JOC Article

Heteroaromatic Annulation of 2-Methyl/2-Cyanomethylbenzimidazole Dianions with α-Oxoketene Dithioacetals: A Highly Regioselective Synthetic Protocol for 1,2- and 2,3-Substituted/Annulated Pyrido[1,2-*a*]benzimidazoles†

Kausik Panda, J. R. Suresh, H. Ila,* and H. Junjappa*

Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India

hila@iitk.ac.in

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A highly efficient and regioselective annulation protocol for a series of linearly 2,3- and angularly 1,2-substituted and annulated pyrido[1,2-*a*]benzimidazoles involving [3 + 3] cyclocondensation of the dianions generated from 2-methyl (**2A**) and 2-cyanomethyl (**3A**) benzimidazoles with a variety of α-oxoketene dithioacetals has been reported. Thus the dianion **2A** derived from 2-methylbenzimidazole has been shown to undergo regioselective 1,2-addition with various α-oxoketene dithioacetals derived from acyclic (**4a**−**d**) and cyclic ketones (**13a**,**b**, **20**, **29** and **32**) to afford various carbinol acetals which on intramolecular cyclocondensation in the presence of phosphoric acid furnish the corresponding 1-methylthio-2,3-substituted (**5a**−**c**) and 2,3-fused linear polycyclic (**14a**,**b**, **21**, **30**, and **33**) pyrido[1,2-*a*]benzimidazoles in high yields. Similarly the dianion **3A** from 2-cyanomethylbenzimidazole undergoes one-pot conjugate addition−elimination and cyclocondensation with these α-oxoketene dithioacetals to give 4-cyano-3-(methylthio)-1(or 1,2-)-substituted (**6a**−**d**) and the corresponding angularly 1,2-fused (**16a**,**b**, **23**, **31**, and **34**) polycylic analogues of pyrido[1,2-*a*]benzimidazoles in execellent yields.

Introduction

Compounds containing azaindole ring systems have attracted considerable attention in recent years because of their promising biological activities and use as important building blocks in natural and synthetic bioactive compounds through their isosterism with indole.[1] Among them, the imidazo[1,2-*a*]pyridine (IP)[2] and related structures such as imidazo[1,2-*a*]pyrimidine (IPM),[2b] imidazo-[1,2-*a*]quinoxaline (IQ),[3] or imidazo[2,1-*a*]isoquinoline (IIQ)[4] frameworks have been extensively studied because of their wide range of pharmacological activities, which has prompted chemists to develop many synthetically attractive methods for this class of compounds. In contrast, the related pyrido[1,2-*a*]benzimidazole ring system did not receive much attention until the past decade[5] when some of its derivatives found pharmaceutical applications.[6] Thus many of the pyrido[1,2-*a*]benzimidazolium salts and their 1-azino derivatives are shown to be intercalating agents,[7] whereas structures such as **1a**−**c** are shown (Scheme 1) to exhibit antipro-

† Dedicated to Prof. M. V. George on his 75th birthday.

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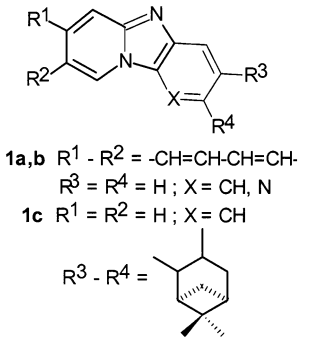
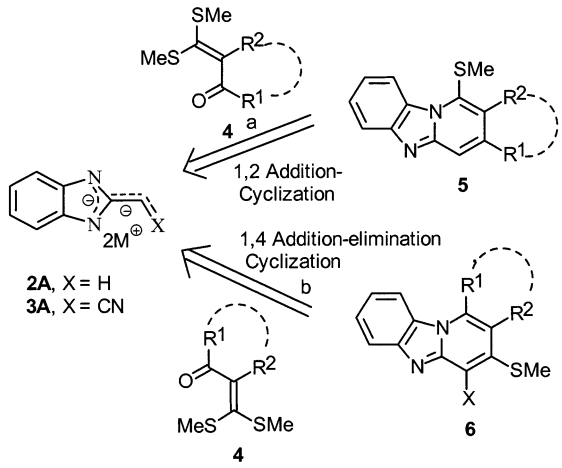
SCHEME 1



liferative activity.[8] Some of these compounds also display interesting photophysical and fluorescent properties.[9] While there are many elegant approaches for imidazo-[1,2-*a*]pyridine[2] and related systems,[1−4] the synthetic routes for pyrido[1,2-*a*]benzimidazoles are less common, which in part can be attributed to the difficulty in the preparation of these heterocycles, often requiring a lengthy and low yielding synthesis.[10]

Assembly of the pyrido[1,2-*a*]benzimidazole framework can be accomplished in a variety of ways with several approaches described in an extensive 1980 review.[11] Only a few new variations have been reported[6b,7a,b,12,13] since then, and to our knowledge, no additional review has appeared. The most common route to pyrido[1,2-*a*]benzimidazoles involves ring closure reactions of 1,2,3-substituted benzimidazole derivatives.[10,11] Thus substituted pyrido[1,2-*a*]benzimidazoles are formed in low yields in uncatalyzed thermal reactions of 1,2-alkyl-substituted benzimidazoles with either methyl propiolate or dimethyl acetylenedicarboxylate (DMAD).[11a] Base-induced cycloannulation of *N*-unsubstituted benzimidazoles having an active methylene substituent (CH_2CN) at the *C*(2) position with 1,3-dicarbonyl compounds has been reported to give various substituted pyrido[1,2-*a*]-benzimidazoles in moderate to high yields.[11a] However, use of unsymmetrically substitued 1,3-dicarbonyl compounds or substituted benzimidazoles in this type of condensation is complicated by formation of isomeric mixtures as a result of availability of several modes of ring closure. The other important approaches make use of ring closure reactions of pyridine derivatives such as 2-aminopyridine with either *o*-chloronitrobenzene, *p*-benzoquinone, or 2-chlorocyclohexanone yielding substituted pyrido[1,2-*a*]benzimidazoles in moderate to high yields.[11a] However, all these methods suffer from some limitations such as low yields, drastic reaction conditions,

SCHEME 2



or generality over a wide range of substrates. Therefore development of new general regiospecific methods for this class of compounds is highly desirable.

During the course of our heteroaromatic annulation studies involving [3 + 3] cyclocondensation of α-oxoketene dithioacetals (1,3-bielectrophilic components) with various heteroallyl anions (1,3-binucleophilic components),[14] we had the opportunity to explore regiospecific formation of substituted and annulated pyrido[1,2-*a*]benzimidazoles by coupling of these oxoketene dithioacetals with dianions **2A** and **3A** derived from 2-methyl- or 2-cyanomethylbenzimidazoles retrosynthetically depicted in the Scheme 2. We have demonstrated in our earlier studies that it is possible to tune up reactivity of ambident heteroallyl anions derived from various methyl-substituted heterocycles toward α-oxoketene dithioacetals in either a regiospecific 1,2-fashion or a conjugate 1,4-addition−elimination pathway.[15] In general the heteroallyl anions stabilized by an electron-withdrawing group such as nitrile are shown to add to α-oxoketene dithioacetals initially in conjugate addition−elimination fashion[15a,b,h,i] whereas the corresponding lithiomethyl species generated by deprotonation of methyl-substituted heterocycles

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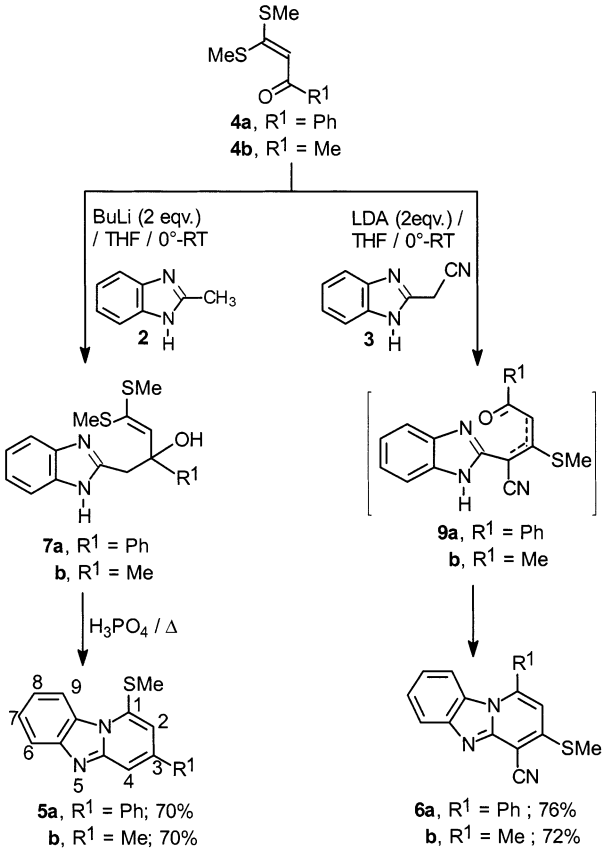
SCHEME 3

