g (0.08 mol) of ethyl diazoacetate. After addition, vpc showed a 1:3 ratio of product to starting material. Another 20 g (0.16 mol) of ethyl diazoacetate was added in the same manner, and then the mixture was treated with PhH, filtered, and chromatographed on 500 g of Florisil using PhH to elute. Most of the resinous material remained on the column and the product was rapidly eluted. The eluted material was rechromatographed on 500 g of Florisil using PhH containing increasing amounts of acetone to elute. The exo isomer **15** was eluted first followed by the endo isomer **40**. Nmr ($CDCl_3$) for **15**: δ 1.28 (t, 3 H, CH_3, J = ~7.0 Hz), 1.56 (d of d, 1 H, C_1H, J = ~2.0 and ~3.0 Hz), 3.33 (d of d, 1 H, $C_{6b}H$, J = ~3.0 and ~7.0 Hz), 3.80 (s, 3 H, OCH_3), 4.23 (q, 2 H, OCH_2, J = ~7.0 Hz), 4.29 (d of d, 1 H, $C_{1a}H$, J = ~2.0 and ~7.0 Hz); ir ($CHCl_3$) 1708 and 1635 cm^{-1}. Nmr ($CDCl_3$) for **40**: δ 1.0 (t, 3 H, CH_3, J ~7.0 Hz), 2.02 (d of d, 1 H, C_1H, J = ~7.0 and ~9.5 Hz), 3.27 (d of d, 1 H, $C_{6b}H$, J = ~9.5 and ~7.0 Hz), 3.82 (s, 3 H, OCH_3), 3.96 (q, 2 H, OCH_2, J = ~7.0 Hz), 4.18 (d of d, 1 H, $C_{1a}H$, J = ~7.0 and ~7.0 Hz); ir ($CHCl_3$) 1720 and 1635 cm^{-1}.

Preparation of Acids Ib and IIb (Tables II and III). Saponification of Ia and IIa was carried out in 95% EtOH at 50° using 1.5–3 equiv of 5 *N* NaOH.

***exo*-2-(*p*-Chlorobenzoyl)-5-methoxy-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic Acid (14).** A stirred suspension of 6.7 g (0.02 mol) of **15** in 80 ml of 95% EtOH at 50° was treated dropwise with 5 ml of 5 *N* NaOH. Heating was continued for 2 hr. As the starting material dissolved, the sodium salt of **14** precipitated. The reaction mixture was poured into H_2O, extracted with Et_2O, and acidified with 3 *N* HCl. The resulting precipitate was recrystallized: nmr (DMSO-d_6) δ 1.62 (d of d, 1, H, C_1H, J = ~2.0 and ~3.2 Hz), 3.2 (d of d, 1 H, $C_{6b}H$, J = ~3.2 and ~7.0 Hz), 3.78 (s, 3 H, OCH_3), 4.19 (d of d, 1 H, $C_{1a}H$, J = ~2.0 and ~7.0 Hz), 12.63 (broad band, 1 H, COOH); ir (KBr) 1700 and 1608 cm^{-1}.

***exo*-5-Chloro-2-(*p*-chlorobenzoyl)-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic Acid (36).** A stirred solution of 10 ml of SO_2Cl_2 and 10 ml of acetone was cooled to −5° and treated

