HETEROCYCLES, Vol. 60, No. 1, 2003, pp. 131 - 141
Received, 10th October, 2002, Accepted, 18th November, 2002, Published online, 25th November, 2002

SYNTHESIS OF DIBENZO[*a,f*]QUINOLIZINIUM AND 2-PHENYLOXAZOLO[3,2-*a*]QUINOLINIUM PERCHLORATES *via* ACID-CATALYZED CYCLIZATION OF 1-(2-OXO-2-PHENYL)ETHYL)-2(1*H*)-ONES

I-Li Chen,[a] Yeh-Long Chen,[a] Tai-Chi Wang,[b] and Cherng-Chyi Tzeng[a*]

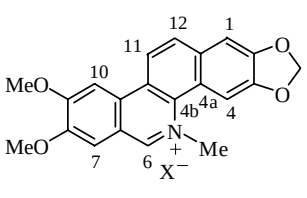
[a]School of Medicinal and Applied Chemistry, College of Life Science, Kaohsiung Medical University, Kaohsiung City, Taiwan

[b]Department of Pharmacy, Tajen Institute of Technology, Pintung, Taiwan

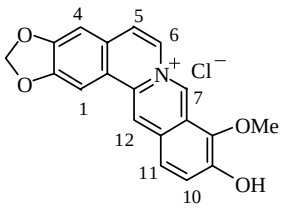
Abstract - Treatment of certain *N*-alkylated quinolin-2(1*H*)-ones with concentrated H_2SO_4 afforded oxazolo[3,2-*a*]quinolin-10-ylium perchlorates *via* a *Z*-form enol intermediate while others gave dibenzo[*a,f*]quinolizinium perchlorates *via* an *E*-form enol intermediate. We examined the structure of starting *N*-alkylated quinolin-2(1*H*)-ones and found that a methoxy group substituted at R_4 is required for the formation of tetracyclic dibenzo[*a,f*]quinolizinium perchlorates.

There are two types of tetracyclic quarternary aromatic alkaloids: *N*-Alkylquinolinium salts such as nitidine and fagaronine[1,2] and quinolizinium salts such as coralyne and deoxythalidastine.[3-5] Nitidine and fagaronine belong to benzo[*c*]phenanthridine ring while coralyne and deoxythalidastine belong to dibenzo[*a,g*]-quinolizinium skeleton. Both types of alkaloids were found to have anticancer activities.

Figure 1



Nitidine



Deoxythalidastine

Due to limited natural resources, synthetic studies of these bioactive alkaloids and their derivatives attracted much attention.[6-9] Among the possible dibenzoquinolizinium isomers, we were particularly interested in

dibenzo[*a*,*f*]quinolizinium series because of its structural similarity to both dibenzo[*a*,*g*]quinolizinium and benzo[*c*]phenanthridine tetracycles. It is the isomer of the former and possesses the same type of ring connection with the later one. Interchange of 4b-CH and the neighboring quaternary nitrogen at 5-position converts the benzo[*c*]phenanthridine ring to the dibenzo[*a*,*f*]quinolizinium series. However, only two papers have been appeared so far describing the preparation of this skeleton through the photochemical method.[10,11] The present report describes acid-catalyzed ring cyclization of 1-[2-oxo-2-(4-methoxyphenyl)ethyl]-quinolin-2(1*H*)-ones to form dibenzo[*a*,*f*]quinolizinium salts *via* an *E*-form intermediate. On the other hand, other 2-phenyloxazolo[3,2-*a*]quinolinium perchlorates[12] were synthesized by acid-catalyzed ring cyclization of 1-(2-oxo-2-phenyl)ethyl)quinolin-2(1*H*)-ones[13] *via* the *Z*-form intermediate.

Scheme 1

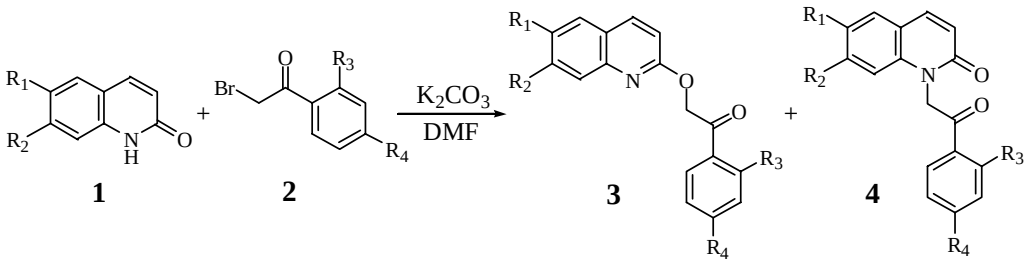


Table 1. Alkylation of Quinolin-2(1*H*)-ones

Entry	R_1	R_2	R_3	R_4	Yield (%)	Ratio (**3**/**4**)
a	H	H	H	H	48	0/1
b	H	OAc	H	H	60	1/4
c	H	OAc	H	Me	68	1/1.8
d	OAc	H	H	H	63	1/2.3
e	OAc	H	H	Me	76	1/2.4
f	H	H	H	OMe	91	1/3
g	H	OAc	H	OMe	59	1/2.7
h	H	OAc	OMe	OMe	81	1.7/1
i	OAc	H	H	OMe	73	1/2.2
j	OAc	H	OMe	OMe	88	1.7/1

Alkylation of 6-acetoxyquinolin-2(1*H*)-one (**1d**) with 2-bromoacetophenone and K_2CO_3 gave a mixture of 6-acetoxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (**4d**) and 6-acetoxy-2-(2-oxo-2-phenylethoxy)-quinoline (**3d**) in a ratio of 2.3:1 (Table 1, Entry d).[13] The mixture of **4b-j** and **3b-j** was obtained from **1b-j**

and **2b-j** respectively under the same reaction conditions. However, when quinolin-2(1*H*)-one (**1a**) was reacted with 2-bromoacetophenone and K_2CO_3, the sole *N*-alkylated product (**4a**) (Entry a) was obtained in 48% yield.

