Compound 7 eluted at t_R 7.12 min, and 8 eluted at t_R 9.02 min. Removal of solvent by lyophilization afforded pure 7 and 8 as highly hygroscopoic white powders: ^{1}H-NMR (D_2O) of 7, δ 7.41 (s, 1 H, thymine 6-proton), 6.20 (m, 1 H, 1′-proton), 5.10 (m, 1 H, 3′-proton), 4.14 (m, 1 H, 4′-proton), 3.10 [q, 6 H, $(CH_3CH_2)_3^+NH$], 2.98–2.82 (m, 2 H, $-CH_2SO_3^-$), 2.39 (m, 2 H, 2′-proton), 2.12–1.88 (m, 2 H, 5′-proton), 2.04 (s, 3 H, $OCOCH_3$), 1.82 (s, 3 H, thymine 5-CH_3), 1.18 [t, 9 H, $(CH_3CH_2)_3^+NH$]; MS (pos-FAB) m/z 102 $[(Et)_3NH]^+$, MS (neg-FAB) m/z 361 $(M - H)^-$. Anal. Calcd for $C_{19}H_{33}N_3O_8S\cdot4.3H_2O$: C, 42.19, H, 7.70; N, 7.69. Found: C, 42.21; H, 7.65; N, 8.01. 8: ^{1}H-NMR (D_2O) δ 7.30 (s, 1 H, thymine 6-proton), 6.80 (m, 1 H, 1′-proton), 6.44 (m, 1 H, 2′-proton), 5.82 (m, 1 H, 3′-proton), 4.93 (m, 1 H, 4′-proton), 3.10 [q, 6 H, $(CH_3CH_2)_3^+NH$], 2.98–2.82 (m, 2 H, $-CH_2SO_3^-$), 2.12–1.88 (m, 2 H, 5′-proton), 1.80 (s, 3 H, thymine 5-CH_3), 1.18 [t, 9 H, $CH_3CH_2)_3^+NH$]; MS (pos-FAB) m/z 102-$[(Et)_3NH]^+$, MS (neg-FAB) 301 m/z $(M - H)^-$. Anal. Calcd for $C_{17}H_{29}N_3O_6S\cdot1.5H_2O$: C, 47.44; H, 7.44; N, 9.77. Found: C, 47.62; H, 7.80; N, 10.11.

Addition of 10% AcOH to the DMF solution afforded impure 7 in 43% yield after XAD-4 chromatography.

Compound 7 could also be prepared via 3-*O*-acetylation of 9 with $AcOAc/NEt_3$/DMAP in acetonitrile in 67% yield.

2,3-Dehydro-1,2,3,5,6-pentadeoxy-1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidinyl)-β-D-*erythro*-hexofuranuronosulfonic Acid (8). Sultone 5 (100 mg, 0.33 mmol) was dissolved in a mixture of hot absolute EtOH (100%) (1.0 mL) and 1 N aqueous NaOH solution (2 mL, 6 equiv). The mixture was heated under reflux for 18 h, cooled, and extracted with EtOAc (3 × 3 mL) and the aqueous layer lyophilized to afford the impure sodium salt of 8 as a white hydroscopic solid. The above product was converted to its triethylammonium salt via XAD-4 chromatography, as described for the preparation of 6, to afford 87% of a product identical to compound 8 isolated from the reaction of NaOAc with sultone 5 (see above).

1,2,5,6-Tetradeoxy-1-(3,4-dihydro-5-methyl-2,4-dioxo-1-(2*H*)-pyrimidinyl)-β-D-*erythro*-hexofuranuronosulfonic Acid (9). Sultone 5 (100 mg, 0.33 mmol) was dissolved in concentrated NH_4OH (2 mL, 0.880 sp gr) and the solution heated under reflux for 3 days with intermittent addition of NH_4OH (2 mL) every 12 h. The reaction mixture was extracted with EtOAc (3 × 10 mL) and the aqueous layer lyophilized to afford 9 as a white, highly hygroscopic solid (90 mg, 81% yield): ^{1}H-NMR (D_2O) δ 7.38 (s, 1 H, thymine 6-proton), 6.18 (m, 1 H, 1′-proton), 4.28 (m, 1 H, 3′-proton), 3.93 (m, 1 H, 4′-proton), 2.95 (m, 2 H, $-CH_2SO_3^-$), 2.29 (m, 2 H, 2′-proton), 2.00 (m, 2 H, 5′-proton), 1.82 (s, 3 H, thymine 5-CH_3); MS (neg-FAB) m/z 319 $(M - H)^-$. Anal. Calcd for $C_{17}H_{31}N_3O_7S\cdot2H_2O$: C, 44.64; H, 7.66; N, 9.19. Found: C, 44.68; H, 7.81; N, 9.51.

2,3-Anhydro-1,2,5,6-tetradeoxy-1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidinyl)-β-D-*erythro*-hexofuranuronosulfonic Acid (11). Sultone 2 (0.5 g, 1.65 mmol) was dissolved in NH_4OH solution (5 mL, 0.880 sp gr) and the mixture heated under reflux for 30 h with intermittent addition of NH_4OH (2 mL) every 8 h. The reaction mixture was extracted with EtOAc (3 × 10 mL) and the aqueous layer lyophilized to afford the ammonium salt of 11 as a pale brown solid (0.42 g, 79% yield), which was used directly with the preparation of 6: ^{1}H-NMR (D_2O) δ 7.48 (s, 1 H, thymine 6-proton), 5.81 (m, 1 H, 1′-proton), 5.31 (m, 1 H, 3′-proton), 4.45 (m, 1 H, 4′-proton), 2.95 (m, 2 H, $-CH_2SO_3^-$), 2.61 (m, 2 H, 2′-proton), 1.98 (m, 2 H, 5′-proton), 1.82 (s, 3 H, thymine 5-CH_3); MS (neg-FAB) m/z 301 $(M - H)^-$.

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Nucleophilic Addition of 2-Indolylacyl Anion Equivalents to *N*-Alkylpyridinium Salts

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The reactions of the anions derived from dithioacetals 1–3 and α-amino nitriles 4 toward pyridinium salts 5 are studied. Depending on the nucleophile used, 2-(dihydropyridylmethyl)indoles 6 and 7, which can be cyclized to tetracyclic methanoazocinindole systems 10 and 11, respectively, or 2-substituted 3-(dihydropyridyl)indoles 8 and 9 are formed.

The nucleophilic addition of ester enolates to *N*-alkylpyridinium salts has proved to be a useful and straightforward method in alkaloid synthesis.[1] Following this methodology, from 1-, 2-, and 3-indoleacetic ester anions, and subsequent cyclization of the resulting 1,4-dihydropyridines, we have recently reported a general method for the synthesis of tetracyclic substructures of *C*-mavacurine, *Strychnos*, and akuammiline-type alkaloids, respectively,[2] from which the synthesis of the indole alkaloids vinoxine[2,3] and tubifolidine[4,5] was accomplished.

In contrast, although the synthetic usefulness of acyl anion equivalents is well-known,[6] there are no studies about their reactivity as nucleophiles toward pyridinium salts.[7,8] In this context, we planned to explore the scope and synthetic usefulness of the addition of 2-indolylacyl anion equivalents to pyridinium salts.[9]

A priori, depending on factors such as the softness or hardness of the nucleophile and the reversibility of the

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(2) Bennasar, M.-L.; Alvarez, M.; Lavilla, R.; Zulaica, E.; Bosch, J. *J. Org. Chem.* **1990**, *55*, 1156.

(3) Bennasar, M.-L.; Zulaica, E.; Jiménez, J.-M.; Bosch, J. *Tetrahedron Lett.* **1990**, *31*, 747.

(4) Amat, M.; Linares, A.; Bosch, J. *J. Org. Chem.* **1990**, *55*, 6299.

(5) Alvarez, M.; Salas, M.; de Veciana, A.; Lavilla, R.; Bosch, J. *Tetrahedron Lett.* **1990**, *31*, 5089.

(6) Gröbel, B. T.; Seebach, D. *Synthesis* **1977**, 357. (b) Albright, J. D. *Tetrahedron* **1983**, *39*, 3207. (c) Ager, D. J. *Umpoled Synthons. A Survey of Sources and Uses in Synthesis*; Hase, T. A., Ed.; Wiley: New York, 1987; Chapter 2.

