Synthesis and Autoxidation of New Tetracyclic 9*H*,10*H*-Indolizino[1,2-*b*]indole-1-ones

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The new tetracyclic 9*H*,10*H*-indolizino[1,2-*b*]indole-1-one derivatives (**7a**−**d**, **7ea**, **7eb**) have been synthesized by modified Fischer indole synthesis from the enol ether of 2,5-dihydroxy-7-methyl-6-cyano-indolizine (**3**) and arylhydrazines (**4a**−**g**). Attempted *N*-methylation of **7a**−**d** produced a series of autoxidized products including 10-hydroperoxy-1-methoxyindolizino[1,2-*b*]indole (**9a**−**d**) as the major product accompanied with methylperoxides (**10a**−**d** and **11a**−**d**) and 2-formyl-3-(pyridine-2-yl)indole (**12a**, **12c**) derivatives as the minor products. A plausible mechanism of the autoxidation is postulated based on the isolation of some intermediates. The reaction is thought to proceed through azaenolate/enamine intermediates following a novel type of autoxidation.

Introduction

Indoles are constituent of various important alkaloids. Due to their rich biological activity, continuous research on indole derivatives is still of great interest. Fischer indole synthesis[1] is widely used to construct indole derivatives by reaction of ketones with phenylhydrazines to form a hydrazone intermediate followed by rearrangement and elimination of ammonia under acidic conditions.[2,3] Various modifications of Fischer indole synthesis are available.[4,5] Besides Fischer indole synthesis, palladium catalyzed cyclization,[6] titanium induced synthesis[7] and radical cyclization[8] are also available in the literature. It is known that indole undergoes oxidation by air and light (autoxidation) to form indoxyl which can further form dimer or trimer.[9] Indole also undergoes autoxidation by PtO_2 and the C_2-C_3 bond is subsequently cleaved to give the ring expanded product.[10] On the other hand, the C_2-ethyl group of 2,3-diethylindole was reported to afford 2-acetyl-3-ethylindole via autoxidation.[11]

Autoxidation is a slow atmospheric oxidation of a C−H bond to a C−OOH bond and occurs when the compound is allowed to stand in air and is catalyzed by light.[12] The autoxidized products usually are hydroperoxide derivatives, which can often be further transformed into alcohol, ketone/aldehyde derivatives, etc.[13] Autoxidation is a free radical process in which some bonds (such as tertiary, allylic, and benzylic) are found to be autoxidized faster than others.[14] Autoxidation of a ketone is sluggish in nature. However, when a ketone forms stable enol, the latter is found to be autoxidized to afford α-hydroperoxy ketone.[15] This finding was used for the synthesis of 17α-hydroxysteroid derivatives.[16] Oxygen itself (a diradical) is too unreactive to be the species that actually abstracts the hydrogen. However, a trace of free radical, which is produced by some initiating process, will react with oxygen to give the hydroperoxide. In some cases (in alkaline media), an allylic radical can also be generated by the oxidation of an allylic carbanion.[17]

Autoxidation of indole has also been well studied.[18] In the presence of air and light, indole is converted to indoxyl, which reacts further to give either indigo or trimer.[9] The latter is probably formed by way of leuco-indoxyl red and indoxyl red. Autoxidation of an indole derivative, tetrahydrocarbazole, has also been carefully investigated.[19] It is a free-radical process, initiated by abstraction of hydrogen from the nitrogen by molecular oxygen. The resulting mesomeric carbazole radical then combines with the hydroperoxy radical to give hydroperoxide. This peroxide is stable when dry but very unstable in polar solvents, presumably due to polarization of $N_1=C_2$ bond of indole, promoting the internal

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(1) Brown, R. K; *The Chemistry of Heterocyclic Compounds*; Houlihan, J. W., Ed.; Interscience: New York, 1972; pp 228−558.
(2) Fischer, E.; Hess, O. *Chem. Ber.* **1884**, *17*, 559−568.
(3) Robinson, B. *The Fischer Indole Synthesis*; John Wiley and Sons: Chichester, 1982.
(4) Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 10251−10263.
(5) Gassman, P. G.; van Bergen, T. J.; Gilbert, D. P.; Cue, B. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 5495−5508.
(6) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652−7662.
(7) Furstner, A.; Jumbam, D. J. *Tetrahedron* **1992**, *48*, 5991−6010.
(8) Tokuyama, H.; Yamashita, T.; Reding, M. T.; Kaburagi, Y.; Fukuyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 3791−3792.
(9) Oddo, B. *Gazz. Chim. Ital.* **1920**, *50*, 268−275.
(10) Perkin, A. G.; Thomas, F. *J. Chem. Soc.* **1909**, *95*, 793−797.
(11) Leete, E. *J. Am. Chem. Soc.* **1961**, *83*, 3645−3653.
(12) Ingold, K. V. *Acc. Chem. Res.* **1968**, *1*, 1−9.
(13) March, J. *Advanced Organic Chemistry*, 3rd ed; John Wiley & Sons: 1985; pp 633−635.
(14) Voronov, V. V.; Vingradov, A. N.; Belayev, V. A. *Russ. Chem. Rev.* **1970**, *39*, 944−952.
(15) Bailey, E. J.; Barton, D. H. R.; Elks, J.; Templeton, J. F. *J. Chem. Soc.* **1962**, 1578−1591.
(16) Gardner, J. N.; Popper, T. L.; Carlon, F. E.; Gnoj, O.; Herzog, H. L. *J. Org. Chem.* **1968**, *33*, 3695−3699.
(17) Barton, D. H. R.; Jones, D. L. *J. Chem. Soc.* **1965**, 3563−3570.
(18) Remers, W. A. *The Chemistry of Heterocyclic Compounds*; Houlihan, J. W., Ed.; Interscience: New York, 1972; pp 145−152.
(19) Witkop, B.; Patrick, J. B. *J. Am. Chem. Soc.* **1951**, *73*, 2196−2200.