Scheme 2

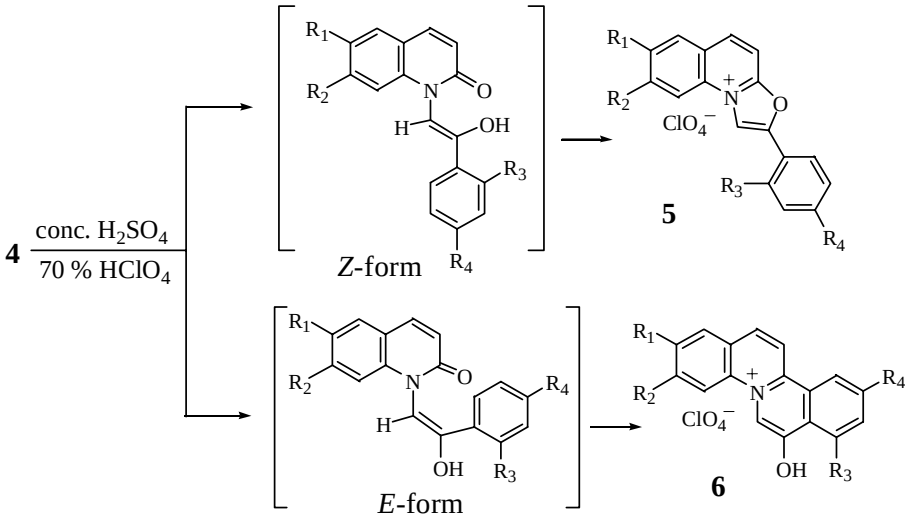


Table 2. Preparation of Oxazolo[3,2-*a*]quinolinium Perchlorates (**5a-e**) and Dibenzo[*a*,*f*]quinolizinium Perchlorates (**6f-j**) from *N*-Alkylated Quinolin-2(1*H*)-ones (**4a-j**)

Entry	R_1	R_2	R_3	R_4	Yield (%)	Ratio (**5**/**6**)
a	H	H	H	H	92	1/0
b	H	OH	H	H	80	1/0
c	H	OH	H	Me	94	1/0
d	OH	H	H	H	75	1/0
e	OH	H	H	Me	80	1/0
f	H	H	H	OMe	80	0/1
g	H	OH	H	OMe	65	0/1
h	H	OH	OMe	OMe	94	0/1
i	OH	H	H	OMe	83	0/1
j	OH	H	OMe	OMe	98	0/1

Although synthesis of 2-phenyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (**5a**) was previously described by Bradsher and Zinn in 1967,[12] the NMR spectral data were not reported. Under the same H_2SO_4-catalyzed cyclization conditions, oxazolo[3,2-*a*]quinolin-10-ylium perchlorate (**5b-e**) were obtained from **4b-e**

respectively through a *Z*-form enol intermediate in a yield of 75-94% (Table 2, Entries b-e). However, reaction of **4f-j** with catalytic H_2SO_4 gave dibenzo[*a,f*]quinolizinium perchlorates (**6f-j**) respectively through an *E*-form enol intermediate. We examined the structure of starting *N*-alkylated quinolin-2(1*H*)-ones (**4a-f**) and found that a methoxy group substituted at R_4 is required for the formation of tetracyclic dibenzo[*a,f*]-quinolizinium perchlorates.

In summary, the present report describes acid-catalyzed ring cyclization of 1-[2-oxo-2-(4-methoxyphenyl)-ethyl]-2(1*H*)-ones (R_4 = OMe) to form dibenzo[*a,f*]quinolizinium salts *via* an *E*-form enol intermediate. On the other hand, certain 2-phenyloxazolo[3,2-*a*]quinolinium perchlorates were synthesized by acid-catalyzed ring cyclization of 1-(2-oxo-2-phenyl)ethyl)-2(1*H*)-ones (R_4 = H or Me) *via* the *Z*-form enol intermediate.

EXPERIMENTAL

Melting points were determined on a Electrothermal IA9100 melting point apparatus and are uncorrected. Nuclear magnetic resonance (^{1}H and ^{13}C) spectra were recorded on a Varian Gemini 200 spectrometer or Varian-Unity-400 spectrometer. Chemical shifts were expressed in parts per million (δ) with tetramethylsilane (TMS) as an internal standard. TLC was performed on silica gel 60 F-254 plates purchased from E. Merck and Co. The elemental analyses were performed in the Instrument Center of National Science Countil at National Cheng-Kung University and National Chung-Hsing University using Heraeus CHN-O Rapid EA.