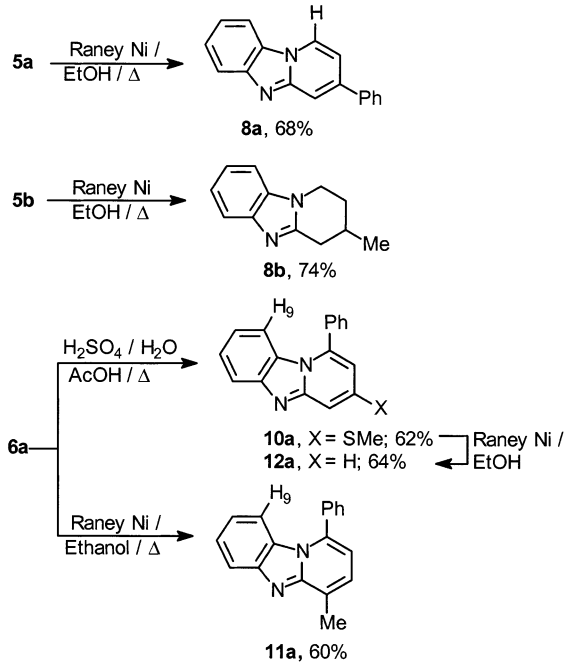


were found to be less discriminate, displaying either a 1,2- or a 1,4-addition pattern.[14,15] Subsequent acid-induced (or spontaneous) cycloaromatization of these adducts leads to formation of either linearly substituted/annulated (1,2-addition) or angularly substituted/annulated (conjugate addition−elimination) benzoheterocycles (or bridged azaheterocycles) in highly regiospecific fashion. We therefore envisaged in line with these earlier studies that it should be possible to develop a general protocol for regioselective synthesis of either 2,3-substituted/annulated (**5**) or the corresponding angularly 1,2-substituted/fused (**6**) pyrido[1,2-*a*]benzimidazoles by cycloannulation of α-oxoketene dithioacetals with respective 2-substituted benzimidazole dianions **2A** and **3A** as shown in the Scheme 2. We have successfully achieved these objectives and report our findings in the present paper.

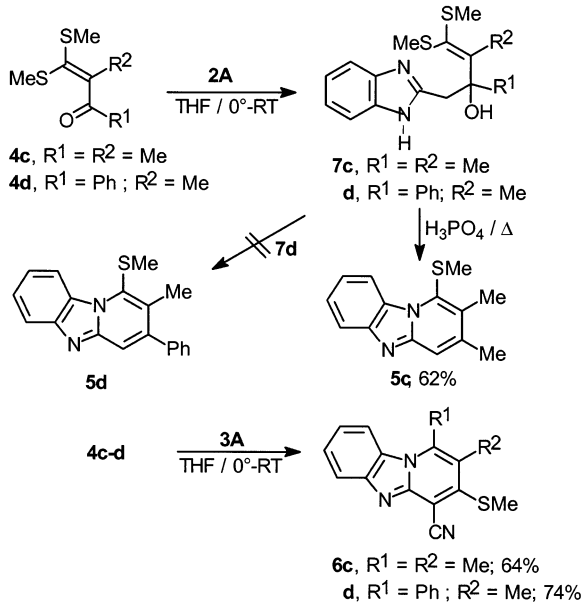
Results and Discussion

Cycloannulation of dianion **2A** derived from 2-methylbenzimidazole **2** with acyclic α-oxoketene dithioacetals **4a**−**d** was first investigated (Schemes 3−5). Dianion **2A** was generated by deprotonation of **2** with BuLi followed by its reaction with ketene dithioacetal **4a** to afford the carbinol acetal **7a** in nearly quantitative yield. When **7a** was subjected to cycloaromatization in the presence of H_3PO_4, workup and TLC analysis of the reaction mixture showed formation of a single product (70%) characterized as 1-(methylthio)-3-phenylpyrido[1,2-*a*]benzimidazole (**5a**) on the basis of its spectral and analytical data (Scheme 3).The regiochemistry of the product **5a** was further

SCHEME 4



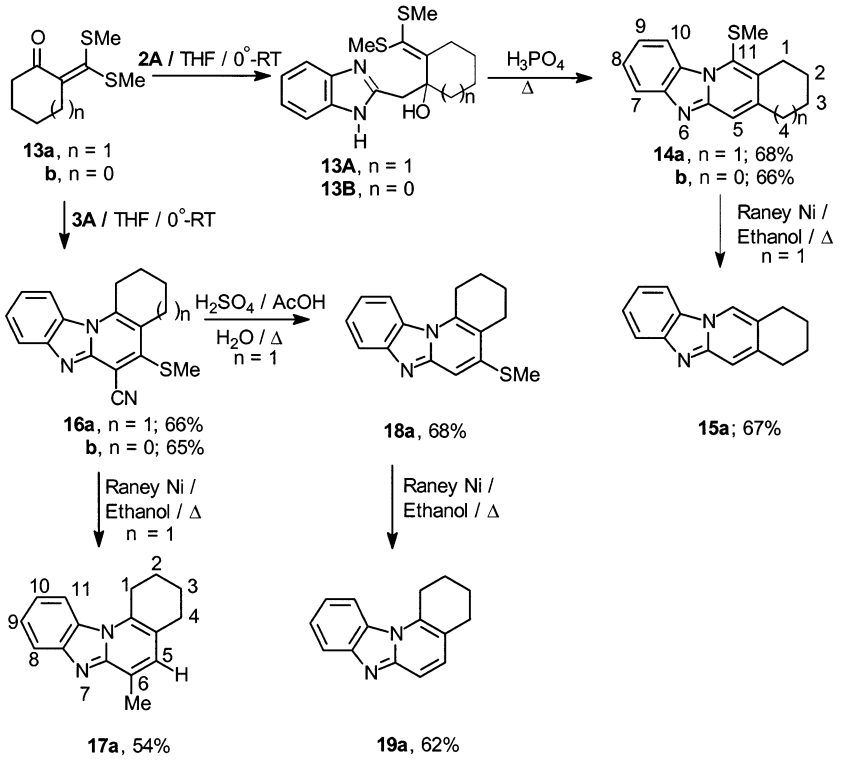
SCHEME 5



established by its Raney-Ni dethiomethylation to afford sulfur-free compound **8a** in 68% yields (Scheme 4). The corresponding 4-bis(methylthio)-3-buten-2-one (**4b**) also underwent 1,2-addition with **2A** followed by acid-induced cyclization of the resulting carbinol acetal **7b** under identical conditions to furnish the corresponding 3-methyl-1-(methylthio)pyrido[1,2-*a*]benzimidazole (**5b**) in 70% yield (Scheme 3). Attempted reductive dethiomethylation of **5b** resulted in concomitant reduction of the pyridine ring also to give 3-methyl-1,2,3,4-tetrahydropyrido-[1,2-*a*]benzimidazole (**8b**) in 74% yield (Scheme 4).

