The Synthesis of Novel Polycyclic Heterocyclic Ring Systems *via* Photocyclization. **11** [1]. Synthesis and Total Assignment of the ^{1}H and ^{13}C NMR Spectra of Isomeric Benzothienonaphthoquinolines Using Multiple Inverse Detected Two-Dimensional NMR Methods

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Two novel heterocyclic ring systems, namely, [1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline and [1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline have been synthesized and characterized by inverse detected two-dimensional nmr methods. Unequivocal total assignments of the proton and carbon nmr spectra were made through the concerted utilization of HMQC (Heteronuclear Multiple Quantum Correlation) and a combination of HMBC (Heteronuclear Multiple Bond Correlation) and HMQC-TOCSY (HMQC with proton TOtal Correlation SpectroscopY).

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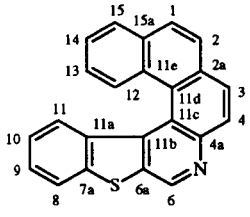
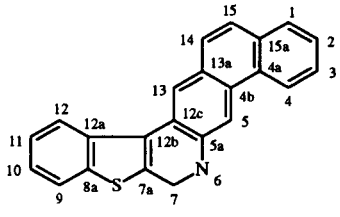
Introduction.

Polynuclear aromatic and heteroaromatic compounds offer considerable challenge to the spectroscopist when it becomes necessary to establish either total assignments and/or the structure of an unknown compound in this class. Thus it is often useful to have at hand complex molecules with unequivocally assigned spectra that can be used for the development of new two-dimensional nmr applications. It was, in part, for this purpose that the title compounds, [1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**1**) and [1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**2**) were synthesized and their ^{1}H and ^{13}C nmr spectra totally assigned.