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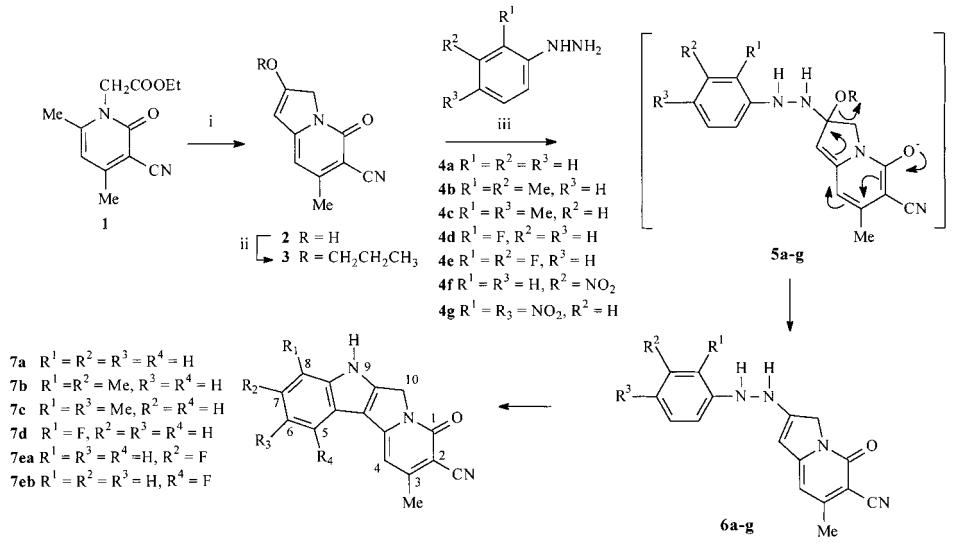
Scheme 1[a]



[a] Reaction conditions: (i) KO-t-Bu/dioxane, rt, 10 min, 76%; (ii) propanol/TsOH/toluene, reflux, 8 h, 80%; (iii) $C_6H_5NHNH_2$/AcOH/HCl, reflux, 3 h.

addition of oxygen to the carbon end of this bond to produce a quasistable endoperoxide. It can readily open to give a diketone derivative.

In our ongoing research toward the synthesis of indole derivatives, we synthesized the new tetracyclic 9*H*,10*H*-indolizino[1,2-*b*]indole-1-one derivative (**7a**) by the condensation of the known 2,5-dihydroxy-7-methyl-6-cyanoindolizine (**2**)[20] with various arylhydrazines (**4a**) via modified Fischer indole synthesis. Attempted *N*-methylation of **7a**, surprisingly, gave a mixture of 10-hydroperoxy-1-methoxy-indolizino[1,2-*b*]indole (**9a**) (major product) together with its *N*-methyl-10-hydroperoxy- and *N*-methyl-10-methylperoxy derivatives (**10a** and **11a**, respectively), 2-formyl-3-(pyridin-6-yl)indole (**12a**), and *N*-methyl-10-methoxyindolizinoindole **13a** (minor products). Apparently, the C_{10}−N bond of the indolizine residue of indolizinoindole was cleaved to form 3-(pyridin-6-yl) indole via an autoxidation process. The new finding prompted us to study the autoxidation of indolizinoindole derivatives. We report herein the synthesis of the new tetracyclic 9*H*,10*H*-indolizino[1,2-*b*]indole-1-one derivatives and their autoxidation.

Results and Discussion

The new tetracyclic indolizino[1,2-*b*]indole derivative **7a** was synthesized from the known compound (**2**) (Scheme 1), which was prepared by the intramolecular cyclization of **1** in the presence of base catalyst.[20] The enol **2** was treated with phenylhydrazine (**4a**) in glacial acetic acid, and the product ene-hydrazine derivative **6a** was further converted into indolizinoindole **7a** via Fischer indole synthesis in poor yield (30%). However, we found that the desired indolizinoindole **7a** can be prepared in high yield (>80%) by the reaction of *n*-propyl enol ether **3** with phenylhydrazine (**4a**) in a mixture of AcOH/HCl (3:1 v/v) in a one pot-reaction similar to Fischer indole synthesis. Compound **3** was prepared by the reaction of **2** with *n*-propanol in the presence of toluenesulfonic acid. Apparently, the electron withdrawing properties of the carbonyl and cyano functions of **3** facilitate the Michael type addition of arylhydrazine to form the intermediate **5a** which underwent elimination of propanol to give ene-hydrazine **6a** (Scheme 1), followed by ring cyclization and elimination of ammonia to furnish the indolizinoindole derivative **7a**. In a similar manner, a series of tetracyclic indolizinoindoles (**7b**−**d**, **7ea**, and **7eb**) was synthesized in good yield by the reaction of **3** with various phenylhydrazines (**4b**−**f**). However, reaction of **3** with 3-fluorohydrazine (**4e**) afforded a mixture of regioisomers of **7ea** and **7eb** (in a ratio of 1:3), which we were unable to separate by column chromatography. The reaction of **3** with nitro-substituted phenylhydrazines, **4f** and **4g**, did not yield the corresponding indolizinoindoles under various acidic conditions, probably due to the deactivating effect of the nitro group. Instead, we isolated the intermediates, ene-hydrazine **6f** and **6g**.

Attempts were directed toward the *N*-methylation of **7a**, and we surprisingly found that the reaction did not give the expected *N*-methyl derivative. Instead, a mixture of oxidized products was formed depending on base used and reaction time (Scheme 2). One major product, the 10-OOH-indolizinoindole derivative (**9a**) (43%) and its *N*,*O*-methyl substituted derivatives **10a** (6%) and **11a** (5%) along with 2-formyl-1-methyl-3-(pyridin-2-yl)indole (**12a**) (5%), were isolated when **7a** was treated with K_2CO_3/MeI/DMF under nitrogen for 8 h at room temperature (Table 1). When the reaction was carried out with KO-*t*-Bu/Me_2SO_4/THF/DMF, 80 °C, for 1 h under nitrogen, **9a** and **12a** appeared on thin-layer chromatography (SiO_2, hexane/EtOAc, 1:3 v/v). After 8 h, compounds **9a** (major product, 40%), **10a** (1%), **11a** (5%), **12a** (5%), and 10-methoxyindolizinoindole (**13a**, 2%) were isolated by column chromatography (Table 1). When the same reaction was performed under oxygen at 80 °C, it proceeded at a faster rate and the same oxidized products were isolated in better a yield of **9a** (58%), **10a** (8%), **12a** (8%), and **13a** (4%). In a similar manner, the tetracyclic indolizinoindoles (**7b**−**d**) were also subjected to *O*-methylation/autoxidation under the same reaction conditions (KO-*t*-Bu/Me_2SO_4/THF/DMF) in a nitrogen or oxygen atmosphere.

(20) Gewald, K.; Jansch, J. H. *J. Prakt. Chem. (Leipzig)* **1976**, *318*, 313−320.