We next investigated the cycloannulation of dianion **3A** derived from 2-cyanomethylbenzimidazole **3** with the acyclic ketene dithioacetals **4a**,**b** (Scheme 3). Thus when **4a** or **4b** was reacted with **3A**, workup of the reaction mixture gave only a single product in both cases, which

SCHEME 6



were characterized as 4-cyano-1-phenyl(or 1-methyl)-3-(methylthio)-pyrido[1,2-*a*]benzimidazoles **6a** (76%) and **6b** (72%), respectively (Scheme 3). Our attempts to isolate conjugate adducts **9a**,**b** under various conditions in the presence of different bases (NaH, BuLi) were not successful. The regiochemistry of one of the products **6a** was established by its acid-induced hydrolysis−decarboxylation to **10a** and also by its Raney-Ni dethiomethylation−reduction to the product **11a** (Scheme 4). The characteristic spectral feature that distinguished the two regioisomers **5a** and **10a** was the chemical shift of the H-9 proton, which appeared at higher field (δ 6.47, d, J = 8.5 Hz) in the ^{1}H NMR spectrum of **10a** in comparison to **5a** (δ 8.67, d, J = 8.6 Hz) presumably due to the shielding effect of the 1-phenyl group in **10a**.[16] The product **10a** was further desulfurized to give parent 1-phenylpyrido[1,2-*a*]benzimidazole (**12a**) in 64% yield (Scheme 4).

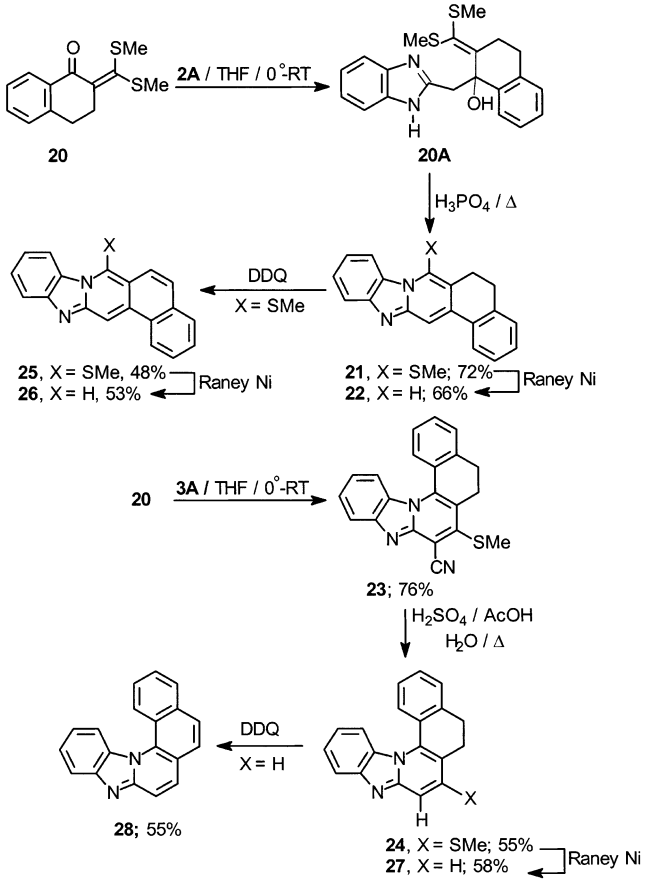
The methodology was next extended for the synthesis of tetrasubstituted pyrido[1,2*a*]benzimidazoles by subjecting the α-oxoketene dithioacetals **4c**,**d** to cyclocondensation with **2A** and **3A** (Scheme 5). Thus the ketene dithioacetal **4c** from ethylmethyl ketone underwent smooth 1,2-addition with the dianion **2A** followed by cyclization of the resulting carbinol **7c** to afford 2,3-dimethyl-1-(methylthio)pyrido[1,2-*a*]benzimidazole **5c** in 62% yield. However, the carbinol dithioacetal **7d** from ketene dithioacetal **4d** (from propiophenone) failed to cyclize to the corresponding 2-methyl-3-phenyl derivative **5d** under similar conditions or in the presence of other Lewis and protic acids (BF_3·Et_2O, TFA, PTSA) yielding only an intractable mixture of products. This may be due to the presence of a bulkier phenyl group in the carbinol **7d**, which sterically inhibits formation of cyclic planar transition state for cyclization. On the other hand, both **4c** and **4d** underwent smooth cyclization with dianion **3A** yielding 1,2,3,4-tetrasubstituted pyrido[1,2-*a*]benzimidazoles **6c**,**d** in high yields under identical conditions to those described earlier (Scheme 5).

After successfully achieving and establishing the synthesis of regioselectively substituted pyrido[1,2-*a*]benzimidazoles **5a**−**c** and **6a**−**d**, we next undertook the synthesis of linearly and angularly fused [1,2-*a*]pyridobenzimidazoles as depicted in Schemes 6−9. Cyclocondensation of cyclic α-oxoketene dithioacetals **13a**,**b** derived from cyclohexanone and cyclopentanone with dianions **2A** and **3A** was first investigated (Scheme 6). Thus the linearly fused 12-(methylthio)-2,3-cyclohexapyrido[1,2-*a*]benzimidazole **14a** was obtained in 68% yield when **13a** was reacted with dianion **2A** under earlier described conditions followed by acid-induced cyclization of the resulting carbinol **13A**.[17] The product **14a** was converted to the sulfur-free pyrido[1,2-*a*]benzimidazole **15a** by treatment with Raney-Ni. The corresponding 2,3-cyclopentapyrido[1,2-*a*]benzimidazole **14b** was also obtained from **13b** and **2A** following the identical conditions (Scheme 6). Similarly, the one-step cycloannulation of dianion **3A** with **13a** and **13b** afforded the angularly 1,2-fused substituted pyrido[1,2-*a*]benzimidazoles **16a**,**b** in 66% and 65% yields, respectively (Scheme 6). Reductive dethiomethylation of one of the products **16a** with Raney-Ni yielded **17a** in which the connectivity between the 6-methyl group and the H-5 proton was established by

(16) The ^{1}H NMR spectra of all the newly synthesized 1-phenylpyrido[1,2-*a*]benzimidazole **6a**, **6d**, and **11**−**12a** displayed a higher field shift of the H-9 proton (δ 5.92−6.44) due to the shielding effect of the 1-phenyl group.

(17) All the carbinols obtained by 1,2-addition of anion **2A** to various oxoketene dithioacetals were characterized with the help of ^{1}H and ^{13}C NMR spectral data.

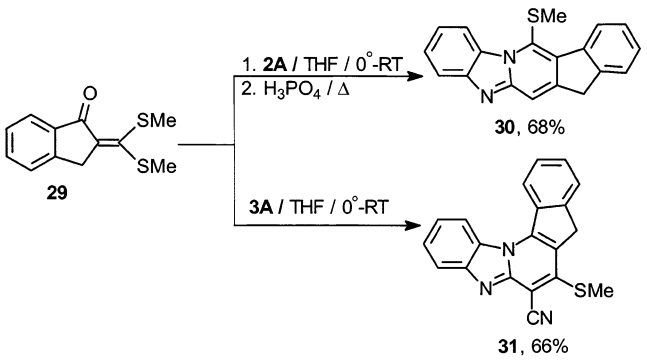
SCHEME 7



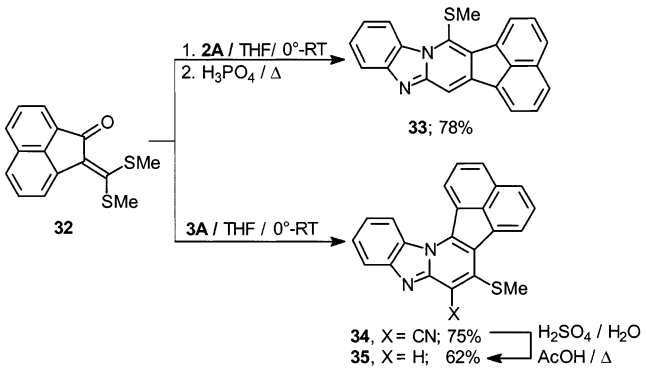
the NOE difference experiment thus confirming the regiochemical assignments. The product **16a** was subjected to acid-induced hydrolysis−decarboxylation to give **18a** followed by its Raney-Ni dethiomethylation to afford **19a** in 62% yield (Scheme 6).