1-(2-Oxo-2-phenylethyl)quinolin-2(1*H*)-one (4a). Quinolin-2(1*H*)-one (0.29 g, 2 mmol), K_2CO_3 (028 g, 2 mmol) and dry DMF (10 mL) were stirred at rt for 5 min. To this solution was added 2-bromoacetophenone (0.40 g, 2 mmol) in dry DMF (10 mL) in one portion. The resulting mixture was continued to stir at rt for 24 h. (TLC monitoring) and then poured into ice water (100 mL). The mixture was extracted with CH_2Cl_2 (3 x 50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (silica gel; CH_2Cl_2/AcOEt = 20:1) and recrystallization from hexane/CH_2Cl_2 gave 4a (0.25 g, 48 %). mp 164-165 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.82 (s, 2H), 6.77 (d, 1H, *J* = 9.6 Hz), 6.98 (d, 1H, *J* = 8.4 Hz), 7.20 (m, 1H), 7.57 (m, 5H), 7.75 (d, 1H, *J* = 9.6 Hz), 8.08 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 48.71, 114.04, 120.79, 121.12, 122.31, 128.11, 128.91, 129.04, 130.72, 134.00, 134.82, 139.50, 139.93, 162.15, 192.34. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.44; H, 5.04; N, 5.32.

2-(7-Acetoxyquinolin-2-yloxy)-1-phenylethanone (3b) and 7-acetoxy-1-(2-oxo-2phenylethyl)quinolin-2(1*H*)-one (4b). Prepared from 7-acetoxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 1:1) gave **3b** (12 %) and **4b** (47 %). **3b**: mp 110-112 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 5.74 (s, 2H), 7.08 (d, 1H,

J = 8.8 Hz), 7.12 (dd, 1H, *J* = 8.2, 2.0 Hz), 7.42 (d, 1H, *J* = 2.4 Hz), 7.51 (t, 2H, *J* = 8.0 Hz), 7.61 (tt, 1H, *J* = 7.6, 1.2 Hz), 7.71 (d, 1H, *J* = 8.4 Hz), 8.03 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.14, 67.64, 112.58, 118.74, 119.32, 123.41, 127.94, 128.45, 128.80, 133.56, 135.01, 138.98, 146.76, 151.56, 161.30, 169.26, 194.21. Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 71.09; H, 4.81; N, 4.01.

4b: mp 154-155 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.24 (s, 3H), 5.84 (s, 2H), 6.65 (d, 1H, *J* = 9.4 Hz), 7.07 (dd, 1H, *J* = 8.4, 2.0 Hz), 7.31 (d, 1H, *J* = 2.0 Hz), 7.62 (m, 2H), 7.73 (d, 1H, *J* = 7.2 Hz), 7.81 (d, 1H, *J* = 8.4 Hz), 8.02 (d, 1H, *J* = 9.4 Hz), 8.13 (m, 2H). ^{13}C NMR (50 MHz, DMSO-d_6) δ 20.82, 49.29, 108.15, 116.53, 118.01, 120.07, 128.24, 128.89, 130.04, 134.03, 134.64, 139.79, 140.83, 152.53, 161.13, 168.93, 192.91. Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 70.99; H, 4.81; N, 4.37.

2-(7-Acetoxyquinolin-2-yloxy)-1-*p*-tolylethanone (3c) and 7-acetoxy-1-(2-oxo-2-*p*-tolylethyl)quinolin-2(1*H*)-one (4c). Prepared from 7-acetoxyquinolin-2(1*H*)-one and 2-bromo-4'-methylacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 10:1) gave **3c** (24 %) and **4c** (44 %). **3c**: mp 112-113 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.43 (s, 3H), 5.72 (s, 2H), 7.08 (d, 1H, *J* = 8.8 Hz), 7.12 (dd, 1H, *J* = 8.8, 2.2 Hz), 7.30 (m, 2H), 7.43 (d, 1H, *J* = 2.2 Hz), 7.71 (d, 1H, *J* = 8.8 Hz), 7.94 (m, 2H), 8.02 (d, 1H, *J* = 8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.10, 21.71, 67.54, 112.59, 118.71, 119.223, 123.36, 127.80, 128.39, 129.43, 132.45, 138.87, 144.40, 146.76, 151.50, 161.33, 169.21, 193.71. Anal. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.81; H, 5.20; N, 4.02.

4c: mp 189-190 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.45 (s, 3H), 5.71 (s, 2H), 6.71 (d, 1H, *J* = 9.4 Hz), 6.73 (d, 1H, *J* = 1.6 Hz) , 6.97 (dd, 1H, *J* = 8.4, 2.0 Hz), 7.33 (m, 2H), 7.57 (d, 1H, *J* = 8.6 Hz), 7.72 (d, 1H, *J* = 9.4 Hz), 7.98 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.06, 21.72, 48.79, 107.28, 116.22, 118.52, 120.68, 128.25, 129.53, 129.96, 132.24, 139.28, 140.62, 145.00, 152.45, 161.98, 168.88, 191.55. Anal. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.83; H, 5.25; N, 4.07.