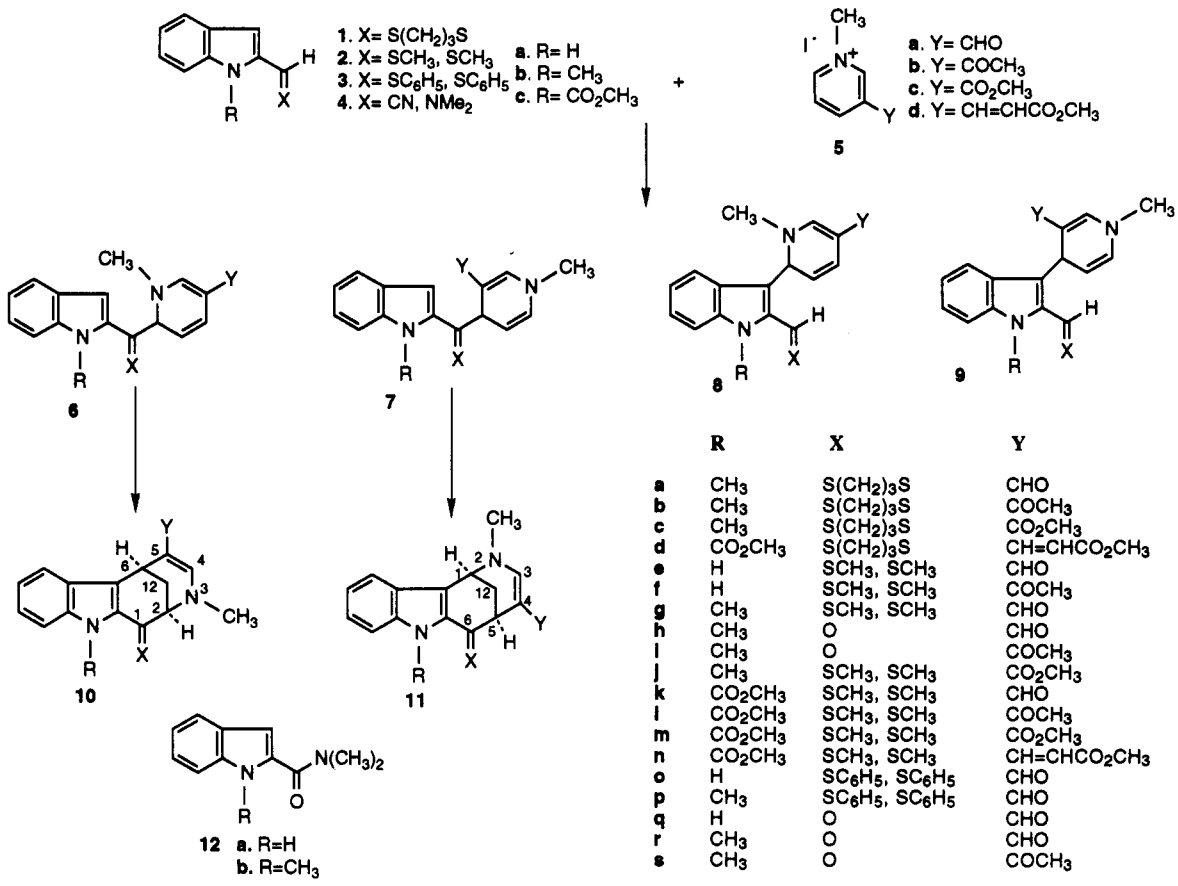
(7) Bennasar, M.-L.; Zulaica, E.; Torrens, A.; Pérez, A.; Bosch, J. *Tetrahedron Lett.* **1990**, *31*, 1893.

(8) For the reaction of dithiane anions with pyridines, see: Taguchi, T.; Nishi, M.; Watanabe, K.; Mukaiyama, T. *Chem. Lett.* **1973**, 1308.

(9) For other reactions of anions derived from 2-(1,3-dithian-2-yl)-indoles, see: Rubiralta, M.; Díez, A.; Reig, I.; Castells, J. *Heterocycles* **1990**, *31*, 173 and references cited therein.

0022-3263/92/1957-2835$03.00/0

Scheme I



	R	X	Y
a	CH_3	$S(CH_2)_3S$	CHO
b	CH_3	$S(CH_2)_3S$	$COCH_3$
c	CH_3	$S(CH_2)_3S$	CO_2CH_3
d	CO_2CH_3	$S(CH_2)_3S$	$CH=CHCO_2CH_3$
e	H	SCH_3, SCH_3	CHO
f	H	SCH_3, SCH_3	$COCH_3$
g	CH_3	SCH_3, SCH_3	CHO
h	CH_3	O	CHO
i	CH_3	O	$COCH_3$
j	CH_3	SCH_3, SCH_3	CO_2CH_3
k	CO_2CH_3	SCH_3, SCH_3	CHO
l	CO_2CH_3	SCH_3, SCH_3	$COCH_3$
m	CO_2CH_3	SCH_3, SCH_3	CO_2CH_3
n	CO_2CH_3	SCH_3, SCH_3	$CH=CHCO_2CH_3$
o	H	SC_6H_5, SC_6H_5	CHO
p	CH_3	SC_6H_5, SC_6H_5	CHO
q	H	O	CHO
r	CH_3	O	CHO
s	CH_3	O	$COCH_3$

process,[10] the nucleophilic attack can occur at the pyridine α- or γ-positions to give 1,2- or 1,4-dihydropyridines, respectively. On the other hand, the 2-indolylacyl anion can react either by the latent acyl carbon or by the indole 3-position to give 2-(dihydropyridylmethyl)indoles **6** and **7** or 3-(dihydropyridyl)indoles **8** and **9**, respectively (Scheme I). The usefulness of 1,4-dihydropyridines **9** arises from their potential activity as calcium antagonists[11] whereas dihydropyridine systems of types **6** and **7** could constitute valuable synthetic precursors of several classes of 2-acylindole alkaloids.

The 2-indolylacyl anion equivalents studied were those derived from dithianes **1a–c**, bis(methylthio)acetals **2a–c**, bis(phenylthio)acetals **3a–b**, and α-amino nitriles **4a–b**.[12] All pyridinium salts tried (**5a–d**) possess an electron-withdrawing substituent at the β-position. The results are shown in Table I. Although dihydropyridines of types **6** and **7** were usually unstable, some of them were characterized by their NMR data. However, in most cases, they were not isolated but directly treated with acid in order to obtain the corresponding cyclized tetracyclic derivatives, **10** and **11**, respectively. This cyclization failed from bis(methylthio)acetals **6e** and **7g**, due either to their instability or to the fact that deprotection to give a 2-acylindole system occurs under the acidic reaction conditions before cyclization. In fact, in some cases (**10h** and **10i**) tetracyclic 2-acylindoles were obtained after cyclization.

The constitution of the resulting isomeric dihydropyridines **6–9** and tetracycles **10** and **11** was unambiguously established from their NMR data. Thus, a diagnostic signal for the assignment of 1,2- and 1,4-dihydropyridines (**6**, **8** vs **7**, **9**) was that corresponding to the sp^3 methine carbon at C-2 or C-4, respectively (Table II). On the other hand, tetracycles **10** and **11** were easily distinguished by the chemical shift values of protons and carbons (Table III) at the bridgehead positions. For compounds **10a** and **10h** this assignment was confirmed since a positive NOE effect was observed in the signals due to 6-H and 2-H upon irradiation of 7-H and 3-CH_3, respectively.

The results of Table I, although apparently erratic, show some general trends.

(i) Dithiane **1b** and bis(methylthio)acetals **2a,b** react at the latent acyl carbon upon the pyridine α- and, in some cases, γ-positions. N_{ind}-Methyl-substituted dithioacetals (**1b** and **2b**) give better yields than the corresponding unsubstituted ones (**1a** and **2a**); in fact, dithiane **1a** was unreactive toward all pyridinium salts tried. The nature of the electron-withdrawing substituent on the pyridinium salts exerts an important effect: the best yields (40% for the addition–cyclization sequence) were obtained when this substituent is methoxycarbonyl (salt **5c**), whereas when it is acrylate (**5d**) the addition does not take place. The latter result contrasts with the useful reactivity of β-[(methoxycarbonyl)vinyl]pyridinium salts with ester enolates.[2] Also, it is worth noting that tetracyclic *Strychnos*-type systems **11**, i.e., those formed by cyclization of 1,4-dihydropyridines **7**, were only obtained from the methoxycarbonyl-substituted pyridinium salt **5c**.

(ii) In sharp contrast with the above series, dithioacetals **1c** and **2c**, having a methoxycarbonyl group upon the indole nitrogen, react at the indole 3-position upon the γ-position of the pyridinium salt to give 3-(1,4-dihydropyridyl)indoles **9**, and the best yields were obtained from the pyridinium salt **5d**; except for this salt, low yields (**9k**)

(10) For a detailed discussion, see ref 1a.
(11) Triggle, D. J. In *Comprehensive Medicinal Chemistry*; Hansch, C., Ed.; Pergamon Press: Oxford, 1990; Vol. 3, p 1070.
(12) For the reaction of α-(dimethylamino)pyrrole-2-acetonitrile anions with alkyl halides, see: Bray, B. L.; Muchowski, J. M. *J. Org. Chem.* 1988, *53*, 6115.