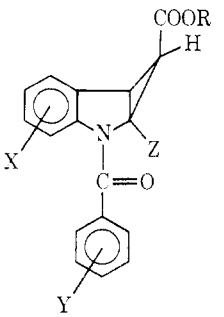
Table II



Compd	R	X	Y	Z	Yield, %	Crystn solvent	Mp, °C	Formula
12	H	H	H	H	62	PhH–EtOH	241–243	$C_{17}H_{13}NO_3$
13	C_2H_5	H	H	H	20	Isooctane–$(i\text{-Pr})_2O$	94–96	$C_{19}H_{17}NO_3$
14	H	5-OCH_3	*p*-Cl	H	67	EtOH–H_2O	250–252	$C_{18}H_{14}ClNO_4$
15	C_2H_5	5-OCH_3	*p*-Cl	H	27	$(i\text{-Pr})_2O$	135–138	$C_{20}H_{18}ClNO_4$
16	H	H	*p*-Cl	CH_3	75	PhH–isooctane	183–185	$C_{18}H_{14}ClNO_3$
17	C_2H_5	H	*p*-Cl	CH_3	27	$(i\text{-Pr})_2O$	129–131	$C_{20}H_{18}ClNO_3$
18	H	5-OCH_3	*p*-Cl	CH_3	81	PhH–isooctane	213–215	$C_{19}H_{16}ClNO_4$
19	C_2H_5	5-OCH_3	*p*-Cl	CH_3	28	$(i\text{-Pr})_2O$–pet. ether	118–120	$C_{21}H_{20}ClNO_4$
20	H	5-OCH_3	*m*-CF_3	H	77	EtOH	250–253	$C_{19}H_{14}F_3NO_4$
21	C_2H_5	5-OCH_3	*m*-CF_3	H	34	$(i\text{-Pr})_2O$	140–142	$C_{21}H_{18}F_3NO_4$
22	H	5-OCH_3	*o*-Cl	CH_3	85	EtOH–H_2O	220–223	$C_{19}H_{16}ClNO_4$
23	C_2H_5	5-OCH_3	*o*-Cl	CH_3	25	PhH–isooctane	113–119	$C_{21}H_{20}ClNO_4$
24	H	4-OCH_3 5-OCH_3	*p*-Cl	CH_3	70	MeOH–H_2O	217–221	$C_{20}H_{18}ClNO_5$
25	C_2H_5	4-OCH_3 5-OCH_3	*p*-Cl	CH_3	36	$(i\text{-Pr})_2O$	160–162	$C_{22}H_{22}ClNO_5$
26	H	5-OCH_3	H	H	94	MeOH–H_2O	228–230	$C_{18}H_{15}NO_4$
27	C_2H_5	5-OCH_3	H	H	34	$(i\text{-Pr})_2O$	129–132	$C_{20}H_{19}NO_4$
28	H	H	*o*-Cl	H	61	EtOH–H_2O	281–283	$C_{17}H_{12}ClNO_3$
29	C_2H_5	H	*o*-Cl	H	32	$(i\text{-Pr})_2O$	90–93	$C_{19}H_{16}ClNO_3$
30	H	H	*p*-OCH_3	H	89	MeOH–H_2O	235–238	$C_{18}H_{15}NO_4$[a]
31	C_2H_5	H	*p*-OCH_3	H	25	$(i\text{-Pr})_2O$	99–104	$C_{20}H_{19}NO_4$
32	H	H	*p*-Cl	H	36	PhH–isooctane	235–237	$C_{17}H_{12}ClNO_3$
33	C_2H_5	H	*p*-Cl	H	32	$(i\text{-Pr})_2O$	106–108	$C_{19}H_{16}ClNO_3$
34	H	5-Cl	H	H	72	MeOH–H_2O	210–215	$C_{17}H_{12}ClNO_3$
35	C_2H_5	5-Cl	H	H	79	$(i\text{-Pr})_2O$–ligroine	79–80	$C_{19}H_{16}ClNO_3$
36	H	5-Cl	*p*-Cl	H	50	MeOH–H_2O	226–228	$C_{17}H_{11}Cl_2NO_3$

[a] C: calcd, 69.89; found, 70.36.

Table III



Compd	R	X	Y	Z	Yield, %	Crystn solvent	Mp, °C	Formula
37	H	H	H	H	88	PhH–EtOH	213–215	$C_{17}H_{13}NO_3$
38	C_2H_5	H	H	H	10	$(i\text{-Pr})_2O$	114–116	$C_{19}H_{17}NO_3$
39	H	5-OCH_3	*p*-Cl	H	57	PhH–isooctane	205–207	$C_{18}H_{14}ClNO_4$
40	C_2H_5	5-OCH_3	*p*-Cl	H	4	$(i\text{-Pr})_2O$	94–96	$C_{20}H_{18}ClNO_4$
41	C_2H_5	H	*p*-Cl	CH_3	7	$(i\text{-Pr})_2O$	126–128	$C_{20}H_{18}ClNO_3$