Further scope of the methodology is demonstrated by the synthesis of linearly and angularly fused pentacyclic pyrido[1,2-*a*]benzimidazoles **21** and **23** by performing cycloannulation reactions on oxoketene dithioacetal **20** derived from α-tetralone with dianions **2A** and **3A**, respectively (Scheme 7). Thus when oxoketene dithioacetal **20** was reacted with dianion **2A**, the corresponding carbinol **20A** was isolated in 91% yield. Subsequent cyclization of **20A** with H_3PO_4 under earlier described conditions afforded the pentacyclic pyrido[1,2-*a*]benzimidazole **21** in 72% yield. The reaction of **20** with dianion **3A** also followed the similar conjugate addition−cyclization trend affording the corresponding angularly 1,2-fused pentacyclic pyridobenzimidazole **23** in high yield under identical conditions. The regiochemistry of the products **21** and **23** was established by desulfurization of **21** to **22** and acid-assisted hydrolysis−decarboxylation of **23** to **24**. The product **21** was converted to the linearly fused parent pentacyclic pyrido[1,2-*a*]benzimidazoles **26** by subjecting it to successive dehydrogenation (DDQ) and dethiomethylation with Raney-Ni (Scheme 7). The angularly fused parent pyrido[1,2-*a*]benzimidazole **28** was also obtained from **24** following a similar two-step sequence (Scheme 7). The methodology was also extended to cyclic ketene dithioacetal **29** available from indanone, which produced the expected linearly and angularly fused

SCHEME 8



SCHEME 9



pentacyclic pyrido[1,2-*a*]benzimidazoles **30** and **31** in good yields on treatment with dianions **2A** and **3A**, respectively, under identical conditions (Scheme 8).

Finally, the versatility of this annulation methodology was evident from the synthesis of planar hexacyclic pyrido[1,2-*a*]benzimidazoles **33** and **34** which were obtained in good yields by cycloannulation of anions **2A** and **3A** with ketenedithioacetal **32** derived from acenaphthen-1-one (Scheme 9) under the described conditions. The angularly fused product **34** was subjected to acid-induced hydrolysis−decarboxylation to provide **35** in 62% yield.

Conclusion

In summary, we have demonstrated a highly efficient and regiospecific annulation protocol for a series of linearly 2,3- and angularly 1,2-substituted and annulated pyrido[1,2-*a*]benzimidazoles involving [3 + 3] cyclocondensation of the dianions derived from 2-methyl- (**2A**) and 2-cyanomethyl- (**3A**) benzimidazole with a variety of α-oxoketene dithioacetals via a highly regioselective 1,2-addition (with **2A**) or 1,4-addition−elimination (with **3A**) pathway (Scheme 2). Depending on the structures of acyclic and cyclic α-oxoketene dithioacetals the methodology allows access to a wide range of hitherto unknown novel planar polycyclic (tetra, penta, hexa) linearly or angularly fused pyrido[1,2-*a*]benzimidazole ring systems, some of which may prove useful as potential DNA binders. A few of these newly synthesized pyrido[1,2-*a*]-benzimidazoles display fluorescent properties which are under investigation. We are currently studying the generality of this cycloannulation process for regiospecific construction of other bridged azaindoles such as pyrido-[1,2-*a*]imidazoles and pyrido[1,2-*a*]pyrroles which will be published later.

Experimental Section

General. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ and TMS was used as an internal reference. Melting points are uncorrected. Chromatographic purification was done by column chromatography, using 60−120 mesh silica gel obtained from Acme Synthetic Chemicals. All reactions were monitored by TLC on glass plates coated with silica gel (Acme) containing 13% calcium sulfate as binder and visualization was effected with short-wavelength UV light (254 nm) or acidic $KmnO_4$ solution. THF was dried over sodium wire with benzophenone and distilled.

The chemically pure diisopropylamine, ethanol, H_2SO_4, AcOH, ammonia solution, and dioxane were purchased from standard firms and further dried whenever needed by standard procedures.

All the ketones, i.e., acetophenone, propiophenone, acetone, ethylmethyl ketone, cyclohexanone, and cyclopentanone, required for the preparation of α-oxoketene dithioacetals were purchased from the standard firms whereas the α-tetralone,[18a] indan-1-one,[18b] acenaphthene-1-one,[18c] and 2-methyl-[18d] and 2-cyanomethylbenzimidazoles[18e] were prepared according to the reported procedures. All the known α-oxoketene dithioacetals **4a**−**d**, **13a**,**b**, **20**, and **29** and the unknown **32** were prepared from the appropriate ketones according to our earlier reported method.[18f]

3-(Bismethylthio)acenaphthene-1-one (32). Yield 72%; yellow crystals (chloroform−hexane); mp 78 °C; R_f 0.6 (9:1 hexanes−EtOAc); IR (KBr) 1676, 1506, 1420, 1362 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H, SCH_3), 2.63 (s, 3H, SCH_3), 7.60 (t, J = 7.36 Hz, 1H, ArH), 7.66 (t, J = 7.56 Hz, 1H, ArH), 7.76 (d, J = 8.32 Hz, 1H, ArH), 8.00 (dd, J = 8.04, 6.84 Hz, 2H, ArH), 8.36 (d, J = 7.08 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 19.4, 121.0, 121.3, 124.5, 127.6, 128.2, 130.3, 130.8, 133.4, 135.0, 137.1, 156.2, 189.4: MS (*m*/*z*, %) 272 (M$^+$, 100), 255 (14.9). Anal. Calcd for $C_{15}H_{12}OS_2$ (272.40): C, 66.14; H, 4.40. Found: C, 66.43; H, 4.21.

General Procedure for the Addition of Dianion 2A to α-Oxoketene Dithioacetals. To a stirring solution of 2-methylbenzimidazole (1.0 g, 8 mmol) in THF (30 mL) at 0 °C was added BuLi (15%, 7.5 mL, 20 mmol) under nitrogen atmosphere. The reaction mixture immediately developed a yellowish brown color, indicating the formation of monoanion, that changed to a curdy white suspension within 5 min showing the formation of dianion. After further stirring for 1 h, a solution of appropriate ketene dithioacetal (8 mmol) in THF (15 mL) was added at 0 °C and the reaction mixture was brought to room temperature and left overnight under stirring (monitored by TLC). It was then poured into a cold saturated NH_4Cl solution (50 mL) and extracted with $CHCl_3$ (3 × 50 mL), and the combined organic layer was washed with water (3 × 50 mL), dried (Na_2SO_4), and evaporated to give the corresponding carbinols in almost quantitative yields which were pure enough to be characterized by ^{1}H and ^{13}C NMR spectra and used as such for further transformation. Analytically pure samples of few carbinols were obtained by column chromatography over silica gel with hexanes−EtOAc (8:2) as eluent.

2-[4-Bis(methylthio)-2-hydroxy-2-phenylbut-3-ene-1-yl]benzimidazole (7a). Yield 94% (2.67 g); brown crystals (chloform−hexane); mp 134 °C; R_f 0.3 (9:1 hexanes−EtOAc); IR (KBr) 3355, 3161, 2920, 1674, 1582 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.00 (s, 3H, SCH_3), 2.12 (s, 3H, SCH_3), 3.37 (d, J = 14 Hz, 1H, CH), 3.50 (d, J = 15.2 Hz, 1H CH), 6.38 (s, 1H, ArH), 7.19−7.23 (m, 3H, ArH), 7.25−7.32 (m, 2H, ArH), 7.46 (d, J = 8.0 Hz, 2H, ArH), 7.51−7.53 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCI_3$) δ 16.8, 16.8, 43.9, 114.7, 115.5, 119.0, 122.2, 124.6, 125.2 126.0, 127.2, 128.3, 128.6, 135.3, 136.6, 146.6, 151.2; MS (*m*/*z*, %) 290 (100), 275 (90).

General Procedure for H_3PO_4-Induced Cyclization of the Carbinols 7a−d: Synthesis of 2,3-Substituted (5a−c) and 2,3-Annulated Pyrido[1,2-*a*]benzimidazoles (14a,b, 21, 30, and 33). The crude carbinols (∼8 mmol) obtained from the earlier reactions were dissolved in H_3PO_4 (85%, 20 mL) and the solution was heated at 90−100 °C for 4−5 h (monitored by TLC). The reaction mixture was brought to room temparature, poured into ice-cold water (50 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined organic extracts were washed with water (3 × 50 mL), dried (Na_2SO_4), and evaporated to give crude products which were purified by column chromatography over silica gel with hexanes−EtOAc (8:2) as eluent.