Table I. Reactions of 2-Indolylacyl Anion Equivalents Derived from 1–4 toward Pyridinium Salts 5

2-indolylacyl anion equiv derived from	pyridinium salt	products (yield, %)
1a	**5a** or **5d**	*a*
1b	**5a**	**6a** (30) or **10a** (35)[b]
1b	**5b**	**10b** (23)[b]
1b	**5c**	**10c** + **11c** (1:1, 40)[b]
1b	**5d**	*c*
1c	**5a**, **5b**, or **5c**	*a*
1c	**5d**	**9d** (45)
2a	**5a**	**6e** (7)[d]
2a	**5b**	**10f** (15)[b]
2a	**5d**	*c*
2b	**5a**	**6g** + **7g**[d] (1:1, 15) or **10g** + **10h** (1:5, 20)[b]
2b	**5b**	**10i** (16)[b]
2b	**5c**	**10j** + **11j** (1:1, 40)[b]
2b	**5d**	*c*
2c	**5a**	**9k** (15) or **8e** + **9e** (1:1, 50)[e]
2c	**5b**	**9l**[f]
2c	**5c**	**9m**[f]
2c	**5d**	**9n** (58)
3a	**5a**	**8o** (8)
3a	**5b** or **5d**	*a*
3b	**5a**	**8p** (10)
3b	**5b** or **5d**	*a*
4a	**5a**	**8q** + **9q** (9:1, 22), **12a** (5)
4a	**5b**	*a*
4a	**5d**	**12a** (21)
4b	**5a**	**8r** + **9r** (3:1, 42), **12b** (5)
4b	**5b**	**8s** + **9s** (3:1, 30), **12b** (8)
4b	**5d**	**12b** (19)

[a] Complex mixture. [b] After acidic treatment. [c] No reaction was observed. [d] This dihydropyridine did not cyclize after acidic treatment. [e] *n*-BuLi was used as the base. [f] Hardly purifiable product.

and complex or hardly purifiable (**9l,m**) mixtures were obtained. No products coming from the attack by the acyl carbon (**6** and **7**) were detected. In this series **c**, the anion was generated using LDA as the base instead of *n*-BuLi. The use of *n*-BuLi brings about deprotection of the *N*-methoxycarbonyl substituent generating an indolyl anion which reacts at its 3-position to give a mixture of 1,2- and 1,4-dihydropyridines (**8e** and **9e**, respectively).[13]

(iii) The anions derived from bis(phenylthio)acetals **3a,b** only react, but in very low yield (~10%), with the formyl-substituted pyridinium salt **5a** at the indole 3-position to give 1,2-dihydropyridines (**8o** and **8p**, respectively). The bulky dithioacetal moiety could account for the regioselectivity and the low reactivity of these anions.

(iv) Amino nitriles derived from **4a** and **4b** react at the indole 3-position upon the pyridine α- and γ-positions to give mixtures of dihydropyridines **8** and **9**. Again, the acrylate substituent on the pyridinium ring proved to be useless, and the yields are higher when the indole nitrogen is alkyl substituted. In all cases, hydrolysis of the amino nitrile functionality occurs either under the reaction conditions or during workup to give the corresponding indole-2-carbaldehydes. The formation of amides **12** as byproducts (5%), or even as the only isolable products (~20%) in those cases in which the pyridinium salt does not react, deserves comment. Although nitriles **4a,b** slowly undergo oxidation to the respective amides under neutral conditions (on storage or during column chromatography), the isolation of significant amounts of amides from the above reactions could be indicative of an oxidation process involving a single electron transfer from the nucleophile to the pyridinium ring[14] to give a radical, which would be stabilized by a captodative effect[15] and could undergo either further oxidation to amide[16] or coupling with the pyridine ring.

Due to the nature of the nucleophiles employed, the ratio of products derived from an α- or a γ-attack on the pyridinium salt must reflect a kinetic distribution rather than a thermodynamic one. It seems reasonable to assume that equilibration between 1,2- and 1,4-dihydropyridines of types **6** and **7** does not occur with dithioacetal anions and that rapid irreversible aromatization of the indole ring also blocks a further equilibrium between dihydropyridines coming from attack by the indole 3-position. However, it is difficult to rationalize all the results only on the basis of the hardness and softness of the nucleophile, and other factors (steric, electronic, nature of the electron-withdrawing substituent, participation of radical species) are probably involved.

Experimental Section

Melting points were determined in a capillary tube and are uncorrected. Unless otherwise noted, ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 200 and 50.3 MHz, respectively, using Me_4Si as internal standard. Chemical shifts are reported in ppm downfield (δ) from Me_4Si, and coupling constants are expressed in hertz. In the description of NMR spectra of compounds **6–9**, umprimed numbers refer to pyridine whereas the numbering of indole is marked with primes. Only noteworthy IR absorptions (cm^{-1}) are listed. TLC was carried out on SiO_2 (silica gel 60 F_{254}, Merck, 0.063–0.200 mm), and the spots were located with iodoplatinate reagent. Column chromatography was carried out on SiO_2 (silica gel 60, SDS, 0.060–0.2 mm). Flash chromatography was carried out on SiO_2 (silica gel 60, SDS, 0.040–0.060 nm). Drying of organic extracts during the workup of reactions was performed over anhydrous Na_2SO_4. Unless otherwise stated, dihydropyridines were purified after workup by flash chromatography (AcOEt). Microanalyses were performed by Centro de Investigación y Desarrollo (C.S.I.C.), Barcelona. All reactions were performed, at least, in triplicate. Formation of the anions derived from **1–4** under the reported reaction conditions was confirmed by deuteration experiments.

2-[Bis(methylthio)methyl]indole (2a). A solution of indole-2-carbaldehyde[17] (2 g, 13.8 mmol), CH_3SH (4 mL, 68.9 mmol), and TsOH (1.3 g, 6.89 mmol) in anhydrous CH_2Cl_2 (200 mL) was stirred at −30 °C for 1 h. The organic solution was washed with 10% aqueous NaOH, dried, and evaporated to give an oil. Column chromatography (CH_2Cl_2) gave **2a**: 2.5 g (81%); IR (NaCl) 3400 (NH); ^1H NMR (60 MHz) 2.0 (s, 6 H, SCH_3), 4.8 (s, SCH), 6.2 (d, J = 2, 3-H), 6.6–7.1 (m, 3 H), 7.3 (m, 4-H), 8.0 (br, NH). Anal. Calcd for $C_{11}H_{13}NS_2$: C, 59.17; H, 5.86; N, 6.27. Found: C, 59.40; H, 5.52; N, 6.15.

2-[Bis(methylthio)methyl]-1-methylindole (2b). This compound was prepared as described for **2a**, starting from 1-methylindole-2-carbaldehyde[18] (3.1 g, 19.5 mmol): 3.8 g (82%); mp 85–86 °C (Et_2O); ^1H NMR (60 MHz) 2.0 (s, 6 H, SCH_3), 3.5 (s, NCH_3), 4.8 (s, SCH), 6.2 (s, 3-H), 6.7–7.1 (m, 3 H), 7.3 (m, 4-H). Anal. Calcd for $C_{12}H_{15}NS_2$: C, 60.71; H, 6.36; N, 5.90. Found: C, 60.34; H, 6.37; N, 5.93.

Methyl 2-(1,3-Dithian-2-yl)indole-1-carboxylate (1c). A mixture of dithiane **1a**[19] (1.5 g, 6.3 mmol), tetrabutylammonium

(13) For the synthesis of 3-(dihydropyridyl)indoles by reaction of indolyl anions with pyridinium salts, see: (a) Bosch, J.; Alvarez, M.; Lavilla, R. *Heterocycles* **1989**, *29*, 237. (b) Lavilla, R.; Gotsens, T.; Bosch, J. *Synthesis* **1991**, 842.

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(15) (a) Viehe, H. G.; Janousek, Z.; Merényi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148. (b) Viehe, H. G.; Merényi, R.; Janousek, Z. *Pure Appl. Chem.* **1988**, *60*, 1635.

(16) The oxidation of α-aminonitriles to amides under alkaline conditions is a known process: (a) Aurich, H. G. *Tetrahedron Lett.* **1964**, 657. (b) Grierson, D. S.; Urrea, M.; Husson, H.-P. *Heterocycles* **1985**, *23*, 2493.

(17) Harley-Mason, J.; Pavri, E. H. *J. Chem. Soc.* **1963**, 2565.