Scheme 2

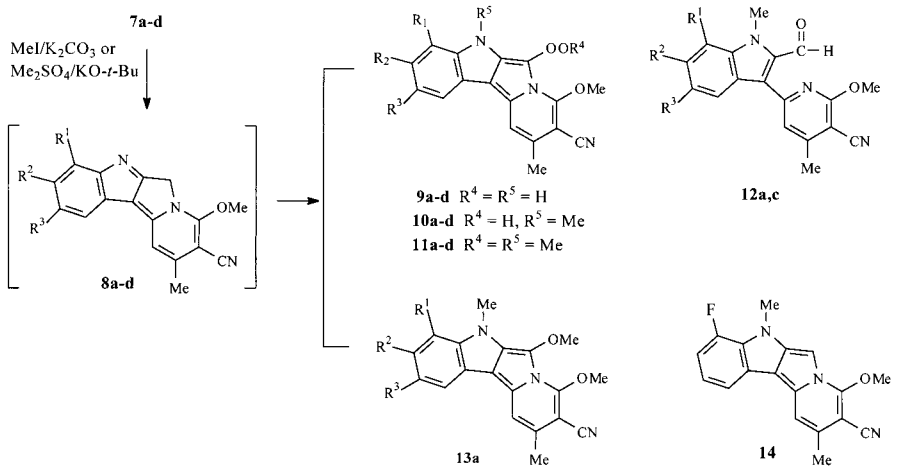


Table 1. Products of O-Methylation/Autoxidation of 2-Cyano-3-methyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one Derivatives

compound	reaction conditions	product	under N_2 yield (%)	under O_2 yield (%)
7a	A[a]	**9a**	43	
		10a	6	
		11a	5	
		12a	5	
16	A[a]	**17**	3	
		18	10	
		19	3	
7a	B[b]	**9a**	40	58
		10a	1	8
		11a	5	2
		12a	5	8
		13a	2	4
7b	B[b]	**9b**	42	55
		10b	6	2
		11b	4	1
7c	B[b]	**9c**	50	60
		10c	6	4
		11c	7	2
		12c	ND[c]	3
7d	B[b]	**9d**	ND[c]	7
		10d	2[d]	5
		14	37[d]	35

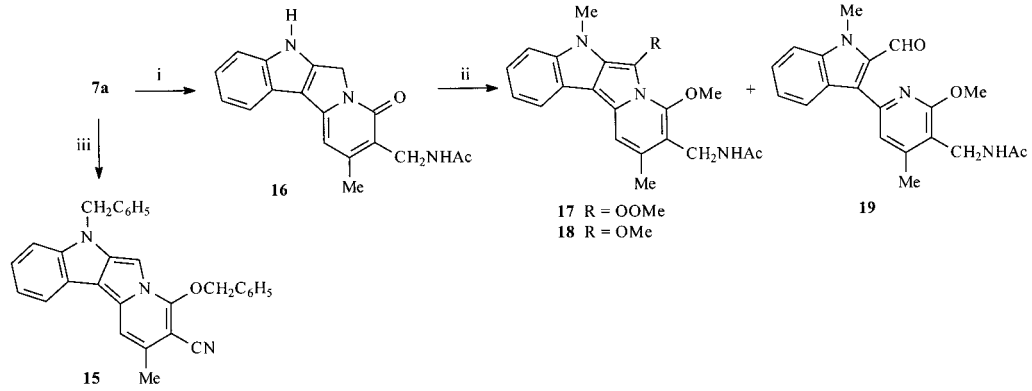
[a] Reaction condition A: MeI (excess)/K_2CO_3 (3 eq.)/DMF, room temperature, 8 h. [b] Reaction condition B: Me_2SO_4 (3 equiv)/KO-*t*-Bu (3 equiv)/DMF/THF (1:3), 80 °C, 8 h for reaction under nitrogen, 4 h for reaction under oxygen. [c] ND: not detected. [d] Yield after 24 h reaction.

Table 1 depicts the yield of products and time for the reactions under a nitrogen or oxygen atmosphere. The major products (40−60% isolated yields) were the 10-hydroperoxide derivatives **9a**−**c** except in the case of 8-fluoro-substituted 9*H*,10*H*-indolizinoindole **7d**, where the *N*-Me-indolizinoindole **14** (37%) was the major product. In addition to hydroperoxide substituted derivatives, various autoxidized products such as 10-OOH-indolizinoindoles **10a**−**d** (1−8%) and *N*-Me-10-OOMe-indolizinoindoles **11a**−**c** (2−7%), 2-formyl-1-methyl-3-(pyridin-2-yl)indole **12a**,**c** (3−8%), and *N*-Me-10-OMe-indolizinoindole **13a** (4%) were isolated. It is obvious that the yields of products did not change much, whether the reaction was carried out under nitrogen (8 h) or oxygen (4 h). Though the reaction time was shorter when the reaction was carried under oxygen, the amount of 10-OOMe-substituted products were a little less. The reason for these results may be explained by the fact that, although the reaction was carried out under nitrogen atmosphere, a trace amount of oxygen still remained in the solvent used. On the other hand, it was hard to prevent the contact of atmospheric oxygen when the reaction was worked up. As shown in Table 1, we failed to isolate the 2-formyl-3-(pyridin-6-yl)indole derivatives (**12a**,**c**) and the indolizinoindole derivative **13a** consistently. This may be due to the formation of a very small amount of these products in the course of the reaction and the instability of the aldehyde under basic conditions. The reaction of fluoro-substituted derivative **7d** under the same reaction conditions was sluggish. The reaction was not complete even after 8 h. When the reaction was prolonged for 24 h under a nitrogen atmosphere, the main product was *O*-methylated indolizinoindole **14** (37%) accompanied with a trace amount of 10-methylperoxide **10d** (2%). However, the amount of 10-hydroperoxide and its *N*-methylated compounds (**9d** and **10d**, respectively) were increased when the reaction was carried out under an oxygen atmosphere.

From these results, it is clear that two crucial steps were involved in the course of the autoxidation reaction. In the NMR study, it was found that only indole NH is D_2O exchangeable and hence more acidic than $C_{10}H$. Therefore, the first step is the abstraction of a proton from the indole NH, so *O*-methylation occurred first to yield the azaenolate **8a**−**d** intermediates (Scheme 2). The second step involves the autoxidation. As mentioned above, the majority of fluoro-substituted compound **7d** did not undergo autoxidation, probably due to hydrogen bond formation between fluorine and indole NH.[21] The formation of C−F···H−N bonding is detected by its NMR spectroscopy, a considerably downfield shift of the NH proton of **7d** (δ 12.91) than the other indolizines **7a**−**c** (δ 12.12−12.41) is observed. The question was whether the presence of the dissociable indole NH is necessary for *O*-methylation/autoxidation. To realize this fact, we treated **7a** with benzyl bromide instead of dimethyl sulfate or methyl iodide; the product formed was the *N*,*O*-dibenzylated compound **15** (Scheme 3). Even when the reaction was performed under oxygen, no oxidized products were detected by thin-layer chromatography. This indicated that **7a** was *O*-benzylated first, immediately followed by *N*-benzylation to give the *N*,*O*-dibenzylated product **15**. The *N*,*O*-dibenzylation process is faster than autoxidation, and hence once the *N*-benzylated compound

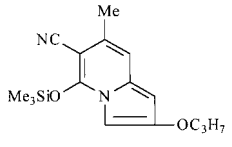
(21) Berkowitz, D. B.; Bose, M.; Pfannenstiel, T. J.; Doukov, T. *J. Org. Chem.* **2000**, *65*, 4498−4508.