2-(6-Acetoxyquinolin-2-yloxy)-1-phenylethanone (3d) and 6-acetoxy-1-(2-oxo-2-phenylethyl)quinolin-2(1*H*)-one (4d). Prepared from 6-acetoxyquinolin-2(1*H*)-one and 2-bromoacetophenone by the same procedure as described for **4a**. Flash chromatography (n-hexane/CH_2Cl_2 = 6:1) gave **3d** (19 %) and **4d** (44 %).[13] **3d**: mp 131-132^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.33 (s, 3H), 5.75 (s, 2H), 7.12 (d, 1H, *J* = 8.8 Hz), 7.27-8.07 (m, 8H), 7.69 (d, 1H, *J* = 8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.15, 67.57, 113.46, 118.43, 124.28, 125.49, 127.94, 128.55, 128.79, 133.56, 135.04, 138.87, 143.98, 146.87, 160.72, 169.60, 194.36. Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 70.80; H, 4.70; N,

4.54.

4d: mp 152-153 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 5.79 (s, 2H), 6.78 (d, 1H, *J* = 9.5 Hz), 6.95-8.11 (m, 8H), 7.70 (d, 1H, *J* = 8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.02, 48.88, 115.08, 120.90, 121.23, 122.12, 124.34, 128.13, 128.94, 134.08, 134.71, 137.35, 139.19, 145.30, 161.85, 169.41, 192.17. Anal. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found: C, 71.01; H, 4.69; N, 4.40.

2-(6-Acetoxyquinolin-2-yloxy)-1-*p*-tolylethanone (3e) and 6-acetoxy-1-(2-oxo-2-*p*-tolylethyl)quinolin-2(1*H*)-one (4e). Prepared from 6-acetoxyquinolin-2(1*H*)-one and 2-bromo-4'-methylacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 9:1) gave **3e** (22 %) and **4e** (54 %). **3e**: mp 89-90 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.44 (s, 3H), 5.75 (s, 2H), 7.12 (d, 1H, *J* = 8.8 Hz), 7.29 (m, 3H), 7.46 (d, 1H, *J* = 2.6 Hz), 7.72 (d, 1H, *J* = 9.0 Hz), 7.97 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.12, 21.73, 67.73, 113.52, 118.41, 124.31, 125.45, 128.03, 128.41, 129.44, 129.70, 132.49, 138.96, 143.78, 144.43, 146.91, 160.78, 169.52. Anal. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.56; H, 5.20; N, 3.81.

4e: m.p.186-188 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.45 (s, 3H), 5.76 (s, 2H), 6.77 (d, 1H, *J* = 9.6 Hz), 6.96 (d, 1H, *J* = 9.6 Hz) , 7.18 (dd, 1H, *J* = 9.0, 2.6 Hz), 7.30 (m, 3H), 7.69 (d, 1H, *J* = 9.6 Hz), 7.97 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.99, 21.74, 48.76, 115.13, 120.83, 121.20, 122.10, 124.29, 128.21, 129.57, 132.26, 137.38, 139.12, 145.05, 145.27, 161.85, 169.37, 191.71. Anal. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.99; H, 5.28, N, 4.29.

1-(4-Methoxyphenyl)-2-(quinolin-2-yloxy)ethanone (3f) and 1-[2-(4-methoxyphenyl)-2-oxoethyl]-quinolin-2(1*H*)-one (4f). Prepared from quinolin-2(1*H*)-one and 2-bromo-4'-methoxyacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 10:1) gave **3f** (23 %) and **4f** (68 %). **3f**: mp 98-99 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.88 (s, 3H), 5.73 (s, 2H), 6.97 (m, 2H), 7.10 (d, 1H, *J* = 8.8 Hz), 7.35 (m, 1H), 7.56 (m, 1H), 7.71 (m, 2H), 8.04 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.45, 67.30, 112.80, 113.91, 124.24, 125.36, 127.17, 127.37, 128.02, 129.46, 130.20, 139.20, 145.95, 160.79, 163.77, 192.83. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.62; H, 5.25; N, 4.75.

4f: mp 170-172 ^{o}C (hexane/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 5.76 (s, 2H), 6.75 (d, 1H, *J* = 9.2 Hz), 6.99 (m, 3H), 7.19 (m, 1H), 7.44 (m, 1H), 7.74 (d, 1H, *J* = 9.2 Hz) , 8.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.43, 55.58, 114.13, 114.22, 120.82, 121.21, 122.28, 127.95, 129.01, 130.50, 130.73, 139.68, 139.89, 162.22, 164.20, 190.82. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C,

73.59; H, 5.18; N, 4.76.

2-(7-Acetoxyquinolin-2-yloxy)-1-(4-methoxyphenyl)ethanone (3g) and 7-acetoxy-1-[2-(4-methoxyphenyl)-2-oxoethyl]quinolin-2(1*H*)-one (4g). Prepared from 7-acetoxyquinolin-2(1*H*)-one and 2-bromo-4'-methoxyacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 10:1) gave **3g** (16 %) and **4g** (43 %). **3g**: mp 124-126 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.89 (s, 3H), 5.72 (s, 2H), 6.99 (m, 2H), 7.10 (m, 2H), 7.45 (d, 1H, *J* = 2.2 Hz), 7.72 (d, 1H, *J* = 8.8 Hz), 8.03 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.14, 55.52, 67.58, 112.68, 113.99, 118.65, 119.33, 123.35, 127.95, 128.43, 130.24, 139.03, 146.62, 151.57, 161.39, 163.86, 169.25, 192.5. Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found: C, 68.23; H, 4.88; N, 3.75.