with 2 g (0.006 mol) of **32**. After addition, the reaction mixture was allowed to warm to 5°, at which temperature the reaction became exothermic. The refluxing mixture was controlled by cooling with ice–H_2O. The mixture was poured into H_2O and the resulting solid was purified by recrystallization: nmr (DMSO-d_6) δ 1.02 (d of d, 1 H, C_1H, J = ~2.0 and ~3.5 Hz), 3.38 (d of d, 1 H, $C_{6b}H$, J = ~3.5 and ~7.0 Hz), 4.26 (d of d, 1 H, $C_{1a}H$, J = ~2.0 and ~7.0 Hz), 6.66 (broad band, COOH + H_2O in DMSO-d_6); ir (KBr) 1720 and 1633 cm^{-1}.

Rearrangement of *exo*-2-(*p*-Chlorobenzoyl)-5-methoxy-1a-methyl-1,1a,2,6b-tetrahydrocycloprop[*b*]indole-1-carboxylic Acid (18) to 1-(*p*-Chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic Acid. A 500-mg sample of 18 was heated 3 min at its melting point. The mixture was cooled and the product was recrystal-

lized from $CHCl_3$ to yield 450 mg (90%), mp 157–160°. A mixture melting point and nmr comparison with indomethacin confirmed the structure.

Rearrangement of *endo*- and *exo*-2-(*p*-Chlorobenzoyl)-5-methoxy-1,1a,2,6b-tetrahydrocyclopropa[*b*]indole-1-carboxylic Acid (39 and 14) to 1-(*p*-Chlorobenzoyl)-5-methoxyindole-3-acetic Acid. Compounds 39 and 14 were rearranged as described above. Both reactions gave a 50% yield of 1-(*p*-chlorobenzoyl)-5-methoxyindole-3-acetic acid after recrystallization from $CHCl_3$: mp 199–200°. *Anal.* ($C_{18}H_{14}ClNO_4$) C, H, N.

Acknowledgment. The authors thank Mrs. Rosa Mealy and Mr. Johnnie Nicholas for pharmacological assistance.

Supplementary Material Available. Nmr spectra for compounds 13 and 38 will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JMED-74-544.

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An Efficient and Selective Method for the Synthesis of 2-(4-Fluorophenyl)-1-(2-hydroxyethyl)-5-nitroimidazole (Flunidazole)

Edward J. J. Grabowski,* Thomas M. H. Liu, Ludwig Salce, and Erwin F. Schoenewaldt

Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065. *Received April 19, 1973*

The specific N-alkylation of 2-substituted 4(5)-nitroimidazoles has become a problem of significant importance because of the utility of these compounds in the treatment of protozoan infections. Generally, the 1-alkylated-2-substituted 5-nitroimidazoles are the preferred isomers because of their superior efficacy in the treatment of these infections.[1,2] Ridd and coworkers have presented a detailed analysis of the factors controlling the site of alkylation in 4(5)-nitroimidazoles and related systems,[3] and the Pfizer group has recently summarized the factors controlling the alkylation of 2-substituted 4(5)-nitroimidazoles in general.[2] Briefly stated their conclusions are: (1) alkylation under basic conditions affords 1-alkyl-4-nitroimidazoles, alkylation having occurred at the more basic nitrogen of the anion; (2) under neutral or mildly acidic conditions alkylation occurs on the unprotonated nitrogen, which is dependent on the equilibrium between the two tautomeric forms of the imidazole; and (3) in strongly acidic media the conjugate acid forms at the more nucleophilic nitrogen, thus favoring the formation of 1-alkyl-5-nitroimidazoles. Despite this information, efficient and isomer-free methods for the synthesis of 1-alkyl-2-substituted 5-nitroimidazoles are lacking.[2]