Scheme 3[a]



[a] Reaction conditions: (i) Raney Ni/H_2 (50 psi)/Ac_2O/AcOH, 6 h, 100%; (ii) K_2CO_3 (3 equiv)/MeI (excess)/DMF, rt, 24 h; (iii) $C_6H_5CH_2Br$ (3 equiv)/KO-*t*-Bu (3 equiv)/THF/DMF, 80 °C, 8 h, 78%.

was formed, the product **15** did not undergo further autoxidation. This is further confirmed by our unpublished result; when compound **3** was *O*-trimethylsilylated, the product **20** bearing an enolate system like **15** did not undergo autoxidation.



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In addition, to understand the effect of the cyano function in *O*-methylation/autoxidation of the tetracyclic ring system, the cyano group of **7a** was converted into the CH_2NHAc (**16**) by treatment with Raney Ni/H_2 ($AcOH/Ac_2O$, 1:5 v/v) (Scheme 3).[22] The product **16** was then subjected to the *O*-methylation/autoxidation under the same reaction conditions (K_2CO_3/MeI/DMF) as described previously. The main oxidized products **17**, **18**, and **19** were isolated from the reaction mixture. It is clear that the cyano function of indolizinoindole does not affect the *O*-methylation/autoxidation

The chemical structures of all oxidized compounds were determined by ^{1}H NMR and mass spectroscopies. The C_{10}-methylene function of **7a** appeared at δ 5.16, while this peak disappeared in the oxidized products (such as **9a**, **10a**, **11a**, and **13a**). Compound **9a** showed an additional peak at δ 3.86, assigned for the OMe group, and at δ 12.48 (D_2O exchangeable), assigned for OOH. Compounds **10a** and **11a**, containing hydroperoxy and methylperoxy functions, respectively, showed singlets at δ 12.42 (D_2O exchangeable) and δ 3.18, respectively. In addition, the *N*-Me function of **10a** and **11a** appeared at δ 4.07 and 3.84, respectively. The MS spectrum of **11a** (M+ 335) showed one peak at 288 *m*/*z*, indicating the elimination of the OOMe group.

The ^{1}H NMR (DMSO-d_6) spectrum of 2-formyl indole **12a** showed three singlets at δ 2.42, 4.02, and 4.11 (each three protons) assigned for Me, NMe, and OMe, respectively. The aromatic protons appeared at δ 7.31 (1H, t), 7.53 (2H, m), 7.73 (1H, d), and 8.08 (1H, d), and the aldehyde proton appeared at δ 10.32. The ^{13}C NMR spectrum of **12a** revealed one aldehyde function at 185 ppm and was confirmed by the DEPT 135 experiment. The fragmentation pattern in the MS spectrum of **12a** (M+ 305) showed one peak at 276 *m*/*z* indicating the elimination of the carbonyl group.

We have isolated several autoxidized products of the tetracyclic indolizinoindoles. As we mentioned previously, two crucial steps were involved in the course of the autoxidation reaction, and both of them are initiated by abstraction of the indole NH proton. The first step involves abstraction of the indole NH and consequently *O*-methylation to form azaenolate **8a**, which tautomerizes to enamine **A** (Scheme 4). The second step (autoxidation) is thought to be a free-radical process similar to the pathway previously described by Barton *et al.*,[17] initiated by the abstraction of the proton from the indole NH resulting in the formation of the carbanion **B**. Oxidation of **B** by triplet oxygen gives radical **C**, which readily reacts with the peroxide anion radical and is subsequently converted to the 10-hydroperoxide **D** intermediate. Tautomerization of **D** to **9a** followed by *N*- or/and *O*-methylation affords **10a** and **11a**. Hino et al.[23] reported that both 2-ethyl ether and 2-thioether of 3-substituted indole were autoxidized to 3-hydroperoxides (or hydroperoxy radicals). This could not rearrange to acyindole or keto-amide as in the case of the 2,3-dialkylindoles due to the presence of the 2-ethoxy group but gave the 3-hydroxyindole derivative. Therefore, the hydroperoxide **D** is readily converted to 10-OH-indolizinoindole **E**, which is then further transformed to 2-formyl-3-(pyridin-2-yl)-indole **12a** via C−N bond cleavage. In the meantime, intermediate **E** tautomerizes (hydride shift) to give **F**, which is then converted into **13a** after *N*,*O*-methylation.

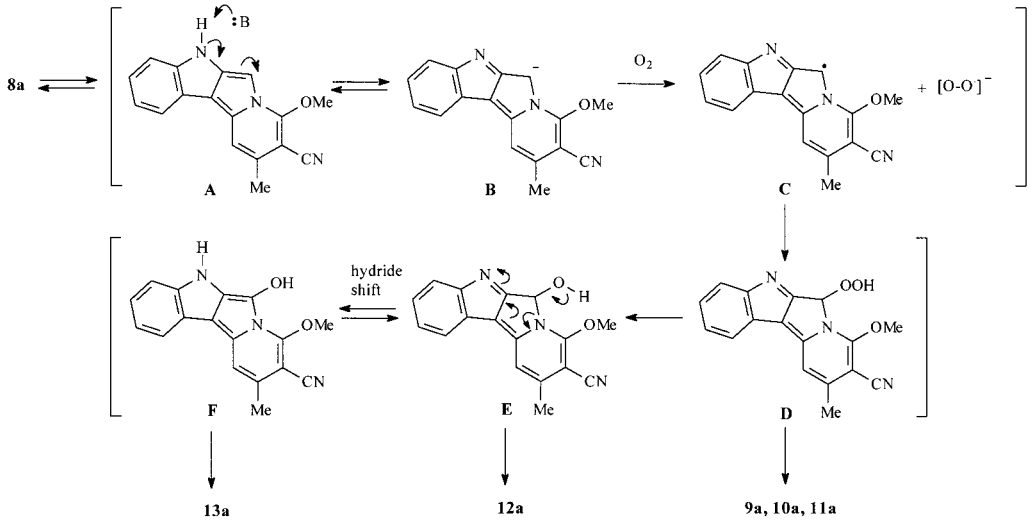
It should be noted that the presence of free indole NH proton is crucial as 8-fluoroindolizinoindole (**7d**) did not undergo autoxidation smoothly. The explanation behind this is the formation of the N−H···F−C bond, which reduces the acidity of the indole NH proton and hence its availability in basic medium. Therefore, *N*,*O*-dimethylated 8-fluoroindolizinoindole (**14**) was the major product in this reaction. Neither **14** nor *O*,*N*-dibenzylated derivative **15** underwent autoxidation since there is no dissociable NH function available.

In summary, we have synthesized a number of new tetracyclic indolizinoindolo derivatives, which underwent a novel *O*-methylation/autoxidation in the presence of *O*-methylating agent under basic conditions to give

(22) Su, T.-L.; Huang, J.-T.; Burchenal, J. H.; Watanabe, K. A.; Fox, J. J. *J. Med. Chem.* **1986**, *29*, 709−715.