4g: mp 141-143 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.90 (s, 3H), 5.70 (s, 2H), 6.73 (d, 1H, *J* = 9.6 Hz), 6.75 (d, 1H, *J* = 2.2 Hz), 6.98 (dd, 1H, *J* = 8.4, 2.2 Hz), 7.00 (m, 2H), 7.58 (d, 1H, *J* = 8.4 Hz), 7.73 (d, 1H, *J* = 9.6 Hz), 8.06 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.13, 48.63, 55.57, 107.39, 114.10, 116.26, 118.59, 120.76, 127.81, 129.99, 130.54, 139.32, 140.74, 152.48, 162.07, 164.22, 168.96, 190.44. Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found: C, 68.28; H, 5.03; N, 3.77.

2-(7-Acetoxyquinolin-2-yloxy)-1-(2,4-dimethoxyphenyl)ethanone (3h) and 7-acetoxy-1-[2-(2,4-dimethoxyphenyl)-2-oxoethyl]quinolin-2(1*H*)-one (4h). Prepared from 7-acetoxyquinolin-2(1*H*)-one and 2-bromo-2',4'-dimethoxyacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 9:1) gave **3h** (51 %) and **4h** (30 %). **3h**: mp 147-149 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.88 (s, 3H), 3.98 (s, 3H), 5.64 (s, 2H), 6.51 (d, 1H, *J* = 2.2 Hz), 6.59 (dd, 1H, *J* = 8.8, 2.2 Hz), 7.07 (d, 1H, *J* = 8.8 Hz), 7.10 (dd, 1H, *J* = 8.8, 2.4 Hz), 7.44 (d, 1H, *J* = 2.2 Hz), 7.70 (d, 1H, *J* = 8.8 Hz), 7.96 (d, 1H, *J* = 8.8 Hz), 8.01 (d, 1H, *J* = 9.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.12, 55.59 (2C), 71.38, 98.07, 105.73, 112.82, 118.49, 118.65, 118.94, 123.25, 128.34, 133.06, 138.71, 146.78, 151.38, 161.31, 161.72, 165.07, 169.25, 193.08. Anal. Calcd for $C_{21}H_{19}NO_6$ H_2O: C, 65.21; H, 5.11; N, 3.62. Found: C, 65.24; H, 5.26; N, 3.32.

4h: mp 177-178 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.27 (s, 3H), 3.89 (s, 3H), 4.00 (s, 3H), 5.63 (s, 2H), 6.54 (d, 1H, *J* = 2.2 Hz), 6.59 (dd, 1H, *J* = 8.8, 2.2 Hz), 6.72 (d, 1H, *J* = 9.6 Hz), 6.76 (d, 1H, *J* = 2.0 Hz), 6.96 (dd, 1H, *J* = 8.4, 2.0 Hz), 7.57 (d, 1H, *J* = 8.4 Hz), 7.72 (d, 1H, *J* = 9.6 Hz), 7.97 (d, 1H, *J* = 8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.13, 53.23, 55.65 (2C), 98.13, 105.87, 107.57, 116.03, 118.32, 118.57, 120.93, 129.82, 133.54, 139.09, 140.85, 152.38, 161.63, 162.22, 165.51, 169.01, 190.66. Anal. Calcd for $C_{21}H_{19}NO_6$: C, 66.13; H, 5.02; N, 3.67. Found: C, 66.06; H, 5.19; N, 3.56.

2-(6-Acetoxyquinolin-2-yloxy)-1-(4-methoxyphenyl)ethanone (3i) and 6-acetoxy-1-[2-(4-methoxy-

phenyl)-2-oxoethyl]quinolin-2(1*H*)-one (4i). Prepared from 6-acetoxyquinolin-2(1*H*)-one and 2-bromo-4'-methoxyacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 10:1) gave **3i** (23 %) and **4i** (50 %). **3i**: mp 112-114 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.89 (s, 3H), 5.74 (s, 2H), 6.98 (m, 2H), 7.12 (d, 1H, *J* = 8.8 Hz), 7.30 (dd, 1H, *J* = 9.0, 2.6 Hz), 7.45 (d, 1H, *J* = 2.6 Hz), 7.74 (d, 1H, *J* = 8.8 Hz), 8.03 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.11, 55.49, 67.54, 113.54, 113.95, 118.41, 124.30, 125.41, 127.93, 128.38, 130.22, 138.96, 143.75, 146.87, 160.80, 163.82, 169.55, 192.61. Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found: C, 68.57; H, 4.99; N, 3.96.

4i: mp 187-188 ^oC (hexane/CH_2Cl_2); ^1H NMR (400 MHz, DMSO-d_6) δ 2.30 (s, 3H), 3.89 (s, 3H), 5.86 (s, 2H), 6.72 (d, 1H, *J* = 9.6 Hz), 7.13 (m, 2H), 7.31 (dd, 1H, *J* = 9.2, 2.8 Hz), 7.37 (d, 1H, *J* = 9.2 Hz), 7.57 (d, 1H, *J* = 2.8 Hz), 7.98 (d, 1H, *J* = 9.6 Hz), 8.12 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.73, 48.68, 55.64, 114.12, 115.98, 120.54, 120.81, 121.46, 124.72, 127.58, 130.53, 137.44, 139.36, 144.81, 160.97, 163.78, 169.42, 191.36. Anal. Calcd for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found: C, 68.48; H, 4.98; N, 4.00.