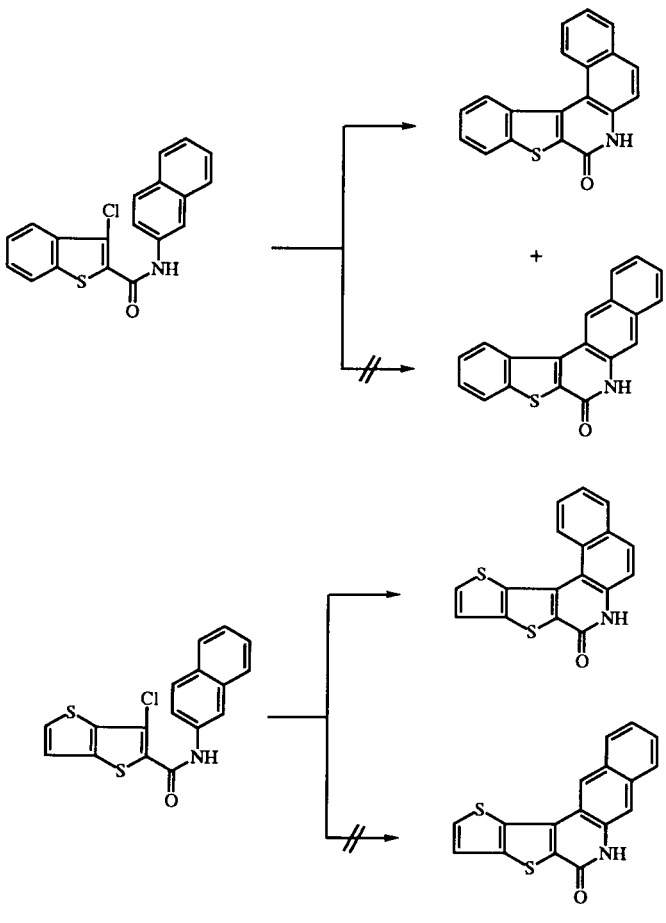
1



2

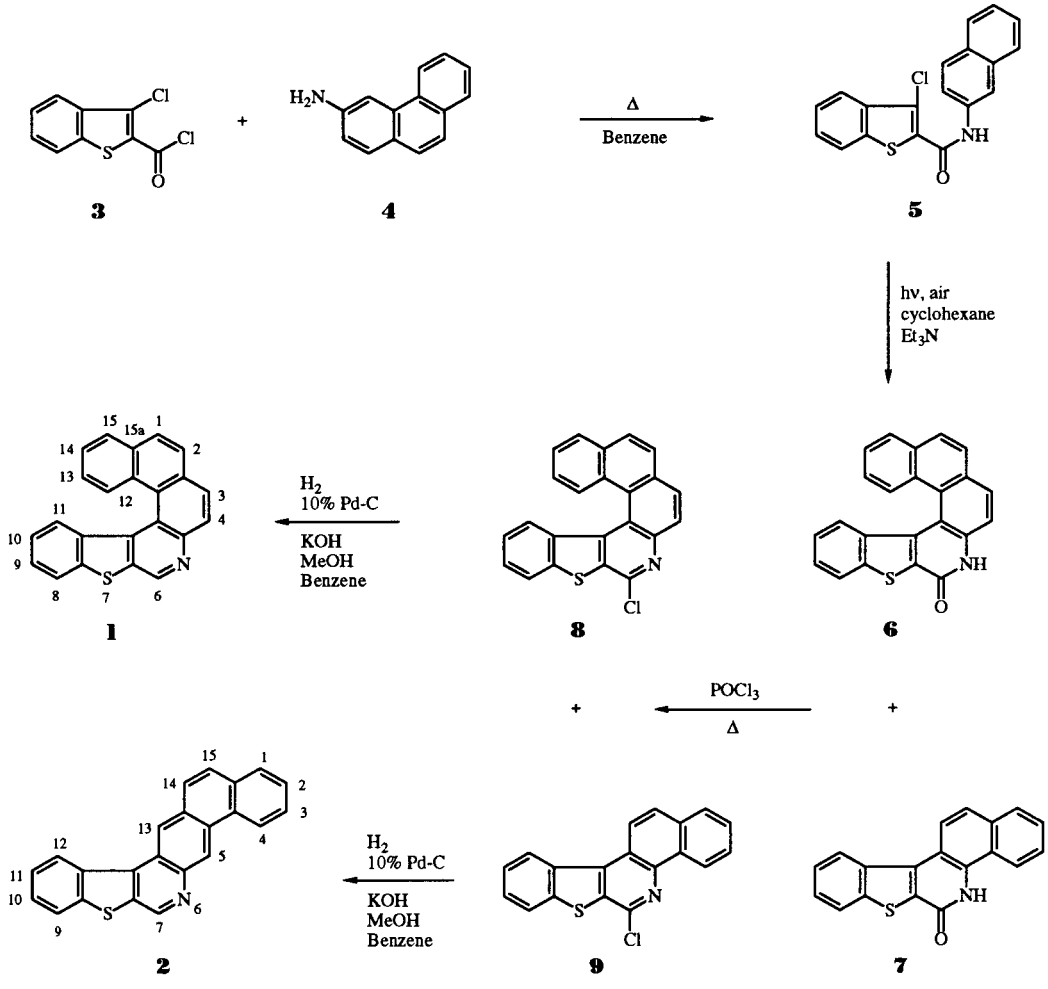
In recent papers [1b,d] we reported that the photoinduced cyclization of 3-chloro-*N*-(2-naphthyl)benzo[*b*]thiophene-2-carboxamide [1b] and 3-chloro-*N*-(2-naphthyl)-thieno[3,2-*c*]thiophene-2-carboxamide [1d] in benzene in the presence of triethylamine yield only benzo[*f*][1]benzothieno[2,3-*c*]quinolin-8(7*H*)-one and benzo[*f*]thieno[2′,3′:4,5]thieno[2,3-*c*]quinolin-8(7*H*)-one, respectively with no corresponding isomers being detected (Scheme 1). As a continuation of our investigation, in this paper we describe the synthesis of two previously unknown ring systems, namely, [1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**1**) and [1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**2**) and their ^{1}H and ^{13}C nmr spectral assignments.

Scheme 1



The synthetic pathway to compounds **1** and **2** is illustrated in Scheme 2. The carbonyl chloride **3** was obtained by treatment of cinnamic acid with thionyl chloride in the presence of pyridine [2,3,4]. When refluxed with 3-aminophenanthrene (**4**) [5] for four hours in benzene, compound **3** was transformed into 3-chloro-*N*-(3-phenanthryl)benzo[*b*]thiophene-2-carboxamide (**5**) in 94% yield. In contrast to 3-chloro-*N*-(2-naphthyl)benzo[*b*]thiophene-2-carboxamide and 3-chloro-*N*-(2-naphthyl)thieno[3,2-*b*]thiophene-2-carboxamide (Scheme 1), when **5** was irradiated with a 450 watt medium pressure mercury lamp in cyclohexane in the presence of triethylamine, an isomeric mixture of [1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**6**) and [1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinolin-7(6*H*)-one (**7**) was obtained in 88% yield. The mixture was used in the next step without further separation and purification due to low solubility. Upon chlorination of the mixture of **6** and **7** with phosphorus oxychloride at 110-120° for five hours, the corresponding isomeric chlorides **8** and **9** were obtained. This isomeric mixture was separated by fractional crystallization and purified by recrystallization to provide 6-chloro[1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**8**) in 57% yield and 7-chloro[1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**9**) in 10% yield. The identification of **8** and **9** was accomplished by their ^{1}H nmr spectra since **9** would give rise to two singlets at 9.16 and 9.40 ppm attributed to H13 and H5, respectively. On the other hand H11, H12 and H13 of **8** are expected to be shifted upfield due to the shielding effect of the terminal rings of the hexahelicene backbone of the molecule [6,7,8] in its ^{1}H nmr spectrum. In addition, compound **9**, being more linear than **8**, should exhibit a higher melting point (265-266° *vs* 231-233°) and a lower solubility than **8** as expected. The unsubstituted [1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**1**) was obtained 50% yield by catalytic dechlorination of **8** with 10% Pd-C in 1:1 benzene-methanol solution containing potassium hydroxide. Dechlorination of **9** was accomplished under more severe reaction conditions due to lower solubility in the reaction medium. Thus, catalytic dechlorination of **9** with 10% Pd-C in 1:1 benzene-methanol solution in the presence of potassium hydroxide was performed at 45 psi on a Parr hydrogenation apparatus to obtain the parent ring system **2** in 44% yield. An HMQC-NOESY study [8] and the complete ^{1}H and ^{13}C assignment