1-(Methylthio)-3-phenylpyrido[1,2-*a*]benzimidazole (5a). Yield 70% (1.62 g); yellow crystals (chloroform−hexane); mp 146 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3173, 3057, 2985, 1991, 1673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70 (s, 3H, SCH_3), 6.92 (d, J = 1.4 Hz, 1H, ArH), 7.34 (dd, J = 3.6, 4.4 Hz, 1H, ArH), 7.41−7.54 (m, 4H, ArH), 7.69 (d, J = 8.2 Hz, 2H, ArH), 7.73 (dd, J = 0.48, 0.72 Hz, 1H, ArH), 7.94 (d, J = 7.5 Hz, 1H, ArH), 8.67 (d, J = 8.6 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.7, 109.7, 111.3, 115.8, 119.3, 120.7, 125.3, 126.9, 128.8, 129.1, 129.9, 138.2, 140.3, 141.4,145.4, 150.0; MS (*m*/*z*, %) 290 (M$^+$, 100), 275 (45.6). Anal. Calcd for $C_{18}H_{14}N_2S$ (290.38): C, 74.45; H, 4.86; N, 9.65. Found: C, 74.28; H, 4.98; N, 9.44.

3-Methyl-1-(methylthio)pyrido[1,2-*a*]benzimidazole (5b). Yield 70% (1.27 g); white crystals (chloroform−hexane); mp 130 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3528, 3445, 1642, 1488, 1451 1323 cm^{-1}; ^{1}H NMR (400 MHz, $CDC1_3$) δ 2.41 (s, 3H, CH_3), 2.63 (s, 3H, SCH_3), 6.46 (s, 1H, ArH), 7.28 (s, 1H, ArH), 7.29 (t, J = 8.3 Hz, 1H, ArH), 7.49 (t, J = 8.0 Hz, 1H, ArH), 7.89 (d, J = 8.0 Hz, 1H, ArH), 8.62 (d, J = 8.5 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 21.5, 112.3, 112.9, 115.7, 119.1, 120.2, 125.1, 130.0, 139. 5, 139.9, 145.0, 150.1; MS (*m*/*z*, %) 228 (M$^+$, 5.6), 214 (100). Anal. Calcd for $C_{13}H_{12}N_2S$ (228.31): C, 68.38; H, 5.26; N, 12.26. Found: C, 68.24; H, 5.42; N, 12.59.

12-(Methylthio)-1,2,3,4-tetrahydrobenzimidazo[1,2-*b*]-isoquinoline (14a). Yield 68% (1.45 g); yellow crystals (chloroform−hexane); mp 115 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3040, 3005, 2937, 2855, 1776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72−1.79 (m, 4H, CH_2), 2.29 (s, 3H, SCH_3), 2.81 (t, J = 6.3 Hz, 2H, CH_2), 3.02 (t, J = 6.3 Hz, 2H,CH_2), 7.19−7.23 (m, 1H, ArH), 7.35 (s, 1H, ArH), 7.40 (t, J = 7.8 Hz, 1H, ArH), 7.80 (d, J = 7.8 Hz, 1H, ArH), 8.92 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 22.0, 23.0, 27.0, 30.2, 116.3, 119.1, 120.4, 124.9, 128.7, 130.2, 132.7, 141.7, 144.9, 148.8, 152.7; MS (*m*/*z*, %) 268 (M$^+$, 100), 253 (25.9). Anal. Calcd for $C_{16}H_{16}N_2S$ (268.38): C, 71.60; H, 6.01; N, 10.43. Found: C, 71.48; H, 6.13; N, 10.40.

5,6-Dihydro-7-(methylthio)benzimidazo[1,2-*b*]benzo[*f*]-isoquinoline (21). Yield 72% (1.82 g); bright yellow crystals (chloroform−hexane); mp 161 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3780, 3687, 2833, 1441 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H, SCH_3), 2.94 (t, J = 7.0 Hz, 2H, CH_2), 3.35 (t, J = 6.6 Hz, 2H, CH_2), 7.26−7.38 (m, 4H, ArH), 7.50 (dd, J = 7.32, 7.08 Hz, 1H, ArH), 7.87 (d, J = 7.5 Hz, 1H, ArH), 7.93 (d, J = 8.28 Hz, 1H, ArH), 8.05 (s, 1H, ArH), 9.04 (d, J = 8.56 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 26.2, 29.1, 112.4, 116.3, 119.5, 121.0, 124.9, 125.1, 127.4, 128.2, 128.4, 129.2, 130.6, 132.2, 132.5, 136.9, 138.2, 145.4, 149.3; MS (*m*/*z*, %) 316 (M$^+$, 100), 301 (15.28). Anal. Calcd for $C_{20}H_{16}N_2S$ (316.42): C, 75.91; H, 5.09; N, 8.85. Found: C, 75.83; H, 5.05; N, 8.73.

14-(Methylthio)benzimidazo[1,2-*f*]fluoranthene (33). Yield 78% (2.11 g); yellow crystals (chloroform−hexane) mp 192 °C; R_f 0.37 (8:2 hexanes−EtOAc); IR (KBr) 3046, 2916, 1746, 1646, 1595, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H, SCH_3), 7.27 (t, J = 7.3 Hz, 1H, ArH), 7.42 (t, J = 7.3 Hz,

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1H, ArH), 7.47−7.57 (m, 2H, ArH), 7.67 (d, J = 8.08 Hz, 1H, ArH), 7.71 (d, J = 8.08 Hz, 1H, ArH), 7.76 (dd, J = 8.28, 10.96 Hz, 2H, ArH), 7.88 (s, 1H, ArH), 8.51 (d, J = 7.5 Hz, 1H, ArH), 8.93 (d, J = 8.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 109.4, 116.2, 119.6, 119.8, 121.5, 122.8, 125.1, 126.1 127.4, 127.9, 128.4, 130.3, 130.4, 130.8, 131.0, 133.7, 134.4, 136.3, 141.5, 145.5, 149.5; MS (m/z, %) 338 (M^+, 65), 323 (72). Anal. Calcd for $C_{22}H_{14}N_2S$ (338.43): C, 78.08; H, 4.16; N, 8.27. Found: C, 78.05; H, 4.22; N, 8.39.

General Procedure for the Cyclization of Dianion 3A with α-Oxoketene Dithioacetals: Synthesis of 1,2-Substituted and Annulated Pyrido[1,2-*a*]benzimidazole (6a−d, 16a,b, 23, 31, and 34). To a stirring solution of LDA [8.0 mmol, prepared from diisopropylamine (2.5 mL, 8.0 mmol), BuLi (15%, 6 mL, 8.0 mmol) in 10 mL of THF] at 0 °C was added a solution of 2-cyanomethylbenzimidazole (0.5 g, 3.2 mmol) in THF (10 mL) when the reaction mixture indicated the formation of dianion **3A** as a deep red solution. It was further stirred for 1 h at 0 °C followed by addition of a solution of oxoketene dithioacetal (3.2 mmol) in THF (15 mL). The reaction mixture was left for overnight stirring and then quenched with cold saturated NH_4Cl (50 mL) followed by extraction with $CHCl_3$ (3 × 50 mL). The combined organic extracts were washed with water (3 × 50 mL), dried (Na_2SO_4), and evaporated to give crude pyrido[1,2-*a*]benzimidazoles as solids which were further purified by passing through a silica gel column with hexanes−EtOAc (8:2) as eluent.

4-Cyano-3-(methylthio)-1-phenylpyrido[1,2-*a*]benzimidazole (6a). Yield 76% (0.76 g); yellow crystals (chloroform−hexane); mp 248 °C; R_f 0.25 (8:2 hexanes−EtOAc); IR (KBr) 3613, 3590, 2214, 1588 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H, SCH_3), 6.44 (d, J = 8.5 Hz, 1H, ArH), 6.58 (s, 1H, ArH), 6.96 (dd, J = 8.28, 1.2 Hz, 1H, ArH), 7.40 (t, J = 8.3 Hz, 1H, ArH), 7.58−7.60 (m, 2H, ArH), 7.63−7.73 (m, 3H, ArH), 7.89 (d, J = 8.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 95.2, 108.2, 113.8, 114.2, 120.0, 121.3, 126.0, 126.2, 128.4, 129.3, 131.0, 132.7, 144.1, 145.1, 147.3, 151.4; MS (m/z, %) 315 (M^+, 100). Anal. Calcd for $C_{19}H_{13}N_3S$ (315.30): C, 72.37; H, 4.15; N, 13.32. Found: C, 72.13; H, 4.32; N, 13.55.