2-(6-Acetoxyquinolin-2-yloxy)-1-(2,4-dimethoxyphenyl)ethanone (3j) and 6-acetoxy-1-[2-(2,4-dimethoxyphenyl)-2-oxoethyl]quinolin-2(1*H*)-one (4j). Prepared from 6-acetoxyquinolin-2(1*H*)-one and 2-bromo-2',4'-dimethoxyacetophenone by the same procedure as described for **4a**. Flash chromatography (CH_2Cl_2/AcOEt = 6:1) gave **3j** (55 %) and **4j** (33 %). **3j**: mp 158-159 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.88 (s, 3H), 3.98 (s, 3H), 5.64 (s, 2H), 6.51 (d, 1H, *J* = 2.2 Hz), 6.58 (dd, 1H, *J* = 8.8, 2.2 Hz), 7.11 (d, 1H, *J* = 8.8 Hz), 7.28 (dd, 1H, *J* = 9.0, 2.6 Hz), 7.44 (d, 1H, *J* = 2.6 Hz), 7.70 (d, 1H, *J* = 8.8 Hz), 7.95 (d, 1H, *J* = 8.8 Hz), 7.98 (d, 1H, *J* = 9.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.10, 55.59 (2C), 71.32, 98.09, 105.69, 113.69, 118.33, 118.58, 124.03, 125.31, 128.43, 133.02, 138.64, 143.98, 146.68, 161.16, 161.27, 165.05, 169.56, 193.24. Anal. Calcd for $C_{21}H_{19}NO_6$: C, 66.13; H, 5.02; N, 3.67. Found: C, 66.11; H, 5.21; N, 3.54.

4j: mp 210-212 ^oC (hexane/CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.89 (s, 3H), 4.00 (s, 3H), 5.68 (s, 2H), 6.54 (d, 1H, *J* = 2.2 Hz), 6.58 (dd, 1H, *J* = 8.8, 2.2 Hz), 6.78 (d, 1H, *J* = 9.6 Hz), 7.00 (d, 1H, *J* = 9.2 Hz), 7.18 (dd, 1H, *J* = 9.2, 2.6 Hz), 7.33 (d, 1H, *J* = 2.6 Hz), 7.68 (d, 1H, *J* = 9.6 Hz), 7.97 (d, 1H, *J* = 8.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.03, 53.17, 55.65 (2C), 98.18, 105.89, 115.46, 118.36, 120.60, 121.16, 122.31, 124.16, 133.52, 137.59, 138.91, 145.14, 161.60, 162.03, 165.51, 169.42, 190.77. Anal. Calcd for $C_{21}H_{19}NO_6$: C, 66.13; H, 5.02; N, 3.67. Found: C, 66.29; H, 5.12; N, 3.64.

2-Phenyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (5a). Compound **4a** (0.2 g, 0.76 mmol) was

dissolved in 99% H_2SO_4 (10 mL) and the solution was stirred at rt for 24 h. The resulting mixture was poured into cold ether (300 mL) and the precipitated solid was collected, dissolved in a minimum quantity of water and 70% perchloric acid added until there was no further precipitation. The precipitated perchlorate salt was collected and recrystallized from MeOH to afford **5a** (0.24g, 92 %). mp 271-272 ^oC [ref[12] 272.5-275 ^oC]; ^1H NMR (400 MHz, DMSO-d_6) δ 7.72 (m, 3H), 8.04 (m, 3H), 8.30 (dt, 1H, *J* = 8.4, 1.2 Hz), 8.48 (d, 1H, *J* = 2.8 Hz), 8.51 (s, 1H), 8.67 (d, 1H, *J* = 8.4 Hz), 9.06 (d, 1H, *J* = 9.2 Hz), 10.18 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 109.21, 110.69, 117.30, 124.24, 125.01, 125.30, 129.20, 129.87, 130.46, 131.02, 131.79, 133.86, 142.22, 152.32, 153.0. Anal. Calcd for $C_{17}H_{12}NO_5Cl$: C, 59.06; H, 3.50; N, 4.05. Found: C, 58.79; H, 3.48; N, 4.00.

The same procedure was used to convert each of the compounds **4b-e** to **5b-e** and **4f-j** to **6f-j**, repectively.

8-Hydroxy-2-phenyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (5b). 80 % yield. mp 267-268 ^oC (MeOH); ^1H NMR (400 MHz, DMSO-d_6) δ 7.51 (dd, 1H, *J* = 8.8, 2.0 Hz), 7.69 (m, 3H), 7.84 (d, 1H, *J* = 2.4 Hz), 8.04 (d, 2H, *J* = 7.2 Hz), 8.16 (d, 1H, *J* = 9.2 Hz), 8.31 (d, 1H, *J* = 9.2 Hz), 8.88 (d, 1H, *J* = 9.2 Hz), 9.96 (s, 1H), 11.72 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 101.01, 104.44, 110.22, 118.64, 120.03, 124.41, 125.23, 129.74, 131.58, 132.39, 133.36, 141.90, 151.74, 153.23, 162.77. Anal. Calcd for $C_{17}H_{12}NO_6Cl$: C, 56.45; H, 3.46; N, 3.87. Found: C, 56.24; H, 3.34; N, 3.87.

