The Synthesis of Novel Polycyclic Heterocyclic Ring Systems *via* Photocyclization. 21 [1,2]. Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]-quinoline, Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*][1,2,4]-triazolo[4,3-*a*]quinoline and Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]-tetrazolo[1,5-*a*]quinoline

Jiann-Kuan Luo* [3], Ronald F. Federspiel and Raymond N. Castle

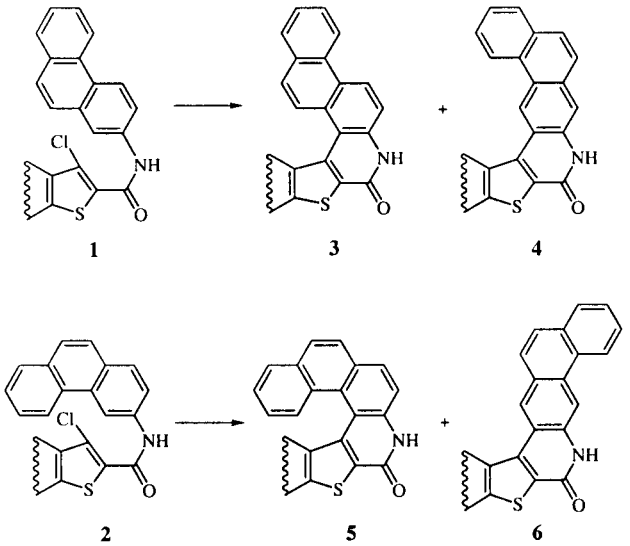
Department of Chemistry
University of South Florida, Tampa, FL 33620-5250
Received May 27, 1999

Photocyclization of 3-chloro-*N*-(3-phenanthryl)naphtho[1,2-*b*]thiophene-2-carboxamide (**12**) furnished only one of the two possible isomers, *i.e.*, naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**13**), which was further elaborated to yield the unsubstituted ring system **7**, its triazole **8** and tetrazole **9**. The structural confirmation of **7** was accomplished by the total assignment of its ^1H and ^{13}C nmr spectra utilizing the concerted two-dimensional nmr spectroscopic experiments.

J. Heterocyclic Chem., **37**, 171 (2000).

The oxidative photocyclization of carboxamides **1** and **2** should theoretically yield a mixture of lactams **3/4** and **5/6**, respectively (Scheme 1). In our recent reports [2e, 2k, 2p, 2r, 2t], we have demonstrated that photocyclization of **1** consistantly affords a mixture of **3** and **4**, with **3** as the major product. On the other hand, the photocyclization of **2** is less predictable, but the angular product, **5**, is always obtained if not both of **5** and **6**. This unusual reactivity prompted us to study a series of photocyclization of isomeric phenanthryl anilides **1** and **2**. It was, in part, for this purpose that we report in this paper the syntheses of three previously unknown heterocyclic ring systems, namely, naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**7**), naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*][1,2,4]-triazolo[4,3-*a*]quinoline (**8**) and naphtho[2',1':4,5]-thieno[2,3-*c*]naphtho[1,2-*f*]tetrazolo[1,5-*a*]quinoline (**9**), and the confirmation of their structures through two-dimensional nmr spectroscopy.

Scheme 1



1 **3** **4**

2 **5** **6**

The synthetic pathway to compounds **7**, **8**, and **9** is illustrated in Scheme 2. Upon treatment of 3-chloronaphtho[1,2-*b*]thiophene-2-carbonyl chloride (**10**) [4,5] with 3-aminophenanthrene (**11**) in benzene 3-chloro-*N*-(3-phenanthryl)naphtho[1,2-*b*]thiophene-2-carboxamide (**12**) was obtained in 80% yield. Irradiation of the amide **12** in a benzene/cyclohexane mixture (v/v, 1:1) containing triethylamine with a 450 watt Hanovia medium pressure mercury vapor lamp provided only one of the two possible cyclization products in 92% yield. The structure of the product was tentatively assigned as naphtho[2',1':4,5]-thieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**13**) based on the lack of two singlets in its proton nmr spectrum. Chlorination of the lactam **13** with phosphorus oxychloride afforded 6-chloronaphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**14**) in 58% yield. Hydrazination of the chloride **14** was carried out by refluxing it with anhydrous hydrazine in a mixture of benzene and ethanol to yield 6-hydrazinonaphtho[2',1':4,5]thieno[2,3-*c*]naphtho-[1,2-*f*]quinoline (**15**) in 87% yield. The unsubstituted novel ring system **7** was realized in 74% yield by refluxing the hydrazine **15** with a mixture of 10% copper sulfate solution and concentrated aqueous acetic acid. When the hydrazine **15** was allowed to react with trimethyl orthoformate in refluxing ethanol, naphtho[2',1':4,5]-thieno[2,3-*c*]naphtho[1,2-*f*][1,2,4]triazolo[4,3-*a*]quinoline (**8**) was obtained in 78% yield, whereas treatment of **15** with sodium nitrite in 70% aqueous acetic acid resulted in a 55% yield of naphtho[2',1':4,5]thieno[2,3-*c*]naphtho-[1,2-*f*]tetrazolo[1,5-*a*]quinoline (**9**).