Scheme 2



of **1** and **2** *via* two-dimensional nmr experiments (*vide infra*) further confirmed our structural assignments of **8** and **9**.

Spectroscopy.

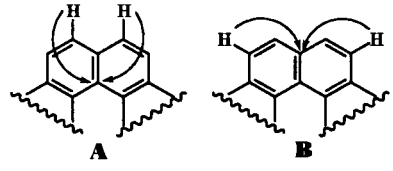
Inverse detected two-dimensional nmr experiments have their greatest potential impact in the form of the vast improvement in sensitivity that they offer over their heteronucleus detected counterparts. This can be exploited with dilute samples due to either lack of material availability or solubility. Alternatively, there are new inverse detected two-dimensional nmr experiments being developed which have no counterpart heteronucleus detected equivalent. Examples here would include HMQC-TOCSY [9] and HMQC-NOESY [10], both of which have potential application in the assignment of polynuclear aromatic spectra.

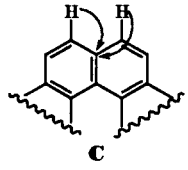
We were interested in obtaining unequivocal proton and carbon resonance assignments for the title compounds and were limited by neither solubility nor availability. In such cases, utilization of inverse detected methods can afford a substantial savings in data accumulation time which are also advantageous.

Direct (one bond, $^1J_{CH}$) heteronuclear correlations were established for **1** using the HMQC pulse sequence originally described by Bax and Subramanian [11]. The data were acquired using 10 mg of **1** dissolved in 0.8 ml of deuteriochloroform recorded as 128 x 2K complex points on a Varian VXR-500S spectrometer. The delay between the proton 90° pulse and the 90° carbon pulse used to create heteronuclear multiple quantum coherence was optimized as a function of $1/2(^1J_{CH})$. Total accumulation time was approximately 30 minutes and the data were processed to yield a final matrix consisting of 1K x 2K real points.

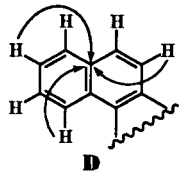
With direct heteronuclear corelations in hand, we can turn our attention to establishing vicinal proton-proton connectivities. An alternative to the COSY experiment is offered by the heteronuclear relayed coherence transfer experiment pioneered by Kessler and Ernst [12] and subsequently modified by Bax [13]. We have made extensive use of this experiment in cases where congestion of the proton nmr spectrum precluded the successful utilization of the COSY experiment [14]. Heteronuclear relay (RCT2D) does have drawbacks, however. Sensitivity is lower than the corresponding heteronucleus detected heteronuclear shift correlation experiments by a factor of two to eight [12]. Optimization of the relay step can be problematic when any substantial variation in proton vicinal coupling constants is encountered [15]. Finally, we have also noted that in four spin systems of polynuclear aromatics the correlation between protons which each have two vicinal neighbors is generally quite weak or absent from the spectrum leading to potential ambiguities in assignments. These problems clearly point to a need for an alternative experiment which offers both superior sensitivity and a freedom from the other shortcomings of the RCT2D experiment. A solution is found in the pulse sequence which has begun to be referred to as the HMQC-TOCSY experiment which was first reported by Lerner and Bax [9].

Having in hand direct ^1H-^{13}C chemical shift correlations, it was necessary to orient the spin systems relative to one another and to assign the quaternary carbon resonances. Probably the two most common correlation methods for orienting successive proton two spin systems of polynuclear aromatic compounds are shown schematically by **A** and **B** and rely on $^3J_{CH}$ coupling pathways which are easier to observe than the corresponding $^2J_{CH}$ coupling pathways illustrated by **C**.





A similar although slightly more complex approach can be utilized to orient a proton four spin system relative to an adjacent two spin system. An example of one set of pathways utilized in such a case is shown schematically by **D**.