(23) Hino, T.; Nakagawa, M.; Akaboshi, S. *Chem. Commun.* **1967**, 656−658.

Scheme 4



various oxidized products. A plausible mechanism of *O*-methylation/autoxidation has been described by the isolation of intermediates. The finding indicates that the initial step of *O*-methylation/autoxidation is the abstraction of indole NH proton to form azaenolates **8a**−**d**, which tautomerize to enamines **A** followed by autoxidation. The novel autoxidation described herein demonstrates oxidation of azaenolates/enamines, which are more easily oxidized by triplet oxygen than activated hydrocarbon C−H.

Experimental Section

General Methods. Melting points were determined on a hot stage apparatus and are uncorrected. Column chromatography was performed on silica gel G60 (70−230 mesh). Thin-layer chromatography was performed on silica gel G60 F_{254} with short-wavelength UV light for visualization. Tetrahydrofuran and DMF were dried using standard procedure.

6-Cyano-2-propyloxy-7-methylindolizine-5-one (3). A solution of 2,5-dihydroxy-7-methyl-6-cyano-indolizine[20] (**2**, 10.0 g, 53.5 mmol) and *p*-toluenesulfonic acid (1.0 g) in dry propanol (150 mL) was refluxed under nitrogen for 48 h. The solvent was evaporated *in vacuo* to dryness and the solid product **3** was purified by silica gel column chromatography using $CHCl_3$ as the eluant. Yield 10.2 g (83%): mp 221−222 °C (EtOH); ^{1}H NMR (DMSO-d_6) δ 1.04 (3H, t, J = 7.2 Hz), 1.84 (2H, m), 2.36 (3H, s), 4.01 (2H, t, J = 6.4 Hz), 4.60 (2H, s, exch), 5.51 (1H, s), 6.04 (1H, s); MS 220 (M^+). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.79; H, 6.13; N, 12.17. Found: C, 67.73, H, 6.14; N, 12.13.

2-Cyano-3-methyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7a). To a solution of **3** (1.54 g, 7 mmol) in AcOH (45 mL) and concentrated HCl (15 mL) was added phenylhydrazine (**4a**, 1.21 g, 7 mmol) at room temperature. The reaction mixture was refluxed under nitrogen for 3 h and was poured into ice water. The resulting solid product was collected by filtration. The filtered cake was washed well with water, dried, and recrystallized from EtOH to give **7a**, 1.47 g (81%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.45 (3H, s), 5.16 (2H, s), 6.91 (1H, s), 7.29 (2H, m), 7.58 (1H, d, J = 8 Hz), 7.94 (1H, d, J = 8 Hz), 12.12 (1H, s, exch); MS 261 (M^+). Anal. Calcd for $C_{16}H_{11}N_3O\cdot{}^1/_{10}H_2O$: C, 73.05; H, 4.29; N, 15.97. Found: C, 72.83, H, 4.28; N, 15.78.

Through use of the same procedure as that for the synthesis of **7a**, the following 9*H*,10*H*-indolizino-[1,2-*b*]indole-1-one derivatives were synthesized.

2-Cyano-3,7,8-trimethyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7b). Compound **7b** was prepared by the reaction of **3** (575 mg, 2.5 mmol) and **4b** (433 mg, 2.5 mmol). Yield, 594 mg (84%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.37 (3H, s), 2.44 (3H, s), 2.50 (3H, s), 5.14 (2H, s), 6.82, (1H, s), 7.12 (1H, d, J = 8 Hz), 7.76 (1H, d, J = 8 Hz), 12.41 (1H, *s*, exch); MS 289 (M^+). Anal. Calcd for $C_{18}H_{15}N_3O\cdot{}^3/_{20}H_2O$: C, 74.09; H, 5.28; N, 14.39. Found: C, 73.98; H, 5.06; N, 14.28.

2-Cyano-3,6,8-trimethyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7c). Compound **7c** was prepared from **3** (575 mg, 2.5 mmol) and **4c** (433 mg, 2.5 mmol). Yield, 527 mg (73%): mp > 300 °C (EtOH); ^{1}H NMR (DMSO-d_6) δ 2.40 (3H, s), 2.43 (3H, s), 2.50 (3H, s), 5.12 (2H, s), 6.86, (1H, s), 6.95 (1H, s), 7.56 (1H, s), 12.31 (1H, s, exch); MS 289 (M^+). Anal. Calcd for $C_{18}H_{15}N_3O\cdot{}^3/_2H_2O$: C, 68.34; H, 5.70; N, 13.28. Found: C, 68.48; H, 5.56; N, 13.57.

2-Cyano-8-fluoro-3-methyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7d). Compound **7d** was prepared by the reaction of **3** (575 mg, 2.5 mmol) and **4d** (407 mg, 2.5 mmol). Yield, 643 mg (92%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.45 (3H, s), 5.12 (2H, s), 6.94 (1H, s), 7.19 (2H, m), 7.18 (1H, d, J = 8 Hz), 12.91 (1H, s, exch); MS 279 (M^+). Anal. Calcd for $C_{16}H_{10}FN_3O$: C, 68.78; H, 3.60; N, 15.04. Found: C, 67.89; H, 3.78; N, 14.92.

2-Cyano-7-fluoro-3-methyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7ea) and 2-Cyano-5-fluoro-3-methyl-9*H*,10*H*-indolizino[1,2-*b*]indole-1-one (7eb). Compounds **7ea** and **7eb** were prepared by the reaction of **3** (110 mg, 0.5 mmol) and **4e** (81 mg, 0.5 mmol). The solid product showed one spot on TLC (SiO_2, EtOAc). The ^{1}H NMR spectrum confirmed that the product contained two regioisomers **7ea** and **7eb** in a ratio of ca. 1:3. Attempts to separate the two isomers by chromatography failed. Yield, 122 mg (87%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) (**7ea**) δ 2.46 (3H, s), 5.18 (2H, *s*), 6.57 (1H, s), 7.05 (1H, m), 7.18 (1H, d, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 12.66 (1H, s, exch); ^{1}H NMR (DMSO-d_6) (**7eb**) δ 2.45 (3H, s), 5.13 (2H, s), 6.57 (1H, s), 7.05 (1H, m), 7.18 (1H, d, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 12.40 (1H, s, exch); MS 279 (M^+). Anal. Calcd for $C_{16}H_{10}FN_3O\cdot{}^1/_{10}H_2O$: C, 67.93; H, 3.70; N, 14.85. Found: C, 67.69; H, 3.55; N, 14.81.