(18) Bennasar, M.-L.; Torrens, A.; Rubiralta, M.; Bosch, J.; Grierson, D. S.; Husson, H.-P. *Heterocycles* **1989**, *29*, 745.

Table II. Significant ^{13}C NMR Data of Dihydropyridines 6–9

	C-2	C-3	C-4	C-5	C-6	NCH_3	Y	C=X	R
6a	69.3	110.6	121.5	111.7	155.7	45.3	184.5	63.9	32.9
6e	67.8	110.9	121.6	111.5	155.5	45.2	184.1	69.2	
6g	68.9	110.1	120.6	112.0	156.2	44.6	184.0	69.5	32.8
7g	149.3	109.2	38.9	105.2	130.7	40.0	187.9	69.5	31.8
8e	56.7	116.3	116.7	108.6	156.9	41.5	183.4	46.5	
8o	57.2	116.5	117.7	109.5	155.9	41.9	184.1	52.1	
8p	57.0	115.9	116.8	110.1	155.0	41.2	183.3	52.7	32.0
8q	56.9	116.6	117.6	109.4	155.3	42.0	183.9	180.8	
8r	56.6	116.3	117.5	109.5	154.8	41.8	183.6	181.3	31.7
8s	55.1	114.5	119.7	109.6	148.5	41.7	23.5, 192.3	181.7	31.4
9d	145.8	106.7	38.2	108.0	130.7	39.9	50.9, 103.3	48.0	53.1
							141.9, 169.2		152.5
9e	148.9	114.4	26.7	109.9	127.8	41.3	188.8	46.2	
9k	151.9	111.7	35.9	105.9	130.0	40.4	188.8	49.8	53.0
									152.6
9n	145.7	106.7	38.4	108.1	130.0	40.0	50.9, 100.0	48.6	53.1
							141.8, 169.2		152.7
9r	148.6	114.6	27.1	110.4	127.7	41.5	188.5	182.9	31.7
9s	142.2	112.3	27.8	110.4	127.5	41.4	24.1, 195.0	183.6	31.4

Table III. Significant ^{13}C NMR Data of Tetracycles 10–11

	C-1	C-2	C-4	C-5	C-6	C-12	NCH_3	Y	R
10a	54.1	62.4	154.1	117.8	20.8	25.0	46.9	184.2	32.9
10b	54.4	61.2	147.6	115.4	21.4	25.1	47.1	23.5, 190.9	32.9
10c	54.4	60.7	145.5	101.1	22.8	25.0	46.4	50.2, 167.4	32.7
10f	59.6	63.6	147.7	116.1	21.2	26.4	45.6	23.2, 192.1	
10g	59.8	67.1	153.1	119.1	21.0	26.7	46.2	184.8	31.7
10h	182.5	64.0	150.0	115.0	21.6	28.9	42.5	184.3	31.3
10i	183.1	62.7	143.8	112.7	21.9	28.6	42.5	23.1, 190.9	31.1
10j	59.6	65.0	144.6	96.9	22.9	26.5	45.7	50.4, 167.6	31.5
11c	48.2	144.4[a]	97.9	35.3	55.4	25.9	41.8	50.6, 169.7	33.5
11j	48.3	144.6[a]	102.5	37.7	60.4	26.8	41.9	50.5, 169.8	32.0

[a] C-3.

hydrogen sulfate (0.2 g), C_6H_6 (70 mL), and 50% aqueous NaOH (25 mL) was vigorously stirred at room temperature for 10 min. Then, methyl chloroformate (1.3 mL, 16.9 mmol) in C_6H_6 (30 mL) was slowly added, and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with C_6H_6, and the organic layer was washed with H_2O, dried, and evaporated. The resulting residue was chromatographed (flash, 4:1 hexane–acetone) to give **1c**: 1.4 g (76%); mp 106 °C (*i*-Pr_2O); IR (KBr) 1715 (CO); ^1H NMR 2.10 (m, CH_2), 2.99 (m, 4 H, CH_2S), 4.09 (s, OCH_3), 6.11 (s, CH), 6.98 (s, 3-H), 7.20–7.40 (m, 2 H), 7.52 (d, J = 7, 4-H), 8.01 (d, J = 8.5, 7-H); ^{13}C NMR 25.1 (CH_2), 30.7 (CH_2S), 42.4 (CH), 53.6 (OCH_3), 111.3 (C-3), 115.7 (C-7), 120.8 (C-4), 123.3 (C-5), 124.9 (C-6), 128.6 (C-3a), 136.2 (C-2), 138.3 (C-7a), 152.1 (CO). Anal. Calcd for $C_{14}H_{15}NO_2S_2$: C, 57.31; H, 5.15; N, 4.77; S, 21.85. Found: C, 57.38; H, 5.12; N, 4.77; S, 21.77.

Methyl 2-[Bis(methylthio)methyl]indole-1-carboxylate (2c). Operating as above, from dithioacetal **2a** (3.3 g, 14.8 mmol) was obtained compound **2c** after flash chromatography (7:3 hexane–acetone): 3.3 g (79%); mp 68 °C (MeOH); IR (KBr) 1715 (CO); ^1H NMR 2.11 (s, 6 H, SCH_3), 4.08 (s, OCH_3), 5.93 (s, CH), 6.85 (s, 3-H), 7.20–7.40 (m, 2 H), 7.51 (d, J = 7, 4-H), 8.03 (d, J = 8, 7-H); ^{13}C NMR 13.3 (SCH_3), 48.9 (CH), 53.7 (OCH_3), 110.3 (C-3), 115.8 (C-7), 120.8 (C-4), 123.3 (C-5), 124.8 (C-6), 128.4 (C-3a), 136.7 (C-2), 137.4 (C-7a), 152.4 (CO). Anal. Calcd for $C_{13}H_{15}NO_2S_2$: C, 55.49; H, 5.37; N, 4.97; S, 22.78. Found: C, 55.43; H, 5.36; N, 4.91; S, 22.76.

2-[Bis(phenylthio)methyl]indole (3a). A solution of indole 2-carbaldehyde (3.25 g, 22.4 mmol), C_6H_5SH (6.87 mL, 67.2 mmol), and TsOH (2.13 g, 11.2 mmol) in anhydrous C_6H_6 (300 mL) was stirred at room temperature for 12 h. The usual workup and further column chromatography (CH_2Cl_2) gave **3a**: 5.5 g (70%); mp 109–110 °C (MeOH); IR (KBr) 3400 (NH); ^1H NMR (60 MHz) 5.3 (s, SCH), 6.1 (d, J = 2, 3-H), 6.6-7.3 (m, 14 H, ArH), 8.1 (br, NH). Anal. Calcd for $C_{21}H_{17}NS_2$: C, 72.58; H, 4.93; N, 4.03; S, 18.45. Found: C, 72.58; H, 4.93; N, 4.00; S, 18.54.

2-[Bis(phenylthio)methyl]-1-methylindole (3b). Operating as above, from 1-methylindole-2-carbaldehyde (6 g, 37.7 mmol) was obtained compound **3b** after column chromatography (CH_2Cl_2): 9.7 g (71%); ^1H NMR (60 MHz) 3.6 (s, NCH_3), 5.3 (s, SCH), 6.2 (s, 3-H), 6.6–7.3 (m, 14 H, ArH). Anal. Calcd for $C_{22}H_{19}NS_2$: C, 73.09; H, 5.29; N, 3.87. Found: C, 73.34; H, 5.20; N, 3.70.

α-(Dimethylamino)indole-2-acetonitrile (4a). A mixture of indole-2-carbaldehyde (7.5 g, 51.7 mmol), $NHMe_2$·HCl (5.48 g, 67.2 mmol), NaCN (3.29 g, 67.2 mmol), MeOH (570 mL), and H_2O (180 mL) was stirred at room temperature for 15 h. The solvent was removed, and the residue was diluted with H_2O and extracted with CH_2Cl_2. The organic extract was successively washed with aqueous $NaHSO_3$ and NaCl solutions, dried, and evaporated to give **4a**: 9 g (87%); mp 123–124 °C (MeOH); IR (KBr) 2210 (CN), 3310 (NH); ^1H NMR (60 MHz) 2.2 (s, 6 H, NCH_3), 4.8 (s, CH), 6.5 (d, J = 1.5, 3-H), 6.8–7.1 (m, 3 H), 7.3 (m, 4-H), 8.1 (br, NH); ^{13}C NMR 41.5 (NCH_3), 57.5 (CH), 102.9 (C-3), 111.8 (C-7), 114.0 (CN), 120.3 (C-4), 121.0 (C-5), 122.9 (C-6), 127.6 (C-3a), 130.9 (C-2), 136.6 (C-7a). Anal. Calcd for $C_{12}H_{13}N_3$: C, 72.33; H, 6.57; N, 21.09. Found: C, 72.33; H, 6.66; N, 21.12.