8-Hydroxy-2-*p*-tolyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (5c). 94 % yield. mp 274-275 ^oC (MeOH); ^1H NMR (400 MHz, DMSO-d_6) δ 2.42 (s, 3H), 7.49 (m, 3H), 7.80 (d, 1H, *J* = 1.2 Hz), 7.90 (m, 2H), 8.13 (d, 1H, *J* = 9.2 Hz), 8.30 (d, 1H, *J* = 8.8 Hz), 8.86 (d, 1H, *J* = 9.6 Hz), 9.88 (s, 1H), 11.67 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.08, 100.96, 104.38, 109.49, 118.62, 120.00, 121.60, 125.13, 130.23, 132.36, 133.28, 141.67, 141.76, 151.97, 152.99, 162.73. Anal. Calcd for $C_{18}H_{14}NO_6Cl$: C, 57.53; H, 3.76; N, 3.73. Found: C, 57.41; H, 3.79; N, 3.67.

7-Hydroxy-2-phenyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (5d). 75 % yield. mp 224-226 ^oC (MeOH); ^1H NMR (400 MHz, DMSO-d_6) δ 7.69 (m, 5H), 8.02 (d, 2H, *J* = 7.6 Hz), 8.37 (d, 1H, *J* = 9.6 Hz), 8.50 (d, 1H, *J* = 9.2 Hz), 8.87 (d, 1H, *J* = 9.6 Hz), 10.06 (s, 1H), 10.88 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 108.99, 110.53, 112.14, 118.87, 124.33, 124.71, 125.22, 126.86, 129.80, 131.66, 140.95, 151.60, 152.09, 157.63. Anal. Calcd for $C_{17}H_{12}NO_6Cl$ 0.6 H_2O: C, 54.81; H, 3.57; N, 3.76. Found: C, 54.67; H, 3.63; N, 3.61.

7-Hydroxy-2-*p*-tolyloxazolo[3,2-*a*]quinolin-10-ylium perchlorate (5e). 80 % yield. mp 255-257 ^oC (MeOH); ^1H NMR (400 MHz, DMSO-d_6) δ 2.43 (s, 3H), 7.51 (d, 2H, *J* = 8.0 Hz), 7.65 (d, 1H, *J* = 2.4 Hz), 7.72 (dd, 1H, *J* = 9.2, 2.8 Hz), 7.90 (d, 2H, *J* = 8.4 Hz), 8.34 (d, 1H, *J* = 9.6 Hz), 8.47 (d, 1H, *J* = 9.2 Hz),

8.84 (d, 1H, *J* = 9.6 Hz), 9.96 (s, 1H), 10.84 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.11, 108.94, 109.82, 112.10, 118.85, 121.57, 124.28, 124.69, 125.18, 126.85, 130.32, 140.70, 141.91, 151.40, 152.34, 157.59. Anal. Calcd for $C_{18}H_{14}NO_6Cl$ 0.3 H_2O: C, 56.72; H, 3.86; N, 3.68. Found: C, 56.81; H, 3.95; N, 3.54.

6-Hydroxy-9-methoxy-4*b*-azoniachrysene perchlorate (6f). 80 % yield. mp 395 °C (decomposed from MeOH/AcOH); ^{1}H NMR (200 MHz, TFA-d_8) δ 4.12 (s, 3H), 7.38 (d, 1H, *J* = 9.0 Hz), 8.09 (m, 2H), 8.33 (m, 3H), 8.54 (d, 1H, *J* = 8.4 Hz), 8.88 (m, 2H), 9.41 (s, 1H). ^{13}C NMR (50 MHz, TFA-d_8) δ 57.62, 109.35, 110.08, 115.23, 117.74, 118.68, 127.74, 129.98, 132.31, 132.66, 133.33, 133.41, 137.10, 144.96, 154.92, 156.47, 162.22. Anal. Calcd for $C_{18}H_{14}NO_6Cl$ 0.3 H_2O: C, 56.72; H, 3.86; N, 3.68. Found: C, 56.77; H, 3.66; N, 3.48.

3,6-Dihydroxy-9-methoxy-4*b*-azoniachrysene perchlorate (6g). 65 % yield. mp 399 °C (decomposed from MeOH/AcOH); ^{1}H NMR (400 MHz, TFA-d_8) δ 4.12 (s, 3H), 7.37 (d, 1H, *J* = 8.8 Hz), 7.67 (dd, 1H, *J* = 8.8, 2.0 Hz), 7.88 (d, 2H, *J* = 9.6 Hz), 8.24 (d, 2H, *J* = 8.8 Hz), 8.73 (d, 1H, *J* = 9.2 Hz), 8.82 (s, 1H), 9.12 (s, 1H). ^{13}C NMR (50 MHz, TFA-d_8) δ 57.63, 103.15, 105.85, 109.54, 115.21, 117.82, 122.40, 123.06, 129.95, 133.31, 134.69, 135.50, 144.34, 155.39, 156.05, 162.26, 164.30. Anal. Calcd for $C_{18}H_{14}NO_7Cl$: C, 55.19; H, 3.60; N, 3.58. Found: C, 55.17; H, 3.76; N, 3.32.