1-Benzyloxy-9-benzyl-2-cyano-3-methylindolizino[1,2-*b*]indole (15). To a mixture of DMF (17 mL), THF (50 mL), and DMF (17 mL) containing KO-*t*-Bu (336 mg, 3 mmol) was added **7a** (261 mg, 1 mmol). After being stirred for 30 min, benzyl bromide (376 μL, 3 mmol) was added to the reaction mixture at 80 °C. It was stirred at 80 °C under nitrogen for 8 h. The solvent was evaporated *in vacuo* to dryness and the residue was triturated with water. The resulting solid was collected by filtration, washed well with water, and dried. The product **15** was purified by column chromatography (SiO_2, 1 cm × 5 cm) using hexane/EtOAc (3:1 v/v) as the eluant and crystallized by ethanol to afford 344 mg (78%) of **15**: mp 251−252 °C; ^{1}H NMR (DMSO-d_6) δ 2.25 (3H, s), 3.76 (2H, d, J = 8 Hz), 4.41 (2H, d, J = 8 Hz), 6.10 (1H, s), 6.34 (2H, d, J = 14 Hz), 6.86−8.03 (13H, m); MS 441 (M^+). Anal. Calcd for

$C_{30}H_{23}N_3O\cdot{}^1/_8H_2O$: C, 80.77; H, 5.26; N, 9.43. Found: C, 80.94, H; 5.13; N, 9.21.

2-*N*-Acetylaminomethyl-3-methyl-9*H*,10*H*-indolizino-[1,2-*b*]indole-1-one (16). A mixture of **7a** (2.61 g, 10 mmol) and Raney Ni (5 g) in a solution of acetic anhydride (30 mL) and acetic acid (10 mL) was hydrogenated at 50 psi for 6 h.[22] The mixture was filtered through a pad of Celite, washed with AcOH, and evaporated in vacuo to dryness. The residue was diluted with ice water (50 mL) and the solid was collected by filtration. The product **16** was recrystallized from EtOH to give 3.06 g (100%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 1.79 (3H, s), 2.31 (3H, s), 4.21 (2H, s), 5.22 (2H, s), 6.61 (1H, s), 7.23 (2H, m), 7.55 (1H, d, J = 8.4 Hz), 7.77 (1H, d, J = 8.4 Hz), 7.81 (1H, s, exch), 12.03 (1H, s, exch); MS 307 (M^+). Anal. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.32; H, 5.58; N, 13.68. Found: C, 70.01, H; 5.24; N, 13.22.

General procedure for *O*-methylation/autoxidation of 9*H*,10*H*-indolizino[1,2-*b*]indole-1-ones. Method A. 10-Hydroperoxy-2-cyano-3-methyl-1-methoxy-indolizino[1,2-*b*]-indole (9a), 9-*N*-Methyl-10-hydroperoxy-2-cyano-3-methyl-1-methoxyindolizino[1,2-*b*]indole (10a), and 9-Methyl-10-methylhydroperoxy-2-cyano-3-methyl-1-methoxy-indolizino[1,2-*b*]indole (11a) and 1-Methyl-2-formyl-3-(1-methoxy-2-cyano-3-methylpyridin-5-yl)indole (12a). To a mixture of 7a (1.31 g, 5 mmol) in dry DMF (50 mL) containing K_2CO_3 (2.05 g, 15 mmol) was added MeI (1.5 mL, 24 mmol) under nitrogen. After being stirred for 8 h at room temperature, the mixture was evaporated in vacuo to dryness. The residue was diluted with water (50 mL), and the resulting solid was collected by filtration, washed with water, and dried. The solid (containing two major products) was dissolved in a small amount of $CHCl_3$ and chromatographed on a silica gel column (2.4 cm × 25 cm). Compound 11a was eluted first with Hexane/EtOAc (3:1 v/v), followed by compounds **12a**, **10a**, and **9a**.

Compound **9a** was eluted by hexane/EtOAc (1:2 v/v). Yield, 660 mg (43%): mp 282−283 °C; ^{1}H NMR (DMSO-d_6) δ 2.45 (3H, s), 3.86 (3H, s), 6.40 (1H, s), 7.21 (1H, t, J = 7.6 Hz), 7.37 (1H, t, J = 7.2 Hz), 7.54 (1H, d, J = 8.4 Hz), 7.65 (1H, d, J = 8 Hz), 12.37 (1H, s, exch), 12.48 (1H, s, exch); MS 307 (M^+), 274 (−OOH). Anal. Calcd for $C_{17}H_{13}N_3O_3\cdot{}^1/_2H_2O$: C, 64.55; H, 4.46; N, 13.28. Found: C, 64.56; H, 4.43; N, 12.91.

Compound **10a** was eluted by hexane/EtOAc (2:1 v/v). Yield 127 mg (6%): mp 248−249 °C; ^{1}H NMR (DMSO-d_6) δ 2.45 (3H, s), 4.07 (3H, s), 4.14 (3H, s), 6.42 (1H, s), 7.27 (1H, d, J = 8.4 Hz), 7.65 (2H, m), 7.72 (1H, d, J = 8.2 Hz), 12.42 (1H, s, exch); MS 321 (M^+), 288 (−OOH). Anal. Calcd for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.70; N, 13.08. Found: C, 67.14; H, 4.86; N, 12.82.

Compound **11a** was eluted by hexane/EtOAc (3:1, v/v) from column chromatography. Yield 83 mg (5%); mp 122−123 °C (EtOH); ^{1}H NMR (DMSO-d_6) δ 2.39 (3H, s), 3.18 (3H, s), 3.84 (3H, s), 4.19 (3H, s), 6.37 (1H, s), 7.24 (1H, d, J = 8.4 Hz), 7.48 (2H, d, J = 7.6 Hz), 7.74 (1H, d, J = 8.4 Hz); MS, 335 (M^+), 288 (−OOMe). Anal. Calcd for $C_{19}H_{17}N_3O_3\cdot{}^1/_8H_2O$: C, 67.58; H, 5.39; N, 12.44. Found: C, 67.59; H, 5.12; N, 12.75.

Compound **12a** was eluted by hexane/EtOAc (3:1 v/v). Yield, 76 mg (8%): mp 220−221 °C; ^{1}H NMR (DMSO-d_6) δ 2.42 (3H, s), 4.02 (3H, s), 4.11 (3H, s), 7.31 (1H, t, J = 7.6 Hz), 7.53 (2H, m), 7.73 (1H, d, J = 8.4 Hz), 8.08 (1H, d, J = 8.4 Hz), 10.32 (1H, s); ^{13}C NMR (DMSO-d_6) δ 19, 32, 54, 93, 111, 114, 119, 121, 122, 124, 124, 127, 132, 138, 152, 155, 163, 185; MS 305 (M^+), 276 (−CHO). Anal. Calcd for $C_{18}H_{15}N_3O_2\cdot{}^1/_5H_2O$: C, 69.99; H, 5.02; N, 13.60. Found: 69.92, H; 5.01; N, 13.43.