α-(Dimethylamino)-1-methylindole-2-acetonitrile (4b). Operating as above, from 1-methylindole-2-carbaldehyde (10 g, 62.8 mmol) was obtained amino nitrile **4b**: 12 g (90%); mp 107–108 °C (MeOH); IR (KBr) 2220 (CN); ^1H NMR (60 MHz) 2.1 (s, 6 H, NCH_3), 3.5 (s, NCH_3), 4.6 (s, CH), 6.5 (s, 3-H), 6.8–7.1 (m, 3 H), 7.4 (m, 4-H); ^{13}C NMR 29.6 (NCH_3) 41.1 (NCH_3), 56.7 (CH), 103.6 (C-3), 109.2 (C-7), 114.0 (CN), 119.9 (C-4), 121.0 (C-5), 122.6 (C-6), 126.5 (C-3a), 131.5 (C-2), 138.5 (C-7a). Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70. Found: C, 73.20; H, 7.36; N, 19.69.

Reaction of Dithiane 1b with Pyridinium Salt 5a. A. *n*-BuLi (1.6 M in hexane, 1.8 mL, 2.9 mmol) was slowly added to a solution of dithiane **1b**[18] (0.7 g, 2.8 mmol) in THF (50 mL) cooled at −20 °C. The resulting solution was stirred at −20 °C for 15 min. Then, pyridinium iodide **5a**[20] (0.7 g, 2.8 mmol) was

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added in portions at −50 °C, and the mixture was allowed to rise to −30 °C, stirred at this temperature for 2 h, quenched with H_2O, and extracted with Et_2O. The resulting residue was chromatographed (flash, AcOEt) to give **1-methyl-6-[2-(1-methyl-2-indolyl)-1,3-dithian-2-yl]-1,6-dihydropyridine-3-carbaldehyde (6a)**: 0.31 g (30%); IR (KBr) 1575 (C=C), 1625 (CO); ^{1}H NMR 1.89 (m, CH_2), 2.73 (m, 4 H, CH_2S), 2.89 (s, NCH_3), 4.04 (s, NCH_3), 4.82 (d, J = 5.2, 2-H), 5.19 (dd, J = 10, 5.2, 3-H), 6.70 (d, J = 10, 4-H), 6.90 (br s, 6-H), 7.08 (s, 3′-H), 7.10–7.40 (m, 3 H, indole), 7.60 (d, J = 7.6, 4′-H), 8.85 (s, CHO); ^{13}C NMR, Table II.

B. To the above reaction mixture was added dropwise enough of a saturated C_6H_6 solution of dry HCl to bring the pH to 3.5–4, and the mixture was allowed to rise to room temperature, stirred for 2 h, poured into saturated aqueous Na_2CO_3, and extracted with Et_2O. Evaporation of the dried extracts followed by flash chromatography (6:1:2 Et_2O–EtOH–DEA) afforded **5-formyl-3,11-dimethyl-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole-1-spiro-2′-(1′,3′-dithiane) (10a)**: 0.37 g (35%); mp 250–251 °C (acetone); IR (KBr) 1600 (CO); ^{1}H NMR 1.60 (dm, J = 13, 1 H, 12-H), 2.05 (m, 3 H, CH_2 and 12-H), 2.80 (m, 4 H, CH_2S), 3.40 (s, NCH_3), 3.91 (d, J = 4.1, 2-H), 4.09 (s, NCH_3), 430 (t, 6-H), 6.71 (s, 4-H), 7.02-7.20 (m, 3 H, indole), 7.96 (d, J = 7.8, 7-H), 8.83 (s, CHO); ^{13}C NMR, Table III. Anal. Calcd for $C_{20}H_{22}N_2OS_2$: C, 64.83; H, 5.98; N, 7.56; S, 17.30. Found: C, 64.97; H, 6.02; N, 7.20; S, 16.90.

5-Acetyl-3,11-dimethyl-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole-1-spiro-2′-(1′,3′-dithiane) (10b). Operating as in the preparation of **10a**, from dithiane **1b** (1 g, 4 mmol) and pyridinium iodide **5b**[21] (0.52 g, 2 mmol), tetracycle **10b** was obtained after flash chromatography (6:1:2 Et_2O–EtOH–DEA): 0.17 g (23%); mp 264–265 °C (acetone–MeOH); IR (KBr) 1600 (CO); ^{1}H NMR 1.65 (dm, J = 14, 1 H, 12-H), 2.09 (s, CH_3CO), 2.15 (m, 3 H, CH_2 and 12-H), 3.01 (m, 4 H, CH_2S), 3.49 (s, NCH_3), 3.94 (dt, J = 4, 1.5, 2-H), 4.12 (s, NCH_3), 4.53 (t, J = 2.4, 6-H), 7.05–7.20 (m, 4 H, indole and 4-H), 8.03 (dm, J = 8, 7-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{21}H_{24}N_2OS_2$: C, 65.59; H, 6.29; N, 7.28; S, 16.67. Found: C, 65.78; H, 6.42; N, 6.97; S, 16.77.

Reaction of Dithiane 1b with Pyridinium Iodide 5c. Operating as above, from dithiane **1b** (1 g, 4 mmol) and pyridinium iodide **5c**[22] (1.1 g, 4 mmol), a 1:1 mixture of tetracycles **10c** and **11c** was obtained after column chromatography (AcOEt): 0.64 g (40%). Both isomers were separated by column chromatography (CH_2Cl_2). **5-(Methoxycarbonyl)-3,11-dimethyl-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole-1-spiro-2′-(1′,3′-dithiane) (10c)**: mp 212–213 °C (acetone-*i*-Pr_2O); ^{1}H NMR 1.72 (dm, J = 14, 1 H, 12-H), 2.15 (m, 3 H, CH_2 and 12-H), 2.95 (m, 4 H, CH_2S), 3.43 (s, NCH_3), 3.69 (s, OCH_3), 3.92 (d, J = 4.4, 2-H), 4.13 (s, NCH_3), 4.23 (t, 6-H), 7.05–7.30 (m, 4 H, indole and 4-H), 7.96 (d, J = 7.8, 7-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{21}H_{24}N_2O_2S_2$: C, 62.97; H, 6.03; N, 6.99; S, 16.00. Found: C, 62.57; H, 6.25; N, 7.20; S, 15.75. **4-(Methoxycarbonyl)-2,7-dimethyl-1,2,5,6-tetrahydro-1,5-methanoazocino[4,3-*b*]indole-6-spiro-2′-(1′,3′-dithiane) (11c)**: mp 165–166 °C (acetone-*i*-Pr_2O); ^{1}H NMR 1.90 (m, 4 H, CH_2 and 12-H), 2.70 (m, 4 H, CH_2S), 3.12 (s, NCH_3), 3.68 (s, OCH_3), 3.85 (br s, 5-H), 4.20 (s, NCH_3), 4.43 (t, 1-H), 7.01–7.26 (m, 4 H, indole and 3-H), 7.56 (d, J = 7.2, 11-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{21}H_{24}N_2S_2O_2$: C, 62.97; H, 6.03; N, 6.99; S, 16.00. Found: C, 62.70; H, 6.27; N, 7.18; S, 15.78.

Methyl 4-[2-(1,3-Dithian-2-yl)-1-(methoxycarbonyl)-3-indolyl]-1-methyl-1,4-dihydropyridine-3(*E*)-acrylate (9d). A solution of dithiane **1c** (0.4 g, 1.36 mmol) in THF (30 mL) was slowly added to a solution of LDA (2 mmol) in THF (5 mL) cooled at −70 °C. After the solution was stirred at −30 °C for 1 h, pyridinium iodide **5d**[23] (0.4 g, 1.36 mmol) was added and allowed to react as described in the preparation of **6a** to give dihydropyridine **9d**: 0.29 g (45%); mp 173–174 °C (acetone); IR (KBr) 1700 (CO); ^{1}H NMR 2.20 (m, CH_2), 2.56 (s, NCH_3), 2.90 (m, 4 H, CH_2S), 3.71 and 3.91 (2 s, 6 H, OCH_3), 4.06 (dd, J = 4.3, 5.1, 4-H), 4.35 (d, J = 4.3, CHS), 4.44 (dd, J = 7.7, 5.1, 5-H), 5.43 (dd, J = 7.7, 1.4, 6-H), 6.20 (d, J = 15.5, CHCO), 6.33 (s, 2-H), 6.90–7.30 (m, 3 H, indole), 7.40 (d, J = 15.5, =CH), 7.67 (d, J = 8, 7′-H); ^{13}C NMR, Table II. Anal. Calcd for $C_{24}H_{26}N_2O_4S_2 \cdot {}^1/_2H_2O$: C, 60.10; H, 5.67; N, 5.84; S, 13.37. Found: C, 60.23; H, 5.69; N, 5.83; S, 13.14.