The total assignments of ^1H and ^{13}C nmr spectra of **7** were achieved by the concerted utilization of COSY [6], HMQC [7], HMBC [8], and NOESY [9] experiments as discussed in previous reports [2d-e, 2j-m, 2o-t]. The ^1H and ^{13}C chemical shifts of **7** are summarized in Table 1.

In conclusion, our study shows that the oxidative photocyclization of 3-chloro-*N*-(3-phenanthryl)naphtho[1,2-*b*]-

Scheme 2

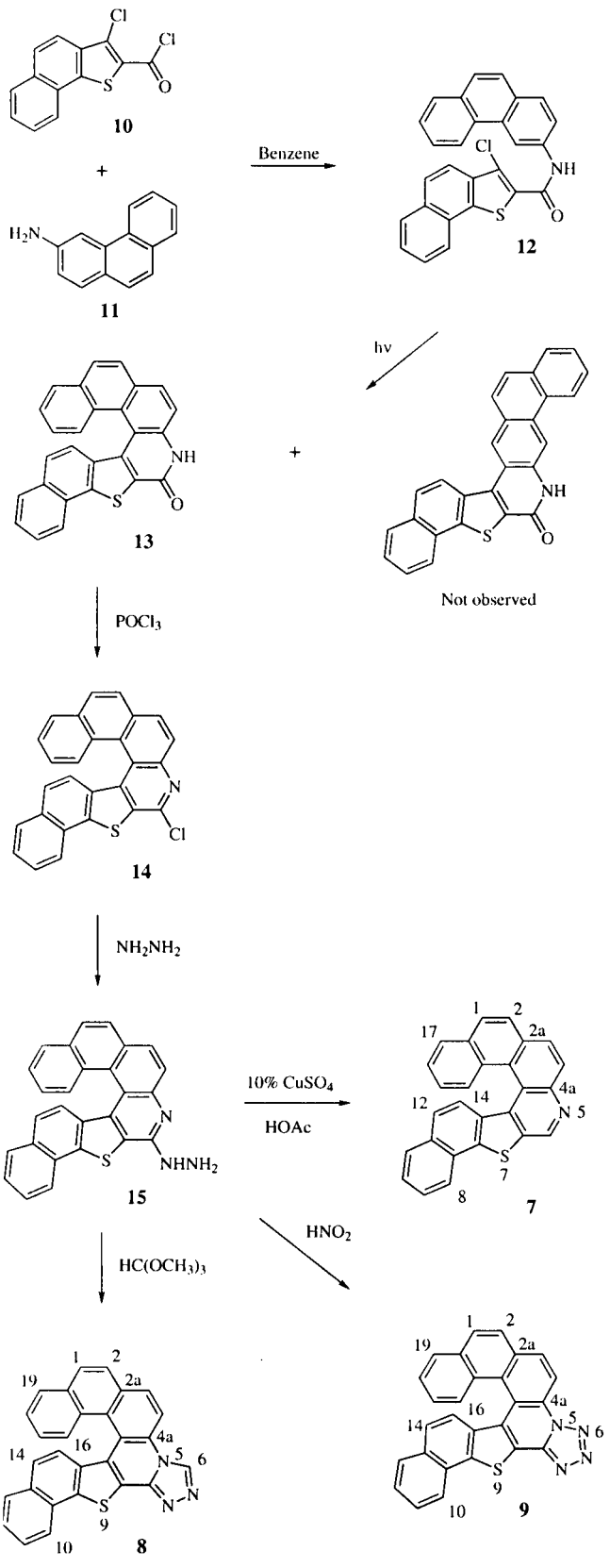


Table 1

^1H and ^{13}C NMR Chemical Shift Assignments and Observed Proton-Carbon Multiple-Bond Correlations for Compound **7** in Deuteriochloroform at 298°K at Observation Frequencies of 360.13 and 90.56 MHz, Respectively