In a similar manner, **16** (307 mg, 1.0 mmol) was treated with MeI (0.5 mL, 7.9 mmol) in DMF (40 mL) containing K_2CO_3 (414 mg, 3 mmol) at room temperature for 24 h, and the following products were isolated after column chromatography.

2-*N*-Acetylaminomethyl-3,9-dimethyl-10-methylperoxyinolizino[1,2-*b*]indole-1-one (17). It was eluted by EtOAc/MeOH (9:1 v/v). Yield, 11 mg (3%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 1.77 (3H, s), 2.22 (3H, s), 3.13 (3H, s), 3.73 (3H, s), 4.08 (3H, s), 4.21 (2H, d, J = 4.8 Hz), 6.05 (1H, s), 7.20 (1H, m), 7.44 (1H, m), 7.21 (1H, d, J = 8 Hz), 7.91 (2H, m); MS 381 (M^+), 334 (−OOMe). Anal. Calcd for $C_{21}H_{23}N_3O_4$: C, 66.13; H, 6.08: N, 11.02. Found: 65.87, H; 5.79; N, 10.73.

2-*N*-Acetylaminomethyl-3,9-dimethyl-10-methoxyindolizino[1,2-*b*]indole-1-one (18). It was eluted by EtOAc/MeOH (9:1 v/v). Yield, 38 mg (10%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 1.82 (3H, s), 2.37 (3H, s), 3.79 (3H, s), 3.85 (3H, s), 3.91 (3H, s), 4.27 (2H, d, J = 4.8 Hz), 7.07 (1H, s), 7.23 (1H, m), 7.38 (1H, m), 7.64 (1H, d, J = 8 Hz), 7.91 (2H, m); MS 365 (M^+). Anal. Calcd for $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34: N, 11.49. Found: 68.84, H; 6.11; N, 11.15.

1-Methyl-2-formyl-3-(1-methoxy-2-*N*-acetylaminomethyl-3-methylpyridin-5-yl)indole (19). It was isolated by ethyl acetate. Yield, 37 mg (3%): mp 162−163 °C; ^{1}H NMR (DMSO-d_6) δ 1.82 (3H, s), 2.38 (3H, s), 3.93 (3H, s), 4.11 (3H, s), 4.21 (2H, d, J = 4.8 Hz), 7.07 (1H, s), 7.23 (1H, m), 7.38 (1H, m), 7.64 (1H, d, J = 8 Hz), 7.91 (2H, m), 10.12 (1H, s); MS 351 (M^+), 322 (−CHO); Calcd for $C_{20}H_{21}N_3O_3\cdot{}^1/_5H_2O$: C, 67.66; H,6.36: N, 11.83. Found: C, 66.72, H; 7.16; N, 11.61.

Method B. In method B the reactions were carried out both under nitrogen and oxygen. The results and yields given here are for the reaction carried out under oxygen (Table 1).

9-Methyl-10-methoxy-2-cyano-3-methyl-1-methoxyindolizino[1,2-*b*]indole (13a). To a mixture of dry DMF (50 mL) and THF (150 mL) containing KO-*t*-Bu (1.68 g, 15 mmol) was added **7a** (1.35 g, 5.0 mmol) at room temperature. After being stirred for 30 min, dimethyl sulfate (1.43 mL, 15 mmol) was added into the reaction mixture at 80 °C, either under nitrogen or oxygen atmosphere, and stirring continued at 80 °C for another 8 h (under nitrogen) or 4 h (under oxygen). The solvent was evaporated in vacuo to dryness. The residue was triturated with water, and the precipitate was collected by filtration, washed with water, and dried. The dried solid was dissolved in a minimum amount of $CHCl_3$ and chromatographed on a silica gel column (3.5 cm × 25 cm) using hexane/EtOAc as the eluent. The products were isolated by column chromatography and are shown in Table 1. Their analytical data (including melting point, ^{1}H NMR, MS spectrum, and elemental analysis) are described as follows:

The reaction produced five spots in TLC (SiO_2, hexane/ethyl acetate = 1:2 as visualized by short wavelength UV light). Every spot was isolated. Compound **13a** (4%) was isolated first followed by compounds **11a** (2%), **10a** (8%), **12a** (8%), and **9a** (58%).

Compound **13a** was eluted by hexane/EtOAc (1:1 v/v). Yield, 63 mg (4%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.50 (3H, s), 3.82 (3H, s), 3.93 (3H, s), 3.96 (3H, s), 7.27 (1H, m), 7.36 (1H, s), 7.41 (1H, m), 7.69 (1H, d, J = 8.4 Hz), 7.98 (1H, d, J = 8.8 Hz); MS 319; Anal. Calcd. for $C_{19}H_{17}N_3O_2\cdot{}^1/_5H_2O$: C, 70.66; H, 5.43; N, 13.01. Found: C, 70.56; H, 5.22; N, 12.91.

Similar treatment of **7b** (289 mg, 1.0 mmol) with KO-*t*-Bu (336 mg, 3.0 mmol) and dimethyl sulfate (0.3 mL) in DMF (17 mL) and THF (50 mL) afforded the following compounds. The reaction produced three products. Compound **11b** was isolated first followed by **10b** and **9b**.

2-Cyano-10-hydroperoxy-1-methoxy-3,7,8-trimethylindolizino[1,2-*b*]indole (9b). Compound **9b** was eluted by hexane/EtOAc (1:2 v/v). Yield, 184 mg (55%): mp 289−290 °C; ^{1}H NMR (DMSO-d_6) δ 2.40 (3H, s), 2.44 (3H, s), 2.50 (3H, s), 4.02 (3H, s), 6.44 (1H, s), 7.05 (1H, brs), 7.35 (1H, brs), 11.69 (1H, s, exch), 12.38 (1H, s, exch); MS 335 (M^+), 302 (−OOH). Anal. Calcd for $C_{19}H_{17}N_3O_3\cdot{}^1/_2H_2O$: C, 66.26; H, 5.26; N, 12.20. Found: C, 66.55; H, 5.65; N, 11.63.

2-Cyano-1-methoxy-10-hydroperoxy-3,7,8,9-tetramethylindolizino[1,2-*b*]indole (10b). Compound **10b** was eluted by hexane/EtOAc (1:1 v/v). Yield, 7 mg (2%): mp 222−223 °C; ^{1}H NMR (DMSO-d_6) δ 2.35 (3H, s), 2.50 (6H, s), 3.82 (3H, s), 4.00 (3H, s), 6.94 (1H, s), 7.33 (1H, d, J = 8 Hz), 7.58 (2H, d, J = 8.0 Hz), 11.72 (1H, s, exch); MS 349 (M^+), 316 (−OOH). Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.53; H, 5.32; N, 11.81.