6-[2-Indolyl[bis(methylthio)]methyl]-1-methyl-1,6-dihydropyridine-3-carbaldehyde (6e). *n*-BuLi (1.6 M in hexane, 6.2 mL, 9.9 mmol) was slowly added to a solution of dithioacetal **2a** (1 g, 4.48 mmol) in THF (60 mL) cooled at −70 °C. After the solution was stirred at −70 °C for 30 min, pyridinium iodide **5a** (1.1 g, 4.48 mmol) was added. Operating as above, dihydropyridine **6e** was obtained: 0.12 g (7%); IR (KBr) 1570 (C=C), 1620 (C=O); ^{1}H NMR 2.04 and 2.09 (2 s, 6 H, SCH_3), 3.17 (s, NCH_3), 4.71 (dd, J = 5.5, 1, 2-H), 5.39 (dd, J = 9.6, 5.5, 3-H), 6.59 (br s, 6-H), 6.62 (s, 3′-H), 6.67 (br d, J = 9.6, 4-H), 7.01–7.20 (m, 2 H, indole), 7.29 (dd, J = 8, 1, 7′-H), 7.50 (dd, J = 7.5, 1, 4′-H), 8.40 (s, CHO), 8.90 (br s, NH); ^{13}C NMR, Table II.

5-Acetyl-3-methyl-1,1-[bis(methylthio)]-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole (10f). A THF solution of the anion derived from dithioacetal **2a** (1 g, 4.48 mmol), prepared as described above, was allowed to react with pyridinium iodide **5b** (0.78 g, 2.98 mmol) as described in the preparation of **10a**. The usual workup and further flash chromatography (AcOEt) gave **10f**: 0.1 g (15%); mp 224–225 °C (acetone); ^{1}H NMR 1.65 (dm, J = 13, 1 H, 12-H), 1.86 and 2.09 (2 s, 6 H, SCH_3), 2.30 (s, CH_3CO), 2.75 (dm, J = 13, 1 H, 12-H), 3.46 (s, NCH_3), 3.77 (d, J = 4.2, 2-H), 4.51 (t, 6-H), 7.01–7.30 (m, 4 H, indole and 4-H), 8.05 (d, J = 7.5, 7-H), 8.10 (br s, NH); ^{13}C NMR, Table III. Anal. Calcd for $C_{19}H_{22}N_2OS_2$: C, 63.65; H, 6.18; N, 7.81; S, 17.88. Found: C, 63.57; H, 6.17; N, 7.70; S, 17.85.

Reaction of Dithioacetal 2b with Pyridinium Iodide 5a. **A.** *n*-BuLi (1.6 M in hexane, 4.3 mL, 6.96 mmol) was slowly added to a solution of dithioacetal **2b** (1.5 g, 6.32 mmol) in THF (75 mL) cooled at −70 °C. After the solution was stirred at −70 °C for 30 min, pyridinium iodide **5a** (1.6 g, 6.32 mmol) was added and allowed to react as described in the preparation of **6a** to give a 3:1 mixture of dihydropyridines **6g** and **7g** (0.3 g, 13%). Both isomers were separated by an additional flash chromatography (7:3 AcOEt-hexane). **1-Methyl-4-[(1-methyl-2-indolyl)[bis(methylthio)]methyl]-1,4-dihydropyridine-3-carbaldehyde (7g)**: IR ($CHCl_3$) 1575 (C=C), 1645 (CO); ^{1}H NMR 2.00 and 2.07 (2 s, 6 H, SCH_3), 2.86 (s, NCH_3), 4.17 (s, NCH_3), 4.49 (d, J = 5.6, 4-H), 4.94 (dd, J = 7.5, 5.6, 5-H), 5.90 (d, J = 7.5, 6-H), 6.75 (s, 3′-H), 6.78 (s, 2-H), 7.05–7.40 (m, 3 H, indole), 7.55 (m, 4′-H), 9.15 (s, CHO); ^{13}C NMR, Table II. **1-Methyl-6-[(1-methyl-2-indolyl)[bis(methylthio)]methyl]-1,6-dihydropyridine-3-carbaldehyde (6g)**: IR ($CHCl_3$) 1570 (C=C), 1620 (CO); ^{1}H NMR 1.91 and 2.15 (2 s, 6 H, SCH_3), 2.75 (s, NCH_3), 4.14 (s, NCH_3), 5.18 (d, J = 5, 2-H), 5.30 (dd, J = 9.5, 5, 3-H), 5.65 (d, J = 9.5, 4-H), 6.93 (br s, 6-H), 6.94 (s, 3′-H), 7.02–7.65 (m, 4 H, indole), 8.85 (s, CHO); ^{13}C NMR, Table II.

B. The above reaction mixture was treated with acid as described in the preparation of **10a**. The usual workup followed by column chromatography (AcOEt) gave a 1:5 mixture of tetracycles **10g** and **10h** (0.36 g, 20%). Both compounds were separated by an additional column chromatography (AcOEt). **5-Formyl-3,11-dimethyl-1,1-[bis(methylthio)]-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole (10g)**: IR (KBr) 1600 (CO); ^{1}H NMR 1.64 (dm, J = 12, 1 H, 12-H), 1.69 (s, SCH_3), 2.31 (s, SCH_3), 2.70 (dt, J = 12, 2.9, 1 H, 12-H), 3.54 (s, NCH_3), 3.90 (m, 2-H), 4.06 (s, NCH_3), 4.35 (t, 6-H), 6.74 (s, 4-H), 7.08–7.25 (m, 3 H, indole), 8.03 (d, J = 7.6, 7-H), 8.90 (s, CHO); ^{13}C NMR, Table III. **5-Formyl-3,11-dimethyl-1-oxo-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole (10h)**: mp 246–247 °C (acetone); IR (KBr) 1600, 1640 (CO); ^{1}H NMR 1.86 (dt, J = 12.7, 3.3, 1 H, 12-H), 2.39 (dt, J = 12.7, 2.8, 1 H, 12-H), 3.21 (s, NCH_3), 3.84 (m, 2-H), 4.01 (s, NCH_3), 4.49 (t, 6-H), 6.68 (s, 4-H), 7.10–7.40 (m, 3 H, indole), 8.19 (d, J = 8.1, 7-H), 8.80 (s, CHO); ^{13}C NMR, Table III. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.91; H, 5.69; N, 9.86.

5-Acetyl-3,11-dimethyl-1-oxo-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole (10i). Operating as in the above procedure B, from dithioacetal **2b** (0.5 g, 2.1 mmol) and pyridinium iodide **5b** (0.26 g, 1.05 mmol), tetracycle **10i** was obtained: 50 mg (16%); mp 228–229 °C (acetone); IR (KBr) 1600, 1640 (CO); ^{1}H NMR 1.85 (dt, J = 12.5, 4, 1 H, 12-H), 2.08 (s, CH_3CO), 2.39 (dt,

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J = 12.5, 2.5, 1 H, 12-H), 3.21 (s, NCH_3), 3.78 (m, 2-H), 4.03 (s, NCH_3), 4.63 (t, 6-H), 7.10–7.40 (m, 4 H, indole, 4-H), 8.25 (d, J = 8.1, 7-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.51. Found: C, 73.21; H, 6.15; N, 9.43.

Reaction of Dithioacetal 2b with Pyridinium Iodide 5c. Operating as above, from dithioacetal **2b** (1 g, 4.2 mmol) and pyridinium iodide **5c** (1.1 g, 4.2 mmol) was obtained a 1:1 mixture of tetracycles **10j** and **11j**: 0.65 g (40%). Both isomers were separated by an additional column chromatography (CH_2Cl_2). **5-(Methoxycarbonyl)-3,11-dimethyl-1,1-[bis(methylthio)]-1,2,3,6-tetrahydro-2,6-methanoazocino[4,5-*b*]indole (10j)**: mp 187 °C (acetone); ^1H NMR 1.63 (dm, J = 13, 1 H, 12-H), 1.70 and 2.29 (2 s, 6 H, SCH_3), 2.60 (dm, J = 13, 1 H, 12-H), 3.42 (s, NCH_3), 3.69 (s, OCH_3), 3.80 (m, 2-H), 4.07 (s, NCH_3), 4.22 (t, 6-H), 7.10–7.30 (m, 4 H, indole, 4-H), 7.97 (d, J = 7.7, 7-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{20}H_{24}N_2S_2O_2$: C, 61.82; H, 6.22; N, 7.21; S, 16.50. Found: C, 61.55; H, 6.20; N, 7.15; S, 16.36. **4-(Methoxycarbonyl)-2,7-dimethyl-6,6-[bis(methylthio)]-1,2,5,6-tetrahydro-1,5-methanoazocino[4,3-*b*]indole (11j)**: mp 204 °C (acetone–i-Pr_2O); ^1H NMR 1.75 and 2.44 (2 s, 6 H, SCH_3), 1.82 and 2.56 (2 dm, J = 12.5, 12-H), 3.18 (s, NCH_3), 3.74 (s, OCH_3), 3.88 (br s, 5-H), 4.16 (s, NCH_3), 4.45 (t, 1-H), 7.10–7.35 (m, 4 H, indole, 3-H), 7.63 (d, J = 7.8, 11-H); ^{13}C NMR, Table III. Anal. Calcd for $C_{20}H_{24}N_2S_2O_2$: C, 61.82; H, 6.22, N, 7.21; S, 16.50. Found: C, 61.52; H, 6.38; N, 7.29, S, 16.27.