3,6-Dihydroxy-7,9-dimethoxy-4*b*-azoniachrysene perchlorate (6h). 94 % yield. mp 370 °C (decomposed from MeOH/AcOH); ^{1}H NMR (400 MHz, TFA-d_8) δ 4.14 (s, 3H), 4.31 (s, 3H), 6.93 (s, 1H), 7.64 (d, 1H, *J* = 8.8 Hz), 7.92 (m, 2H), 8.23 (d, 1H, *J* = 9.2 Hz), 8.70 (d, 1H, *J* = 9.2 Hz), 8.78 (m, 2H). ^{13}C NMR (50 MHz, TFA-d_8) δ 57.75, 58.01, 98.09, 102.97, 106.14, 106.92, 111.10, 118.04, 122.41, 122.67, 130.70, 134.79, 135.31, 144.18, 152.58, 154.51, 162.53, 163.86, 164.62. Anal. Calcd for $C_{19}H_{16}NO_8Cl$ 0.6 H_2O: C, 52.75; H, 4.01; N, 3.24. Found: C, 52.76; H, 4.06; N, 3.20.

2,6-Dihydroxy-9-methoxy-4*b*-azoniachrysene perchlorate (6i). 83 % yield. mp 397 °C (decomposed from MeOH/AcOH); ^{1}H NMR (400 MHz, TFA-d_8) δ 4.12 (s, 3H), 7.38 (d, 1H, *J* = 8.8 Hz), 7.80 (d, 1H, *J* = 2.4 Hz), 7.90 (dd, 1H, *J* = 9.6, 2.4 Hz), 8.04 (d, 1H, *J* = 9.6 Hz), 8.24 (dd, 1H, *J* = 8.8, 2.0 Hz), 8.44 (d, 1H, *J* = 9.2 Hz), 8.71 (d, 1H, *J* = 9.6 Hz), 8.85 (s, 1H), 9.32 (s, 1H). ^{13}C NMR (100 MHz, TFA-d_8) δ 57.67, 109.82, 110.11, 115.58, 117.83, 120.61, 127.25, 128.25, 129.53, 129.98, 132.32, 133.43, 143.71, 153.96, 156.44, 158.60, 162.27. Anal. Calcd for $C_{18}H_{14}NO_7Cl$ 0.5 H_2O: C, 53.95; H, 3.77; N, 3.50. Found: C, 53.76; H, 3.96; N, 3.49

2,6-Dihydroxy-7,9-dimethoxy-4b-azoniachrysene perchlorate (6j). 98 % yield. mp 219 °C (decomposed from MeOH/AcOH); ^{1}H NMR (400 MHz, TFA-d_8) δ 4.15 (s, 3H), 4.30 (s, 3H), 6.95 (s, 1H), 7.79 (d, 1H,

J = 2.4 Hz), 7.90 (dd, 1H, *J* = 9.2, 2.4 Hz), 8.07 (d, 1H, *J* = 9.6 Hz), 8.35 (d, 1H, *J* = 9.2 Hz), 8.67 (d, 1H, *J* = 9.6 Hz), 8.79 (s, 1H), 8.91 (s, 1H). ^{13}C NMR (50 MHz, TFA-d_8) δ 57.80, 58.16, 98.11, 107.00, 119.93, 111.63, 115.71, 120.32, 127.04, 128.14, 129.51, 131.02, 131.32, 143.56, 152.88, 153.12, 158.39, 163.99, 164.89. Anal. Calcd for $C_{19}H_{16}NO_8Cl$ 3.0 H_2O: C, 47.96; H, 4.66; N, 2.94. Found: C, 47.62; H, 4.32; N, 2.93.

ACKNOWLEDGMENTS

We gratefully acknowledge the *National Science Council* for providing financial support and the *National Center for High-Performance Computing* for providing computer resources and chemical database services.

REFERENCES

1. T. Nakanishi, M. Suzuki, A. Saimoto, and T. Kabasawa, *J. Nat. Prod.*, 1999, **62**, 864.
2. H. Ishii, Y-I. Ichikawa, E. Kawanabe, M. Ishikawa, T. Ishikawa, K. Kuretani, M. Inomata, and A. Hoshi, *Chem. Pharm. Bull*., 1985, **33**, 4139.
3. Z. Taira, M. Matsumoto, S. Ishida, T. Ichikawa, and Y. Sakiya, *Chem. Pharm. Bull*., 1994, **42**, 1556.
4. L-K. Wang, B. D. Rogers, and S. M. Hecht, *Chem. Res. Toxicol*., 1996, **9**, 75.
5. A. Ikuta and H. Itokawa, *Phytochemistry*, 1982, **21**, 1419.
6. M. Cushman, D. A. Patrick, P. H. Toma, and S. R. Byrn, *Tetrahedron Lett*., 1989, **30**, 7161.
7. S. Arai and M. Hida, *Adv. Heterocycl. Chem*., 1992, **55**, 261.
8. A. Furstner and A. Ernst, *Tetrahedron*, 1995, **51**, 773.
9. S. Arai, M. Ishikura, and T. Yamagishi, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1561.
10. A. Fozard and C. K. Bradsher, *J. Org. Chem*., 1966, **31**, 3683.
11. L. Marin and C. K. Bradsher, *J. Heterocycl. Chem*., 1970, **7**, 1421.
12. C. K. Bradsher and M. F. Zinn, *J. Heterocycl. Chem*., 1967, **4**, 66.
13. T-C. Wang, Y-L. Chen, C-C. Tzeng, S-S. Liou, W-F. Tzeng, Y-L. Chang, and C-M. Teng, *Helv. Chim. Acta*, 1998, **81**, 1038.