Olofson has recently addressed himself to the problem of the selective alkylation of heterocycles, including imidazoles, and has devised a sequence employing acylation, carbonium ion alkylation, and deacylation.[4] He notes that acylation is an efficient reaction and affords a high selectivity in isomer pereference, possibly due to its reversibility and, therefore, formation of the thermodynamically more stable product. However, this sequence was not applicable in our studies, as the intermediate *N*-acylnitroimidazoles failed to react with carbonium ion reagents.†

Our studies relative to the alkylation of nitroimidazoles arose out of the need to devise an efficient, isomer-free synthesis of 2-(4-fluorophenyl)-1-(2-hydroxyethyl)-5-nitroimidazole (flunidazole, **2**), which has shown appreciable antitrichomonal and antiamebic effects in man.[5]

The specific problem centered about the alkylation of 2-(4-fluorophenyl)-4(5)-nitroimidazole (**1**) which can be readily prepared from either 2-(4-fluorophenyl)imidazole[5a] or 2-phenylimidazole.[6,7] The direct methylation of **1** with dimethoxycarbonium tetrafluoroborate[8] proceeds in 70–75% yield to afford the methyl analog of **2**, 2-(4-fluorophenyl)-1-methyl-5-nitroimidazole.[9] To our knowledge this represents the first reported alkylation of nitroimidazoles with onium salts. An attempt to prepare **2** (*via* acetate **5**) directly from **1** using the Meerwein reagent 2-methyl-1,3-dioxolenium tetrafluoroborate,[10] followed by acid hydrolysis, afforded a 20–30% yield of **2** along with comparable amounts of its 4-nitro isomer and unreacted starting material.†,[9] Most likely steric factors become significant during the attempted acetoxyethylation with this reagent, which are of lesser importance during the methylation with dimethoxycarbonium tetrafluoroborate. As a solution to the problem at hand we envisioned a protection–alkylation–deprotection sequence. Specifically, we wished to methoxymethylate **1** at N-1 under basic conditions, alkylate at N-3 with 2-methyl-1,3-dioxolenium tetrafluoroborate[10] to afford imidazolium salt **4**, and demethoxymethylate to afford acetate **5** which could be hydrolyzed to **2**.

The methoxymethylation of **1** was conducted in toluene at 25–30° employing an excess of triethylamine and chloromethyl methyl ether, anticipating the selective formation of **3a** *via* alkylation of the anion of **1**.[11] Compound **3a** was originally prepared by Drs. Kollonitsch and Marburg of these laboratories and used to prepare **2** by treatment with ethylene oxide–boron trifluoride etherate in a procedure less efficient than that described herein. Work-up after complete consumption of **1** afforded a 3:1 mixture of methoxymethyl compounds **3a** and **3b**, respectively, indicating that **1** and its anion alkylate competitively under the reaction conditions. Isomer assignments are based upon uv and nmr spectra. In accord with previous literature examples the methylene group of **3b** exhibited its resonance slightly downfield (0.31 ppm) of that of **3a** due to the deshielding effect of the nitro group, and the long wavelength maximum of **3a** occurred at slightly shorter wavelength than that of **3b**.[2] Although the alkylation of **1** lacked the desired specificity, **3b** could be readily isomerized to the thermodynamically more stable **3a** by refluxing the reaction mixture for 1 hr.[12] Work-up of the reaction mixture afforded pure **3a** in 97% yield, thus realizing the goal of the protection of **1** at N-1. Compound **3a** was acetoxyethylated by treatment with 2 equiv of 2-methyl-1,3-dioxolenium tetrafluoroborate in dry methylene chloride for 40 hr at reflux. Subsequent work has shown that the same sequence can be run in 1,2-dichloroethane employing a 5-hr reflux period. The resulting imidazolium salt **4** was isolated in 86% yield by filtration, water trituration to remove access Meerwein reagent, and drying and characterized in the usual manner (Scheme I). However, in the normal conversion of **1** to **2**, imidazolium salt **4** was not isolated. Rather, the reaction mixture, containing **4** and excess Meerwein reagent in methylene chloride, was treated with an excess of pyridine for 5 hr at reflux.

†E. J. J. Grabowski, *et al.*, unpublished results.