4-Cyano-1-methyl-3-(methylthio)pyrido[1,2-*a*]benzimidazole (6b). Yield 70% (0.56 g); yellow crystals (chloroform−hexane); mp 258 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3452, 2214, 1623, 1476, 1517 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (s, 3H, CH_3), 3.04 (s, 3H, SCH_3), 6.47 (s, 1H, ArH), 7.31 (t, J = 7.3 Hz, 1H, ArH), 7.52 (t, J = 7.5 Hz, 1H, ArH), 7.95 (d, J = 8.2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 21.7, 105.7, 107.1, 113.9, 114.3, 120.0, 121.8, 126.2, 129.8, 142.8, 145.1, 148.0, 151.6; MS (m/z, %) 253 (M^+, 100), 207 (2.3). Anal. Calcd for $C_{14}H_{11}N_3S$ (253.33): C, 66.37; H, 4.40; N, 16.58. Found: C, 66.13; H, 4.33; N, 16.65.

6-Cyano-5-(methylthio)-1,2,3,4-tetrahydrobenzimidazo-[1,2-*a*]quinoline (16a). Yield 66% (0.61 g); yellow crystals (chloroform−hexane); mp 235 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3710, 2932, 2360, 2337, 2218, 1550 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92−1.96 (m, 2H, CH_2), 2.04−2.10 (m, 2H, CH_2), 2.83 (s, 3H, SCH_3), 2.87 (t, J = 6.1 Hz, 2H, CH_2), 3.43 (t, J = 6.3 Hz, 2H, CH_2), 7.31 (t, J = 8.0 Hz, 1H, ArH), 7.52 (t, J = 7.8 Hz, 1H, ArH), 7.99 (d, J = 8.3 Hz, 1H, ArH), 8.05 (d, J = 8.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8, 21.6, 26.3, 29.0, 125.8, 107.7, 109.8, 115.3, 119.6, 120.3, 120.3, 121.5, 125.8, 125.8, 141.3, 145.0, 145.0; MS (m/z %) 293 (M^+, 100), 278 (11.7). Anal. Calcd for $C_{17}H_{15}N_3S$ (293.39): C, 69.59; H, 5.15; N, 14.32. Found: C, 69.75; H, 5.19; N, 14.13.

8-Cyano-5,6-dihydro-7-(methylthio)benzimidazo[1,2-*a*]-benzo[*h*]quinoline (23). Yield 76% (0.83 g); orange crystals (cloroform−hexane); mp 300 °C; R_f 0.32 (8:2 hexanes−EtOAc); IR (KBr) 3647, 3611, 3043, 2223, 1480, 1443 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (t, J = 6.4 Hz, 1H, CH_2), 2.81 (s, 3H, SCH_3), 2.96 (t, J = 6.4 Hz, 2H, CH_2), 3.47 (d, J = 15.8 Hz, 1H, CH_2), 7.15−7.19 (m, 1H, ArH), 7.29−7.37 (m, 1H, ArH), 7.43−7.52 (m, 3H, ArH), 7.73 (d, J = 8.5 Hz, 1H, ArH), 7.91 (d, J = 7.8 Hz, 1H, ArH), 8.03 (d, J = 8.3 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 25.5, 28.5, 115.0, 115.5, 120.5, 120.8, 125.1, 125.4, 125.9, 126.2, 127.1, 128.0, 128.0, 129.6, 131.2, 138.5, 139.2 145.2, 148.2, 148.6; MS (m/z, %) 341 (M^+, 100), 326 (11.65). Anal. Calcd for $C_{21}H_{15}N_3S$ (341.43): C, 73.87; H, 4.42; N, 12.30. Found: C, 73.74; H, 4.50; N, 12.53.

8-Cyano-7-(methylthio)benzimidazo[1,2-*e*]fluoranthene (34). Yield 75% (0.87 g); red crystals (chloroform−hexane); mp 165 °C; R_f 0.35 (8:2 hexanes−EtOAc); IR (KBr) 3233, 3055, 2218, 1556 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82 (s, 3H, SCH_3), 7.41 (dd, J = 7.0, 8.2 Hz, 1H, ArH), 7.53−7.60 (m, 2H, ArH), 7.65 (t, J = 7.3 Hz, 1H, ArH), 7.80 (d, J = 8.2 Hz, 1H, ArH), 7.98 (d, J = 8.0 Hz, 1H, ArH), 8.03 (d, J = 7.8 Hz, 1H, ArH), 8.50 (d, J = 8.5 Hz, 1H, ArH), 8.58 (d, J = 7.8 Hz, 1H, ArH), 8.64 (d, J = 7.3 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.7, 113.8, 114.9, 115.2, 120.8, 121.8, 123.1, 126.0, 126.5, 126.9, 127.0, 127.5, 127.9, 128.5, 129.0, 129.4, 131.9, 132.4, 135.6, 140.4, 145.0, 145.6, 148.4; MS (m/z, %) 364 (M^+, 100). Anal. Calcd for $C_{23}H_{13}N_3S$ (363.44): C, 76.01; H, 3.60; N, 11.56. Found: C, 76.11; H, 3.51; N, 11.33.

General Procedure for Raney-Ni Dethiomethylation−Reduction of Pyrido[1,2-*a*]benzimidazoles 5a,b, 6a, 14a, 16a, and 21. To an ethanolic solution (20 mL) of appropriate pyrido[1,2-*a*]benzimidazole (5 mmol) was added Raney-Ni (W2) (∼3 g) and the suspension was refluxed with stirring for 6−7 h (monitored by TLC). It was then filtered through a sintered glass funneland washed with hot ethanol and the filtrate was concentrated to afford viscous residue, which was purified by column chromatography over silica gel with hexanes−ethyl acetate (8:2) as eluent.

3-Phenylpyrido[1,2-*a*]benzimidazole (8a). Yield 68% (0.83 g); yellow crystals (chloroform−hexane); mp 175 °C; R_f 0.25 (8:2 hexanes−EtOAc); IR (KBr) 3432, 3240, 3023, 1680, 1643 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 7.08, 0.96, Hz, 1H, ArH), 7.30 (t, 6.8 Hz, 1H, ArH), 7.32(t, J = 7.8 Hz, 1H, ArH), 7.39 (d, J = 7.3 Hz, 1H, ArH), 7.43−7.50 (m, 3H, ArH), 7.65 (d, J = 7.5 Hz, 1H, ArH), 7.90 (s, 1H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 7.94 (d, J = 8.0 Hz, 1H, ArH), 8.45 (d, J = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.3, 110.5, 114.2, 119.6, 121.1, 125.0, 125.8, 126.7, 126.9, 126.9, 128.9, 129.1, 138.2, 142.4, 148.8; MS (m/z, %) 244 (M^+, 100). Anal. Calcd for $C_{17}H_{12}N_2$ (244.36): C, 83.58; H, 4.95; N, 11.46. Found: C, 83.44; H, 4.94; N, 11.58.

4-Methyl-l-phenylpyrido[1,2-*a*]benzimidazole (11a). Yield 60% (0.77 g); yellow low melting solid; R_f 0.25 (8:2 hexanes−EtOAc); IR (CCl_4) 3038, 2921, 2854, 1740, 1696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H, CH_3), 6.50 (d, J = 8.5 Hz, 1H, ArH), 6.53 (d, J = 6.8 Hz, 1H, ArH), 6.88 (dd, J = 7.5, 8.28 Hz, 1H, ArH), 7.21 (d, J = 6.8 Hz, 1H, ArH), 7.28−7.34 (m, 1H, ArH), 7.44−7.54 (m, 5H, ArH), 7.89 (dd, J = 0.52, 8.3 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 112.1, 114.6, 119.6, 120.3, 124.9, 125.9, 126.2, 127.7, 129.1, 129.6, 129.8, 134.5, 138.9, 144.3, 149.7; MS (m/z, %) 258 (M^+, 100), 243 (15). Anal. Calcd for $C_{18}H_{14}N_2$ (258.32): C, 83.69; H, 5.46; N, 10.84. Found: C, 83.76; H, 5.48; N, 10.62.