Reaction of Dithioacetal 2c with Pyridinium Iodide 5a. A. A solution of dithioacetal **2c** (1.5 g, 5.3 mmol) in THF (75 mL) was slowly added to a solution of LDA (7.8 mmol) in THF (15 mL) cooled at −70 °C. After being stirred at −70 °C for 30 min, pyridinium iodide **5a** (1.3 g, 5.3 mmol) was added and allowed to react as described in the preparation of **6a**. The usual workup followed by column chromatography (1:1 hexane-AcOEt and AcOEt) gave **4-[2-[bis(methylthio)methyl]-1-(methoxycarbonyl)-3-indolyl]-1-methyl-1,4-dihydropyridine-3-carbaldehyde (9k)**: 0.32 g (15%); mp 121–122 °C (acetone-i-Pr_2O); IR (KBr) 1630, 1700 (CO); ^1H NMR 2.26 and 2.34 (2 s, 6 H, SCH_3), 2.72 (s, NCH_3), 3.91 (s, OCH_3), 4.39 (m, 4-H, SCH), 4.74 (dd, J = 7.9, 3.6, 5-H), 5.48 (dd, J = 7.9, 1.5, 6-H), 6.70 (d, J = 1.5, 2-H), 6.90–7.30 (m, 3 H, indole), 7.63 (d, J = 7.7, 7′-H), 9.29 (s, CHO); ^{13}C NMR, Table II. Anal. Calcd for $C_{20}H_{22}N_2S_2O_3 \cdot {}^1/_2H_2O$: C, 58.37; H, 5.63; N, 6.80. Found: C, 58.41; H, 5.55; N, 6.52.

B. Dithioacetal **2c** (0.5 g, 1.77 mmol) was allowed to react with n-BuLi (1.6 M in hexane, 2.44 mL, 3.91 mmol) at −70 °C for 30 min and then with pyridinium iodide **5a** (0.44 g, 1.77 mmol) as above. Column chromatography (AcOEt) gave a 1:1 mixture of dihydropyridines **8e** and **9e**: 0.31 g (50%). Both isomers were separated by column chromatography (1:1 hexane–AcOEt and AcOEt). **4-[2-[Bis(methylthio)methyl]-3-indolyl]-1-methyl-1,4-dihydropyridine-3-carbaldehyde (9e)**: ^1H NMR 2.16 and 2.24 (2 s, 6 H, SCH_3), 3.32 (s, NCH_3), 4.88 (d, J = 4.5, 4-H), 5.00 (dd, J = 7.5, 4.5, 5-H), 5.66 (s, SCH), 5.99 (d, J = 7.5, 6-H), 6.80 (d, J = 1.5, 2-H), 7.00–7.50 (m, 4 H, indole), 8.60 (br s, NH), 9.03 (s, CHO); ^{13}C NMR, Table II. **6-[2-[Bis(methylthio)-methyl]-3-indolyl]-1-methyl-1,6-dihydropyridine-3-carbaldehyde (8e)**: mp 193 °C (acetone–MeOH); IR (KBr) 1620 (CO); ^1H NMR 2.15 and 2.18 (2 s, 6 H, SCH_3), 2.90 (s, NCH_3), 5.18 (s, SCH), 5.22 (dd, J = 10, 3, 3-H), 5.85 (br, 2-H), 6.55 (d, J = 10, 4-H), 7.08 (s, 6-H), 7.10–7.65 (m, 4 H, indole), 8.74 (s, CHO), 9.90 (br s, NH); ^{13}C NMR, Table II. Anal. Calcd for $C_{18}H_{20}N_2OS_2$: C, 62.75; H, 5.85; N, 8.13; S, 18.61. Found: C, 62.67; H, 5.84; N, 8,10; S, 18.38.

Methyl 4-[2-[Bis(methylthio)methyl]-1-(methoxycarbonyl)-3-indolyl]-1-methyl-1,4-dihydropyridine-3(*E*)-acrylate (9n). The anion of dithioacetal **2c** (0.4 g, 1.42 mmol) and pyridinium iodide **5d** (0.43 g, 1.42 mmol) were allowed to react as in the above procedure A. The usual workup followed by crystallization from acetone gave dihydropyridine **9n**: 0.38 g (58%); mp 135 °C (acetone); IR (KBr) 1690, 1700 (CO); ^1H NMR 2.26 and 2.73 (2 s, 6 H, SCH_3), 2.59 (s, NCH_3), 3.76 and 3.91 (2 s, 6 H, OCH_3), 4.25 (m, 4-H, SCH), 4.52 (dd, J = 7.7, 5, 5-H), 5.43 (dd, J = 7.7, 1.5, 6-H), 6.30 (d, J = 15, CHCO), 6.36 (s, 2-H), 6.90–7.30 (m, 3 H, indole), 7.41 (d, J = 15, =CH), 7.60 (d, J = 8, 7′-H); ^{13}C NMR, Table II. Anal. Calcd for $C_{23}H_{26}N_2O_4S_2$: C, 60.24; H, 5.71; N, 6.10; S, 13.98. Found: C, 60.34; H, 5.83; N, 6.14; S, 13.80.

6-[2-[Bis(phenylthio)methyl]-3-indolyl]-1-methyl-1,6-dihydropyridine-3-carbaldehyde (8o). n-BuLi (1.6 M in hexane, 2 mL, 3.2 mmol) was slowly added to a solution of dithioacetal **3a** (0.5 g, 1.43 mmol) in THF (30 mL) cooled at −70 °C. After the solution was stirred at −70 °C for 45 min, pyridinium iodide **5a** (0.35 g, 1.43 mmol) was added and allowed to react as described in the preparation of **6a** to give dihydropyridine **8o**: 54 mg (8%); IR (KBr) 1570 (C=C), 1610 (CO), 3220 (NH); ^1H NMR 2.48 (br s, NCH_3), 4.65 (br d, J = 10, 3-H), 5.53 (s, SCH), 5.79 (d, J = 1.8, 2-H), 6.45 (br d, J = 10, 4-H), 6.60 (br s, 6-H), 6.99–7.80 (m, 14 H, ArH), 8.76 (s, NH), 9.35 (s, CHO); ^{13}C NMR, Table II.

6-[2-[Bis(phenylthio)methyl]-1-methyl-3-indolyl]-1-methyl-1,6-dihydropyridine-3-carbaldehyde (8p). Operating as above, from dithioacetal **3b** (0.5 g, 1.38 mmol), n-BuLi (1.6 M in hexane, 1 mL, 1,6 mmol), and pyridinium iodide **5a** (0.34 g, 1.38 mmol) was obtained dihydropyridine **8p**: 60 mg (10%); IR (KBr) 1575 (C=C), 1625 (CO); ^1H NMR 2.35 (br s, NCH_3), 4.10 (br s, NCH_3), 6.90–7.60 (m, 14 H, ArH), 9.50 (s, CHO); ^{13}C NMR, Table II.