Position	δH	δC	Two-Bond Correlation	Three-Bond Correlation
1	8.08	128.7		H17
2	7.99	126.0		H3
2a		131.9		H1, H4
3	8.10	128.8		H2
4	8.28	128.8		
4a		145.8		H3, H6
6	9.54	144.5		
6a		138.6	H6	
7a		139.6		H8, H13
7b		128.6		H9, H11, H12
8	8.29	124.6		H10
9	7.65	126.8		H11
10	7.59	127.4		H8
11	7.82	128.7		H9, H12
11a		132.1		H8, H10, H13
12	7.22	123.6		H11
13	7.01	124.6		
13a		132.9		H12
13b		133.1		H6
13c		119.6		H4
13d		125.6		H2, H3, H14
13e		130.5		H1, H15, H17
14	8.01	128.4		H16
15	7.03	126.1		H17
16	7.48	126.3		H14
17	8.03	128.1		H1, H15
17a		131.7		H2, H14, H16

thiophene-2-carboxamide (**12**) gives only naphtho-[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**13**), which can be further elaborated to provide polycyclic heterocyclic novel ring systems **7**, **8**, and **9**. The confirmation of their structures can be achieved by the concerted utilization of two-dimensional nmr spectroscopic methods.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting apparatus and are uncorrected. The ir spectra were recorded on a Beckmann FT1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm-1. The 1H nmr spectra of the intermediates were obtained on a Bruker AMX360 MHz NMR spectrometer in the solvent indicated with TMS as the internal standard. Chemical shifts are reported in ppm (δ) and J values in Hz. Analysis (tlc) were performed on Sigma precoated silica gel plates containing a fluorescent indicator. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

The ^1H and ^{13}C spectra of **7**, **8**, and **9** were acquired on a Bruker AMX360 MHz NMR spectrometer operating at an observation frequency of 360.13 MHz for ^1H and 90.56 for ^{13}C.

All experiments were performed using an inverse-geometry 5 mm broad band probe. Pulse widths (90°) for ^1H and ^{13}C were 7.8 and

15.5 μsec, respectively. The COSY spectra were recorded using the Bruker pulse program *(COSY90)* [6]. The HMQC experiments were performed using the Bruker pulse program *(invbdgtp)* with the BIRD sequence optimized for direct couplings (165 Hz $^1J_{CH}$) [7]. The HMBC spectra were obtained using the Bruker pulse program *(inv4lplrnd)* [8] optimized for 10 Hz $^3J_{CH}$ couplings. The NOESY experiments were performed using the Bruker pulse program *(noesytp)* [9].

3-Chloro-*N*-(3-phenanthryl)naphtho[1,2-*b*]thiophene-2-carboxamide (**12**).

A mixture of 2.40 g (8.54 mmoles) of 3-chloronaphtho[1,2-*b*]-thiophene-2-carbonyl chloride (**10**) [4,5] and 1.65 g (8.54 mmoles) of 3-aminophenanthrene (**11**) in 80 ml of benzene was heated under reflux for four hours. After cooling to room temperature, the solid was collected by filtration and recrystallized from benzene to yield 3.00 g (6.85 mmoles, 80%) of amide **12** as colorless needles, mp 226-229°; tlc (benzene) R_f 0.67; ir (potassium bromide): 1653 (C=O stretching); ^{1}H nmr (DMSO-d_6): 120°, δ 7.61-8.30 (m, 13H, ArH), 8.66 (dd, $J_{1',2'}$ = 7.0 Hz, $J_{2',4'}$ = 2.4 Hz, 1H, H2'), 9.18 (d, $J_{2',4'}$ = 2.4 Hz, 1H, H4'), 10.38 (br s, 1H, NH).

Anal. Calcd. for $C_{27}H_{16}ClNOS$: C, 74.05; H, 3.68; N, 3.20; S, 7.32. Found: C, 73.74; H, 3.79; N, 2.98; S, 7.35.

Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**13**).

A mixture of 0.50 g (1.14 mmoles) of amide **12**, 240 ml of cyclohexane, 240 ml of benzene and 0.12 g of triethylamine was irradiated with a 450 watt medium pressure Hanovia mercury vapor lamp for four hours. A slow stream of air was passed through the solution during the course of the reaction. The solid was collected by filtration and washed with water to obtain 0.42 g (1.05 mmoles, 92%) of lactam **13**, mp > 300°; ir (potassium bromide): 1635 (C=O stretching); ^{1}H nmr (DMSO-d_6): δ 6.76 (d, $J_{12,13}$ = 9.0 Hz, 1H, H13), 7.00 (m, 1H, ArH), 7.28-8.40 (m, 12H, ArH). The compound was used for the next step without further purification because of low solubility.

6-Chloronaphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**14**).

A mixture of 2.15 g (5.35 mmoles) of lactam **13** and 60 ml of phosphorus oxychloride was heated at 100-110° for four hours. After cooling to room temperature the mixture was slowly poured into 800 ml of ice-water with vigorous stirring. The solid was collected by filtration and washed with water. The solid was recrystallized from cyclohexane/benzene mixture to give 1.30 g (3.10 mmoles, 58%) of chloride **14** as yellow crystals, mp 248-249°; tlc (benzene) R_f 0.58; ^{1}H nmr (deuteriochloroform): δ 6.96 (d, $J_{12,13}$ = 9.0 Hz, 1H, H13), 7.02-7.07 (m, 1H, ArH), 7.22 (d, $J_{12,13}$ = 9.0 Hz, 1H, H12), 7.49 (m, 1H, ArH), 7.59-7.69 (m, 2H, ArH), 7.82 (dd, J = 7.5 Hz, J = 1.5 Hz, 1H, ArH), 7.98 (d, J = 8.6 Hz, 1H, ArH), 7.99 (dd, J = 8.6 Hz, J = 2.0 Hz, 1H, ArH), 8.05 (dd, J = 8.0 Hz, J = 1.5 Hz, 1H, ArH), 8.09 (d, J = 9.0 Hz, 1H, ArH), 8.11 (d, $J_{3,4}$ = 8.6 Hz, 1H, H3), 8.20 (d, $J_{3,4}$ = 8.6 Hz, 1H, H4), 8.31 (dd, $J_{8,9}$ = 8.2 Hz, $J_{8,10}$ = 1.2 Hz, 1H, H8).

Anal. Calcd. for $C_{27}H_{14}ClNS$: C, 77.22; H, 3.36; N, 3.34; S, 7.64. Found: C, 77.27; H, 3.47; N, 3.11; S, 7.83.

6-Hydrazinonaphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**15**).

To a boiling mixture of 0.57 g (1.36 mmoles) of chloride **14** in 10 ml of benzene and 25 ml of absolute ethanol, 10 ml of anhydrous hydrazine was added dropwise over a period of 30 minutes. The resulting solution was heated at 100-110° for 15 hours. After cooling to room temperature the yellow precipitate was collected by filtration and washed with ethanol to produce 0.49 g (1.18 mmoles, 87%) of hydrazine **15** as yellow crystals, mp 268-269° dec.; tlc (chloroform) R_f 0.096; ^{1}H nmr (DMSO-d_6): δ 5.00 (br s, 2H, NH_2), 6.88 (d, $J_{12,13}$ = 9.0 Hz, 1H, H13), 7.01 (t, $J_{14,15}$ = $J_{15,16}$ = 7.3 Hz, 1H, H15), 7.28 (d, $J_{12,13}$ = 9.0 Hz, 1H, H12), 7.47 (t, $J_{15,16}$ = $J_{16,17}$ = 7.3 Hz, 1H, H16), 7.63 (t, $J_{9,10}$ = $J_{10,11}$ = 7.1 Hz, 1H, H10), 7.71 (t, $J_{8,9}$ = $J_{9,10}$ = 7.1 Hz, 1H, H9), 7.85 (d, $J_{1,2}$ = 8.5 Hz, 1H, H2), 7.91-8.08 (m, 6H, ArH), 8.32 (d, $J_{3,4}$ = 7.8 Hz, 1H, H4), 8.91 (br s, 1H, NH). The compound was used for the next step without further purification due to its low solubility.

Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**7**).

To a mixture of 0.12 g (0.29 mmole) of hydrazine **15** in 10 ml of glacial acetic acid and 5 ml of water was added dropwise 10 ml of 10% copper sulfate solution. The mixture was heated under reflux for 24 hours. After cooling to room temperature the mixture was neutralized with 2*N* sodium hydroxide solution. The solid thus obtained was collected by filtration and washed with water. The solid was recrystallized from benzene to give 0.083 g (0.22 mmole, 74%) of the unsubstituted quinoline **7** as yellowish prisms, mp 274-275°; tlc (chloroform) R_f 0.38.

Anal. Calcd. for $C_{27}H_{15}NS$: C, 84.13; H, 3.92; N, 3.63. Found: C, 84.00; H, 4.12; N, 3.49.

Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*][1,2,4]triazolo-[4,3-*a*]quinoline (**8**).

A mixture of 0.15 g (0.36 mmole) of hydrazine **15**, 10 ml of trimethyl orthoformate, and 20 ml of ethanol was heated at 100-110° for 40 hours. After cooling to room temperature the precipitate was collected by filtration. The solid was recrystallized from benzene to afford 0.12 g (0.28 mmole, 78%) of triazole **8** as colorless crystals, mp > 300°; tlc (chloroform:ethyl acetate, 5:1) R_f 0.16; ^{1}H nmr (deuteriochloroform and a drop of trifluoroacetic acid-d): δ 6.81 (d, $J_{14,15}$ = 9.1 Hz, 1H, H15), 7.05 (t, $J_{16,17}$ = $J_{17,18}$ = 7.5 Hz, 1H, H17), 7.24 (d, $J_{14,15}$ = 9.1 Hz, 1H, H14), 7.57 (t, $J_{17,18}$ = $J_{18,19}$ = 7.5 Hz, 1H, H18), 7.68 (t, $J_{11,12}$ = $J_{12,13}$ = 7.6 Hz, 1H, H12), 7.73 (t, $J_{10,11}$ = $J_{11,12}$ = 7.6 Hz, 1H, H11), 7.82 (d, $J_{12,13}$ = 7.6 Hz, 1H, H13), 7.89 (d, $J_{16,17}$ = 7.5 Hz, 1H, H16), 8.03 (d, $J_{1,2}$ = 8.7 Hz, 1H, H2), 8.09 (d, $J_{18,19}$ = 7.5 Hz, 1H, H19), 8.18 (d, $J_{1,2}$ = 8.7 Hz, 1H, H1), 8.28 (d, $J_{10,11}$ = 7.6 Hz, 1H, H10), 8.40 - 8.45 (m, 2H, H3 and H4), 9.94 (s, 1H, H6).

Anal. Calcd. for $C_{28}H_{15}N_3S$: C, 79.03; H, 3.55; N, 9.88. Found: C, 79.07; H, 3.61; N, 9.43.

Naphtho[2',1':4,5]thieno[2,3-*c*]naphtho[1,2-*f*]tetrazolo-[1,5-*a*]quinoline (**9**).

To an ice-chilled solution of 0.05 g (0.12 mmole) of hydrazine **15** in 7 ml of 70% glacial acetic acid was added dropwise a solution of 0.038 g (0.55 mmole) of sodium nitrite in 3 ml of water

with vigorous stirring. The reaction mixture was stirred at ambient temperature for 18 hours. The solid was collected by filtration and washed with water and recrystallized from benzene to afford 0.028 g (0.066 mmole, 55%) of tetrazole **9** as yellowish crystals, mp > 300°; tlc (chloroform) R_f 0.48; ^1H nmr (deuteriochloroform): δ 6.52 (d, $J_{14,15}$ = 9.0 Hz, 1H, H15), 6.82 (t, $J_{16,17} = J_{17,18}$ = 8.0 Hz, 1H, H17), 7.00 (d, $J_{14,15}$ = 9.0 Hz, 1H, H14), 7.42 (t, $J_{17,18} = J_{18,19}$ = 8.0 Hz, 1H, H18), 7.53-7.57 (m, 2H, H11 and H12), 7.60 (d, $J_{16,17}$ = 8.0 Hz, 1H, H16), 7.67 (dd, $J_{12,13}$ = 6.9 Hz, $J_{11,13}$ = 2.2 Hz, 1H, H13), 7.84 (d, $J_{1,2}$ = 8.6 Hz, 1H, H2), 7.94 (d, $J_{18,19}$ = 8.0 Hz, 1H, H19), 7.98 (d, $J_{1,2}$ = 8.6 Hz, 1H, H1), 8.07 (dd, $J_{10,11}$ = 7.1 Hz, $J_{10,12}$ = 2.0 Hz, 1H, H10), 8.14 (d, $J_{3,4}$ = 8.6 Hz, 1H, H3), 8.66 (d, $J_{3,4}$ = 8.6 Hz, 1H, H4).