1,2,3,4-Tetrahydrobenzimidazo[1,2-*b*]isoquinoline (15a). Yield 67% (0.74 g); yellow crystals (chloroform−hexane); mp 152 °C; R_f 0.2 (8:2 hexanes−EtOAc); IR (KBr) 3207, 3042, 2940, 1700, 1600 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84 (s, 4H, CH_2), 2.82 (s, 2H, CH_2), 2.90 (s, 2H, CH_2), 7.26 (t, J = 7.8 Hz, 1H, ArH), 7.34 (s, 1H, ArH), 7.46 (t, J = 7.3 Hz, 1H, ArH), 7.78 (d, J = 8 Hz, 1H, ArH), 7.86(d, J = 8.0 Hz, 1H, ArH), 8.11(s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 22.6, 26.3, 29.5, 110.1, 114.7, 119.2, 119.9, 121.3, 121.9, 125.1, 128.3, 142.3, 144.6, 148.4; MS (m/z, %) 222 (M^+, 100%). Anal. Calcd for $C_{15}H_{14}N_2$ (222.29): C, 81.05; H, 6.34; N, 12.60. Found: C, 81.14; H, 6.30; N, 12.53.

6-Methyl-1,2,3,4-tetrahydrobenzimidazo[1,2-*a*]quinoline (17a). Yield 54% (0.63 g); yellow low melting solid; R_f 0.2 (8:2 hexanes−EtOAc); IR (CCl_4) 2945, 2865, 2739, 1682, 1642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80−1.86 (m, 2H, CH_2), 1.98−2.04 (m, 2H, CH_2), 2.67 (s, 3H, CH_3), 2.75 (t, J = 6.1 Hz,

2H, CH_2), 3.35 (t, J = 6.3 Hz, 2H, CH_2), 7.08 (s, 1H, ArH), 7.25 (t, J = 8.2 Hz, 1H, ArH), 7.46 (dd, J = 7.3, 8.0 Hz, 1H, ArH), 8.03 (d, J = 8.5 Hz, 1H, ArH), 8.09 (d, J = 8.5 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 21.5, 22.3, 27.8, 28.0, 115.5, 118.4, 121.4, 122.9, 125.7, 128.6, 129.6, 133.0, 135.6, 143.1, 153.7; MS (*m*/*z*, %) 236 (M^+, 100), 221 (35). Anal. Calcd for $C_{16}H_{16}N_2$ (236.31): C, 81.31; H, 6.82; N, 11.85. Found: C, 81.40; H, 6.70; N, 11.67.

5,6-Dihydrobenzimidazo[1,2-*b*]benzo[*f*]isoquinoline (22). Yield 66% (0.89 g); yellow crystals (chloroform−hexane); mp 133−134 °C; R_f 0.2 (8:2 hexanes−EtOAc); IR (KBr) 3417, 3053, 2852, 1698, 1627 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (s, 2H, CH_2), 2.85 (s, 2H, CH_2), 7.07 (t, J = 8.0 Hz, 1H, ArH), 7.23−7.26 (m, 2H, ArH), 7.29−7.32 (m, 1H, ArH), 7.32 (s, 1H, ArH), 7.39 (t, J = 7.3 Hz, 1H, ArH), 7.55 (d, J = 9.2 Hz, 1H, ArH), 7.80 (d, J = 8.5 Hz, 1H, ArH), 7.87 (s, 1H, ArH), 7.87 (t, J = 6.8 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 28.8, 115.7, 116.8, 119.4, 119.7, 124.3, 124.5, 125.1, 125.7, 127.9, 128.1, 129.3, 129.8, 130.9, 132.4, 135.3, 138.2, 144.5; MS (*m*/*z*, %) 270 (M^+, 71.2). Anal. Calcd for $C_{19}H_{14}N_2$ (270.33): C, 84.41; H, 5.21; N, 10.36. Found: C, 84.28; H, 5.34; N, 10.49.

General Procedure for Acid-Induced Hydrolysis−Decarboxylation of Pyrido[1,2-*a*]benzimidazoles 6a, 16a, 23, and 34: Synthesis of 10a, 18a, 24, and 35. A suspension of cyano-substituted pyrido[1,2-*a*]benzimidazole (5 mmol) in water (5 mL), AcOH (5 mL), and concentrated H_2SO_4 (5 mL) was refluxed with stirring at 180 °C for 8 h (monitored by TLC). It was then cooled, poured into ice-cold water (25 mL), neutralized with saturated $NaHCO_3$ solution, and extracted with $CHCl_3$ (3 × 50 mL). The combined organic layer was dried (Na_2SO_4) and evaporated to give crude viscous residue that was purified by column chromatography over silica gel with hexanes−EtOAc (8:2) as eluent to give the pure product.

3-(Methylthio)-1-phenylpyrido[1,2-*a*]benzimidazole (10a). Yield 62% (0.90 g); light yellow crystals (chloroform−hexane); mp 170 °C; R_f 0.2 (8:2 hexanes−EtOAC); IR (KBr) 3451, 2982, 2924, 1693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (s, 3H, SCH_3), 6.47 (d, J = 8.5 Hz, 1H, ArH), 6.53 (d, J = 1.4 Hz, 1H, ArH), 6.92 (t, J = 8.2 Hz, 1H, ArH), 7.37 (t, J = 7.5 Hz, 1H, ArH), 7.40 (d, J = 1.9 Hz, 1H, ArH), 7.52−7.66 (m, 5H, ArH), 7.83 (d, J = 8.28 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 108.1, 111.8,111.9, 114.1, 118.9, 120.2, 125.1, 128.9, 129.1, 130.2, 133.6, 139.9, 143.3, 144.5, 149.6; MS (*m*/*z*, %) 290 (M^+, 100). Anal. Calcd for $C_{18}H_{14}N_2S$ (290.38): C, 74.45; H, 4.85; N, 9.64. Found: C, 74.32; H, 4.98; N, 9.68.

5-(Methylthio)-1,2,3,4-tetrahydrobenzimidazo[1,2-*a*]-quinoline (18a). Yield 68% (0.91 g); yellow crystals (chloroform−hexane); mp 168 °C; R_f 0.2 (8:2 hexanes−EtOAc); IR (KBr) 3438, 3265, 2856, 1993, 1735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88−1.94 (m, 2H, CH_2), 2.01−2.07 (m, 2H, CH_2), 2.54 (s, 3H, SCH_3), 2.71 (t, J = 6.12 Hz, 2H, CH_2), 3.38 (t, J = 6.12 Hz, 2H, CH_2), 7.22 (t, J = 7.56 Hz, 1H, ArH), 7.26 (s, 1H, ArH), 7.45 (t, J = 7.32 Hz, 1H, ArH), 7.86 (d, J = 8.28 Hz, 1H, ArH), 8.05 (d, J = 8.28 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 21.6, 21.9, 24.8, 28.2, 106.4, 115.0, 117.1, 119.0, 119.8, 124.6, 129.8, 136.5, 145.0, 148.7, 154.2; MS (*m*/*z*; %) 268 (M^+, 7.0), 266 (75). Anal. Calcd for $C_{16}H_{16}N_2S$ (268.37): C, 71.60; H, 6.01; N, 10.44. Found: C, 71.41, H, 6.12; N, 10.52.

5,6-Dihydro-7-(methylthio)benzimidazo[1,2-*a*]benzo-[*h*]quinoline (24). Yield 55% (0.87 g); yellow crystals (chloroform−hexane); mp 225 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (KBr) 3552, 3061, 2360, 1708, 1614, 1570 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23−2.40 (m, 2H, CH_2), 2.52 (s, 3H, SCH_3), 2.85 (s, 2H, CH_2), 7.02 (t, J = 8.0 Hz, 1H, ArH), 7.27 (s, 1H, ArH), 7.30−7.38 (m, 4H, ArH), 7.67 (d, J = 8.3 Hz, 1H, ArH), 7.80 (d, J = 8.5 Hz, 1H, ArH), 7.82 (d, J = 7.8 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 24.3, 28.5, 108.2, 108.3, 115.5, 115.9, 119.2, 123.0, 124.8, 125.0, 125.6, 127.8, 129.5, 131.4, 134.3, 136.3, 138.0, 143.9, 144.4; MS (*m*/*z*, %) 316 (M^+, 16.3). Anal. Calcd for $C_{20}H_{16}N_2S$ (316.42): C, 75.91; H, 5.09; N, 8.85. Found: C, 75.73; H, 5.16; N, 8.93.

Reductive Dethiomethylation of 10a, 18a, and 24 with Raney-Ni. Reductive dethiomethylation were carried out as reported earlier.