Reaction of Amino Nitrile 4a with Pyridinium Iodide 5a. A solution of amino nitrile **4a** (1 g, 5.02 mmol) in THF (50 mL) was slowly added to a solution of LDA (12.5 mmol) in THF (20 mL) cooled at −70 °C, and the resulting solution was stirred at −70 °C for 30 min. Then, pyridinium iodide **5a** (1.25 g, 5.02 mmol) was added and allowed to react as usual to give a residue which was chromatographed (CH_2Cl_2). The initial elution gave ***N*,*N*-dimethylindole-2-carboxamide**[24] **(12a)**: 47 mg (5%); IR (KBr) 1600 (CO), 3210 (NH); ^1H NMR (60 MHz) 3.2 (s, 6 H, NCH_3), 6.5 (d, J = 1, 3-H), 6.6–7.5 (m, 4 H). Further elution gave a 1:9 mixture of dihydropyridines **9q** and **8q**: 0.3 g (22%). Both isomers were separated by column chromatography (AcOEt). **4-(2-Formyl-3-indolyl)-1-methyl-1,4-dihydropyridine-3-carbaldehyde (9q)**: ^1H NMR 3.33 (s, NCH_3), 5.10 (ddd, J = 7.5, 4.5, 0.5, 5-H), 5.37 (d, J = 4.5, 4-H), 6.01 (dt, J = 7.5, 1.5, 6-H), 6.89 (d, J = 1.5, 2-H), 7.10–7.40 (m, 3 H, indole), 7.75 (d, J = 9, 4′-H), 8.99 (s, CHO), 10.18 (s, CHO). **6-(2-Formyl-3-indolyl)-1-methyl-1,6-dihydropyridine-3-carbaldehyde (8q)**: mp 161–162 °C (acetone–Et_2O); IR (KBr) 1620, 1660 (CO); ^1H NMR 2.89 (s, NCH_3), 5.26 (dd, J = 9.9, 3.8, 3-H), 6.20 (dd, J = 3.8, 1.9, 2-H), 6.58 (br d, J = 9.9, 4-H), 7.06 (br s, 6-H), 7.15–7.50 (m, 3 H, indole), 7.75 (d, J = 9, 4′-H), 8.86 (s, CHO), 10.09 (s, CHO); ^{13}C NMR, Table II. Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.29; N, 10.52. Found: C, 72.03; H, 5.34; N, 10.39.

Reaction of Amino Nitrile 4b with Pyridinium Iodide 5a. Operating as above, amino nitrile **4b** (1.27 g, 6 mmol), LDA (7 mmol) and pyridinium iodide **5a** (1.48 g, 6 mmol) led to a residue which was chromatographed. Elution with CH_2Cl_2 gave ***N*,*N*-dimethyl-1-methylindole-2-carboxamide (12b)**: 60 mg (5%), IR ($CHCl_3$) 1625 (CO); ^1H NMR (60 MHz) 3.0 (s, 6 H, NCH_3), 3.6 (s, NCH_3), 6.4 (s, 3-H), 6.7–7.6 (m, 4 H). Elution with 99:1 CH_2Cl_2–MeOH gave a 1:3 mixture of dihydropyridines **9r** and **8r**: 0.7 g (42%). Both isomers were separated by column chromatography (AcOEt). **4-(2-Formyl-1-methyl-3-indolyl)-1-methyl-1,4-dihydropyridine-3-carbaldehyde (9r)**: mp 205–206 °C (acetone); IR (KBr) 1650 (CO), 1575 (C=C); ^1H NMR 3.30 (s, NCH_3), 4.04 (s, NCH_3), 5.05 (ddd, J = 7.8, 4.4, 0.5, 5-H), 5.40 (br d, J = 4.4, 4-H), 5.95 (dt, J = 7.8, 1.6, 6-H), 6.85 (d, J = 1.6, 2-H), 7.20–7.40 (m, 3 H, indole), 7.75 (d, J = 8, 4′-H), 9.06 (s, CHO), 10.40 (s, CHO); ^{13}C NMR, Table II. Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.77; H, 5.99; N, 9.92. **6-(2-Formyl-1-methyl-3-indolyl)-1-methyl-1,6-dihydropyridine-3-carbaldehyde (8r)**: IR (KBr) 1660, 1630 (CO), 1575 (C=C); ^1H NMR 2.85 (s, NCH_3), 4.10 (s, NCH_3), 5.22 (dd, J = 9.8, 3.5, 3-H), 6.24 (dd, J = 3.5, 1.8, 2-H), 6.55 (br d, J = 9.8, 4-H), 6.92 (br s, 6-H), 7.30–7.50 (m, 3 H, indole), 7.80 (dt, J = 8.2, 0.9, 4′-H), 8.92 (s, CHO), 10.24 (s, CHO); ^{13}C NMR, Table II.

Reaction of Amino Nitrile 4b with Pyridinium Iodide 5b. Operating as above, from amino nitrile **4b** (0.5 g, 2.34 mmol) and pyridinium iodide **5b** (0.61 g, 2.34 mmol) was obtained a residue, and then it was chromatographed. Elution with CH_2Cl_2 gave amide **12b**: 40 mg (8%). Elution with 99:1 CH_2Cl_2–MeOH gave a 1:3 mixture of dihydropyridines **9s** and **8s**: 0.21 g (30%). Both isomers were separated by column chromatography (AcOEt). **3-Acetyl-4-(2-formyl-1-methyl-3-indolyl)-1,4-dihydropyridine**

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(9s): mp 194-195 °C (acetone); IR (KBr) 1650 (CO), 1570 (C=C); ^{1}H NMR 2.06 (s, CH_3CO), 3.26 (s, NCH_3), 4.01 (s, NCH_3), 4.95 (dd, J = 7.7, 4.4, 5-H), 5.43 (d, J = 4.4, 4-H), 5.92 (d, J = 7.7, 6-H), 7.10-7.40 (m, 4 H, indole, 2-H), 7.75 (d, J = 8, 4'-H), 10.31 (s, CHO); ^{13}C NMR, Table II. Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.51. Found: C, 73.66; H, 6.18; N, 9.49. **5-Acetyl-2-(2-formyl-1-methyl-3-indolyl)-1-methyl-1,2-dihydropyridine (8s)**: ^{1}H NMR 2.21 (s, CH_3CO), 2.83 (s, NCH_3), 4.07 (s, NCH_3), 5.08 (br d, J = 9.5, 3-H), 6.15 (br s, 2-H), 6.60 (br d, J = 9.5, 4-H), 7.10-7.50 (m, 4 H, indole, 6-H), 7.79 (d, J = 8, 4'-H), 10.22 (s, CHO); ^{13}C NMR, Table II.

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Concurrent Hydrogen Migration and Nitrogen Extrusion in the Excited States of Alkylchlorodiazirines

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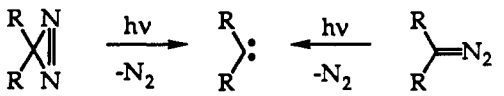
Laser flash photolysis of a series of alkylchlorodiazirines in the presence of pyridine generates easily detected, long-lived ylides. At large pyridine concentrations all of the alkylchlorocarbene generated in a laser flash is completely converted into ylide. The yield of ylide in this regime of pyridine concentration correlates with the α-C-H bond dissociation energy of the alkyl group. This demonstrates that hydrogen migration competes with carbene formation in the excited state of the precursor.

Introduction

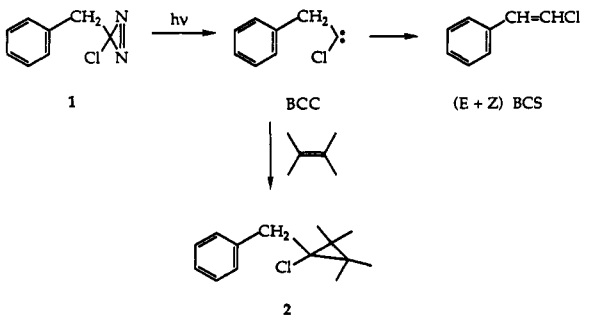
Carbenes have frequently been generated by the photochemical decomposition of diazirines and diazo compounds.[1] It has long been recognized that intramolecular



reactions of the excited states of the precursors may proceed in concert with nitrogen extrusion or that some rearrangement may occur in an excited state of the carbene.[2] In this circumstance the mixture of stable products formed on photolysis would reflect ground-state carbene reactions as well as the chemistry of the excited state of the precursor or the carbene. Identifying the origin (carbene or noncarbene) of a particular product or products is problematic at best.

A good example of these concerns is provided by benzylchlorocarbene BCC. Photolysis of benzylchlorodiazirine (1) in a relatively inert solvent produces a Z and E mixture

Scheme I



of β-chlorostyrenes (BCS's), Scheme I.[3] Upon the addition of a carbene trap (e.g., tetramethylethylene) adducts **2** are formed. The presence of the trap has not only reduced the yield of BCS, but surprisingly the trap leads to a change in the E/Z ratio of the BCS rearrangement product. This result is inconsistent with the simple mechanism of Scheme I and requires that there are at least two pathways by which the chlorostyrenes are formed, a carbene and a noncarbene route. Liu has suggested that BCC forms a complex with alkenes[3] and that the complex can partition between cyclopropane formation and 1,2 hydrogen migration to form BCS with a new $E + Z$ dis-

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