Anal. Calcd. for $C_{27}H_{14}N_4S$: C, 76.04; H, 3.31; N, 13.14. Found: C, 75.97; H, 3.40; N, 12.96.

Acknowledgment.

The authors wish to thank the National Science Foundation (CHE-8813620) for providing funds for the acquisition and operation of the Bruker AM360 NMR spectrometer used in this work.

REFERENCES AND NOTES

[1] Presented at the XVIIth European Colloquium on Heterocyclic Chemistry, Regensburg, Germany, October 6-9, 1996, Abstract SH 61.

[2a] Part **1**: S. L. Castle, J.-K. Luo, H. Kudo and R. N. Castle, *J. Heterocyclic Chem.*, **25**, 1363 (1988); [b] Part **2**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **27**, 1031 (1990); [c] Part **3**: M. J. Musmar and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 203 (1991); [d] Part **4**: J.-K. Luo, A. S. Zektzer and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 737 (1991); [e] Part **5**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 1825 (1991); [f] Part **6**: R. N. Castle, S. Pakray and G. E. Martin, *J. Heterocyclic Chem.*, **28**, 1997 (1991); [g] Part **7**: K. Sasaki and R. N. Castle, *J. Heterocyclic Chem.*, **29**, 963 (1992); [h] Part **8**: K. Sasaki and R. N. Castle, *J. Heterocyclic Chem.*, **29**, 1613 (1992); [i] Part **9**: Ch. Camoutsis and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 153 (1993); [j] Part **10**: M. J. Musmar, A. S. Zektzer, R. N. Castle and N. K. Dalley, *J. Heterocyclic Chem.*, **30**, 487 (1993); [k] Part **11**: J.-K. Luo, A. S. Zektzer, R. N. Castle, R. C. Crouch, J. P. Shockcor and G. E. Martin, *J. Heterocyclic Chem.*, **30**, 453 (1993); [l] Part **12**: J.-K. Luo, S. L. Castle and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 653 (1993); [m] Part **13**: J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **30**, 1167 (1993); [n] Part **14**: M. J. Musmar and R. N. Castle, *J. Heterocyclic Chem.*, **31**, 553 (1994); [o] Part **15**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 317 (1995); [p] Part **16**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 659 (1995); [q] K. Sasaki, O. Tokuda, T. Hirota, J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **32**, 1735 (1995); [r] Part **17**: J.-K. Luo, R. F. Federspiel, R. N. Castle and L. W. Castle, *J. Heterocyclic Chem.*, **33**, 185 (1996); [s] Part **18**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **33**, 923 (1996); [t] Part **19**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **34**, 1597 (1997); [u] Part **20**: J.-K. Luo, R. F. Federspiel and R. N. Castle, *J. Heterocyclic Chem.*, **35**, 1441 (1998).

[3] To whom correspondence should be addressed at the Department of Chemistry, University of South Florida, Tampa, FL 33620-5250 USA.

[4] H. Kudo and R. N. Castle, *J. Heterocyclic Chem.*, **22**, 211 (1985).

[5] T. N. Sidorenko, G. A. Terent'eva, O. S. Andrienko, Yu. V. Savinykh and V. S. Aksenev, *J. Heterocyclic Compd., (USSR)*, **19**, 156 (1983).

[6] A. Bax and R. J. Freeman, *J. Magn. Reson.*, **44**, 542 (1981).

[7] A. Bax and S. Subramanian, *J. Magn. Reson.*, **67**, 565 (1986).

[8] A. Bax and F. Summers, *J. Am. Chem. Soc.*, **108**, 2093 (1986).

[9] J. Jeener, B. H. Meier, P. Bachmann, and R. R. Ernst, *J. Chem. Phys.*, **71**, 4546 (1979).