1-Phenylpyrido[1,2-*a*]benzimidazole (12a). Yield 58% (1.09 g); yellow low melting solid; R_f 0.2 (8:2 hexanes−EtOAc); IR (CCl_4) 3056, 2927, 1686, 1642, 1599 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (d, J = 8.5 Hz, 1H, ArH), 6.59 (d, J = 6.8 Hz, 1H, ArH), 7.33 (dd, J = 7.08, 8.04 Hz, 1H, ArH), 7.39 (dd, J = 6.84, 9.28 Hz, 1H, ArH), 7.45−7.58 (m, 5H, ArH), 7.64 (d, J = 9.0 Hz, 1H, ArH), 7.82 (d, J = 8.3 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.1, 114.1, 116.7, 119.5, 120.3, 125.1, 128.0, 128.9, 129.0, 129.2, 130.0, 134.3, 141.2, 144.6, 149.3; MS (*m*/*z*, %) 244 (M^+, 98), 243 (100). Anal. Calcd for $C_{17}H_{12}N_2$ (244.30): C, 83.58; H, 4.95; N, 11.46. Found: C, 83.75; H, 4.73; N, 11.38.

1,2,3,4-Tetrahydrobenzimidazo[1,2-*a*]quinoline (19a). Yield 62% (0.68 g); yellow low melting solid; R_f 0.2 (8:2 hexanes−EtOAc); IR (CCl_4) 3052, 2935, 2860, 2308, 1734 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.78−1.84 (m, 2H, CH_2), 1.96−2.02 (m, 2H, CH_2), 2.74 (t, J = 6.1 Hz, 2H, CH_2), 3.32 (t, J = 6.3 Hz, 2H, CH_2), 7.13 (d, J = 9.2 Hz, 1H, ArH), 7.20 (t, J = 8.0 Hz, 1H, ArH), 7.41 (t, J = 7.3 Hz, 1H, ArH), 7.48 (d, J = 9.2 Hz, 1H, ArH), 7.85 (d, J = 8.1 Hz, 1H, ArH), 8.06 (d, J = 8.56 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.3, 28.0, 29.6, 114.4, 115.3, 119.2, 119.3, 120.4, 124.8, 129.8,132.8, 137.5, 144.1, 148.4; MS (*m*/*z*; %) 222 (M^+, 100), 194 (85). Anal. Calcd for $C_{15}H_{14}N_2$ (222.28): C, 81.04; H, 6.34; N, 12.60. Found: C, 81.13; H, 6.22; N, 12.53.

5,6-Dihydropyridobenzimidazo[1,2-*a*]benzo[*h*]quinoline (27). Yield 58% (0.48 g); brown crystals (chloroform−hexane); mp 162 °C; R_f 0.4 (8:2 hexanes−EtOAc); IR (KBr) 2960, 2930, 2860, 2359, 1728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80 (t, J = 8.0 Hz, 2H, CH_2), 2.99 (t, J = 8.0 Hz, 2H, CH_2), 7.22−7.28 (m, 1H, ArH), 7.47 (t, J = 8.8 Hz, 1H, ArH), 7.60−7.68 (m, 3H, ArH), 7.82 (d, J = 8.5 Hz, 2H, ArH), 7.92 (d, J = 8.5 Hz, 1H, ArH), 8.23 (d, J = 7.3 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 27.7, 105.3, 109.5, 116.7, 120.4, 120.5, 121.2, 124.4, 127.5, 127.9, 128.4, 128.7, 128.7, 130.3, 131.0, 133.7, 135.9, 152.2; MS (*m*/*z*, %) 270 (M^+, 100), 269 (80). Anal. Calcd for $C_{19}H_{14}N_2$ (270.33): C, 84.41; H, 5.21; N, 10.36. Found: C, 84.27; H, 5.34; N, 10.51.

General Procedure for Dehydrogenation of 21 and 27 with DDQ. To a solution of either **21** or **27** (0.25 g, 0.8 mmol) in dry dioxane (25 mL) was added DDQ (0.5 g, 2.4 mmol) and the reaction mixture was stirred with refluxing for 5 h (monitored by TLC). The dioxan was removed under reduced pressure and the residue was dissolved in $CHCl_3$ (50 mL). The $CHCl_3$ solution was washed with water (3 × 50 mL), dried (Na_2SO_4), and evaporated to give crude residue that was purified by column chromatography over silica gel with hexanes−EtOAc (7:3) as eluent to give pure **25** and **28**.

7-(Methylthio)benzimidazo[1,2-*b*]benzo[*f*]isoquinoline (25). Yield 48% (0.41 g); yellow low melting solid; R_f 0.4 (8:2 hexanes−EtOAc); IR (CCl_4) 3047, 2919, 2849, 1733, 1589 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77 (s, 3H, SCH_3), 7.56 (t, J = 7.5 Hz, 1H, ArH), 7.66−7.70 (m, 2H, ArH), 7.79 (t, J = 6.8 Hz, 1H, ArH), 7.97 (d, J = 8.0 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 8.03 (d, J = 8.0 Hz, 1H, ArH), 8.11 (d, J = 7.5 Hz, 1H, ArH), 8.41 (d, J = 6.8 Hz, 1H, ArH), 8.67 (d, J = 8.0 Hz, 1H, ArH), 8.73 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8, 118.8, 121.1, 124.8, 126.1, 126.3, 126.4, 126.6, 126.7, 127.7, 128.4, 129.1, 129.6, 130.2, 133.6, 134.8, 136.0, 137.0, 137.9, 140.9; MS (*m*/*z*, %) 314 (M^+, 100). Anal. Calcd for $C_{20}H_{14}N_2S$ (314.42): C, 75.91; H, 5.06; N, 8.85. Found: C, 75.82; H, 5.15; N, 8.72.

Benzimidazo[1,2-*a*]benzo[*h*]quinoline (28). Yield 55% (0.56 g); yellow crystals; mp 151 °C; R_f 0.5 (8:2 hexanes−EtOAc); IR (CCl_4) 3056, 2923, 2854, 1641, 1598 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.27 (m, 1H, ArH), 7.49 (t, J = 6.3 Hz, 1H, ArH), 7.63−7.70 (m, 4H, ArH), 7.85 (d, J = 8.8 Hz,

2H, ArH), 7.95 (d, J = 8.8 Hz, 2H, ArH), 8.27 (d, J = 8.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.1, 109.6, 116.8, 120.3, 120.5, 120.6, 120.6, 121.3, 127.5, 127.9, 128.4, 128.6, 128.6, 128.7, 128.8, 130.4, 131.1, 133.8, 135.1; MS (m/z, %) 268 (M^+, 100). Anal. Calcd for $C_{19}H_{12}N_2$ (268.38): C, 71.60; H, 6.01; N, 10.43. Found: C, 71.58; H, 6.11; N, 10.31.

Reductive Dethiomethylation of 25 to 26 with Raney-Ni. Reductive dethiomethylation was carried out as reported earlier.

Benzimidazo[1,2-*b*]benzo[*f*]isoquinoline (26). Yield 53% (0.43 g); yellow crystals (chloroform−hexane); mp 155 °C; R_f 0.3 (8:2 hexanes−EtOAc); IR (CCl_4) 3048, 2849, 2681, 1734, 1508 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 6.3 Hz, 1H, ArH), 7.39−7.48 (m, 4H, ArH), 7.55 (t, J = 7.0 Hz, 1H, ArH), 7.67 (d, J = 7.0 Hz, 2H, ArH), 7.93 (t, J = 7.8 Hz, 2H, ArH), 8.11 (s, 1H, ArH), 8.61 (d, J = 6.8 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 105.4, 109.1, 109.5, 116.8, 120.3, 120.5, 120.6, 121.3, 127.5, 127.9, 128.4, 128.6, 128.6, 128.7, 128.8, 130.4, 131.1, 131.1, 133.8; MS (m/z, %) 268 (M^+, 100). Anal. Calcd for $C_{19}H_{12}N_2$ (268.38): C, 71.60; H, 6.01; N, 10.43. Found: C, 71.67; H, 6.04; N, 10.31.

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Supporting Information Available: Characterization data of products **7b**, **7d**, **20A**, **5c**, **14b**, **30**, **6c**, **6d**, **16b**, **31**, **8b**, and **35** and **NOE** for products **11a** and **17a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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