2-Cyano-1-methoxy-10-methylperoxy-3,7,8,9-tetramethylindolizino[1,2-*b*]indole (11b). Compound **11b** was eluted by hexane/EtOAc (3:1 v/v). Yield, 4 mg (1%): mp 274−275 °C, ^{1}H NMR (DMSO-d_6) δ 2.35 (3H, s), 2.40 (3H, s), 2.44 (3H, s), 3.22 (3H, s), 3.39 (3H, s), 3.83 (3H, s), 6.43 (1H, s), 7.10 (1H, brs), 7.35 (1H, brs), MS 363 (M^+), 316 (−OOH). Anal.

Calcd for $C_{21}H_{21}N_3O_3 \cdot H_2O$: C, 68.99; H, 5.86; N, 11.49. Found: C, 68.88; H, 5.72; N, 11.31.

Similar treatment of **7c** (289 mg, 1.0 mmol) with KO-*t*-Bu (336 mg, 3.0 mmol), and dimethyl sulfate (0.3 mL, 3.0 mmol) in DMF (17 mL) and THF (50 mL) afforded the following compounds. The compound **12c** was isolated first in column chromatography (silica gel; 1.5 cm × 5 cm) followed by **11c**, **10c**, and **9c**.

2-Cyano-10-hydroperoxy-1-methoxy-3,6,8-trimethylindolizino[1,2-*b*]indole (9c). Compound **9c** was eluted by hexane/EtOAc (1:2 v/v). Yield, 198 mg (60%): mp > 270 °C; ^{1}H NMR (DMSO-d_6) δ 2.40 (3H, s), 2.45 (3H, s), 2.50 (3H, s), 4.02 (3H, s), 6.43 (1H, s), 7.09 (1H, s), 7.21 (1H, s), 12.19 (1H, s, exch), 12.42 (1H, s, exch); MS 335 (M^+), 302 (−OOH). Anal. Calcd for $C_{19}H_{17}N_3O_3 \cdot {}^2/_5H_2O$: C, 66.62; H, 5.24; N, 12.27. Found: C, 66.55; H, 5.57; N, 12.19.

2-Cyano-1-methoxy-10-methylperoxy-3,6,8-trimethylindolizino[1,2-*b*]indole (10c). Compound **10c** was eluted by hexane/EtOAc (1:1 v/v). Yield 14 mg (4%): mp 258−259 °C; ^{1}H NMR (DMSO-d_6) δ 2.37 (3H, s), 2.41 (3H, s), 2.56 (3H, s), 3.79 (3H, s), 3.96 (3H, s), 6.46 (1H, s), 7.07 (1H, s), 7.21 (1H, s), 12.26 (1H, s, exch); MS 349 (M^+), 316 (−OOH). Anal. Calcd for $C_{20}H_{19}N_3O_3 \cdot H_2O$: C, 68.31; H, 5.52; N, 11.95. Found: C, 68.32; H, 5.21; N, 11.89.

2-Cyano-1-methoxy-10-methylperoxy-2-cyano-3,6,8,9-tetramethylindolizino[1,2-*b*]indole (11c). Compound **11c** was eluted by hexane/EtOAc (2:1 v/v). Yield, 7 mg (2%): mp 258−259 °C; ^{1}H NMR (DMSO-d_6) δ 2.35 (3H, s), 2.45 (3H, s), 2.56 (3H, s), 2.83 (3H, s), 3.22 (3H, s), 4.34 (3H, s), 6.40 (1H, s), 7.05 (1H, s), 7.21 (1H, s); MS 363 (M^+), 316 (−OOMe). Anal. Calcd for $C_{21}H_{21}N_3O_3 \cdot H_2O$: C, 68.98; H, 5.86; N, 11.49. Found: C, 69.02; H, 5.58; N, 11.13.

5,7-Dimethyl-2-formyl-3-(1-methoxy-2-cyano-3-methylpyridin-5-yl)indole (12c). Compound **12c** was eluted by hexane/EtOAc (3:1 v/v). Yield, 10 mg (3%): mp 208−209 °C; ^{1}H NMR (DMSO-d_6) δ 2.37 (3H, s), 2.47 (3H, s), 2.56 (3H, s), 3.96 (3H, s), 6.98 (1H, s), 7.07 (1H, s), 7.11 (1H, s), 11.26 (1H, s); MS 333 (M^+), 304 (−CHO). Anal. Calcd for $C_{20}H_{19}N_3O_2 \cdot H_2O$: C, 71.57; H, 5.78; N, 12.52. Found: C, 71.48; H, 5.68; N, 12.31.

Similar treatment of **7d** (279 mg, 1.0 mmol) with KO-*t*-Bu (336 mg, 3.0 mmol), and dimethyl sulfate (0.3 mL, 3 mmol), in DMF (17 mL) and THF (50 mL) for 24 h afforded the following compounds. In column chromatography (SiO_2, 1.5 cm × 6 cm) compound **14** was isolated first followed by **10d** and **9d**.

2-Cyano-8-fluoro-10-hydroperoxy-1-methoxy-3-methylindolizino[1,2-*b*]indole (9d). Compound **9d** was eluted by hexane/EtOAc (1:2 v/v). Yield, 22 mg (7%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.41 (3H, s), 4.22 (3H, s), 6.41 (1H, s), 7.26 (2H, m), 7.44 (1H, m), 13.22 (1H, s, exch), 13.42 (1H, s, exch); MS 325 (M^+), 292 (−OOH). Anal. Calcd for $C_{17}H_{12}FN_3O_3$: C, 62.77; H, 3.72; N, 12.92. Found: C, 62.65; H, 3.62; N, 12.56.

2-Cyano-3,9-dimethyl-8-fluoro-10-hydroperoxy-1-methoxyindolizino[1,2-*b*]indole (10d). Compound **10d** was eluted by hexane/EtOAc (2:1 v/v). Yield, 16 mg (5%): mp > 300 °C; ^{1}H NMR (DMSO-d_6) δ 2.43 (3H, s), 3.78 (3H, s), 4.22 (3H, s), 6.43 (1H, s), 7.27 (2H, m), 7.46 (1H, m), 13.29 (1H, s, exch); MS 339 (M^+), 306 (−OOH). Anal. Calcd for $C_{18}H_{14}FN_3O_3$: C, 75.78; H, 4.91; N, 14.73. Found: C, 75.56; H, 4.62; N, 14.57.

2-Cyano-3,9-dimethyl-8-fluoro-1-methoxyindolizino[1,2-*b*]indole (14). Compound **14** was eluted by hexane/EtOAc (3:1 v/v). Yield, 107 mg (35%): mp 279−280 °C; ^{1}H NMR (DMSO-d_6) δ 2.43 (3H, s), 3.79 (3H, s), 4.22 (3H, s), 6.44 (1H, s), 7.35 (2H, m), 7.67 (2H, m); MS 307 (M^+). Anal. Calcd for $C_{18}H_{14}FN_3O$: C, 69.62; H, 6.48; N, 14.33. Found: C, 69.33; H, 6.21; N, 14.27.

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