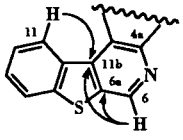


Orientation of a two spin system relative to a four spin system requires the observation of more responses if it is to be successful. An additional complication arises when the orientation of the protons in one of the systems is not fixed relative to the rest of the molecule. In such cases, ambiguous and therefore reversible orientations and assignments may result. Despite the inherent problems, the use of long range heteronuclear chemical shift correlation data provides a far superior means of assigning quaternary carbons than is offered by the INADEQUATE experiment.

The data for the HMBC spectrum of **1** were recorded as 160 x 1K complex points and were zero filled to 1K x 2K real points during the processing. The spectrum was recorded with fixed delays based on the one bond coupling optimized for 165 Hz and the delay for long range coupling optimized for 10 Hz (50 msec). Given the data it is

now possible to quickly complete a total and unequivocal assignment of the proton and carbon nmr spectra of **1**.

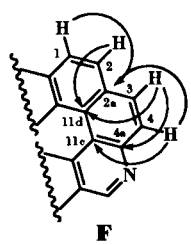
The most convenient point of entry into the assignment process is afforded by the H6 singlet resonating at 9.47 ppm which is directly correlated with the carbon resonating at 144.51 ppm. Long range couplings to H6 are observed to three quaternary carbons resonating at 133.53, 137.47 and 145.70 ppm. The quaternary carbon resonating furthest upfield of this group has no other long range couplings. Upon consideration of the structure of **1**, C6a would be expected to exhibit this behavior, the coupling observed arising due to $^2J_{CH}$ which is typically larger in pyridine systems. The middle carbon of the group just defined exhibits couplings to both the H6 resonance and to the furthest upfield doublet resonating at 7.01 ppm. Based on this, the doublet may be assigned unequivocally as H11 and the carbon in question must thus be C11b, exhibiting three bond couplings to both of the protons involved. Finally, the carbon resonating downfield in this group may be assigned as C4a through both a process of elimination and a consideration of the chemical shift. These correlation pathways are shown by **E**.



E

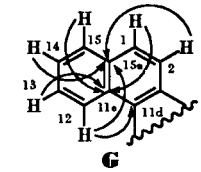
Given the means of unequivocally assigning the resonance at 7.01 ppm as H11, which on the basis of chemical shift could be assigned as either H12 or H11, we can readily assign the balance of the proton and carbon resonances in the ring containing H11 through concerted usage of HMQC, HMQC-TOCSY and HMBC spectra.

Continuing the opposite direction around the helicene core of the molecule, we can link successive spin systems through the quaternary carbon resonances as discussed and illustrated schematically above. The assignment and orientation of H3 and H4 relative to C4a is straightforward, the former long range coupled to C4a, the latter providing the means of assigning C11c. Orientation of H1 and H2 relative to the H3–H4 spin system is accomplished through the three bond couplings of H1 and H4 to C2a and H2 and H3 to C11d. These correlation pathways are illustrated by **F**.



F

This leaves only the assignment and orientation of the four spin system which, as noted above, is only slightly more complex than the orientation of a pair of two spin systems relative to one another. Thus, H1 and H15 exhibit strong long range coupling response to C11e while H13 exhibits only a weak response; H12, H14 and H2 all exhibit long range couplings to C15a, H12 also exhibiting a long range coupling to C11d which irrefutably establishes the orientation of the H12–H15 spin system. This final set of connectivity pathways is shown by **G**.



G

The spectral assignment of [1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**2**) was analyzed and accomplished in a fashion identical to that described in the assignment of the spectra of **1**.

Establishment of direct heteronuclear correlations is straightforward except for three protonated carbon atoms resonating at 127.12, 127.20 and 127.34 ppm. The ^{1}H nmr spectrum of **2** exhibits three singlets at 9.37, 9.27 and 8.98 ppm. The resonance at 9.27 ppm is assigned to H7 which is directly correlated with C7 resonating furthest downfield at 145.96 ppm, based on a consideration of the chemical shift.

Perhaps the most useful and interesting information in the COSY spectrum of **2** is the long-range couplings. The differentiation of H5 and H13 is made through the COSY and long-range heteronuclear chemical shift correlation spectra. In the COSY spectrum of **2**, H5 exhibits long-range couplings to H4 [16], H7 [17,18,19], H13 and H14 [16], whereas H13 couplings to H5, H12 [17-20], H14 [16,17] and H15 [17,19] are observed. Given the assignment of H7 resonating at 9.27 ppm, the assignment of H5 resonating at 9.37 ppm as the proton long-range coupled [17-19] to H7 is established. Consequently, the remaining singlet resonating at 8.98 ppm is identified as H13. The frequently encountered long-range "bay" coupling in phenanthrene systems [16] is observed between H5 and H4 locating at 8.71 ppm, which in turn long-range couples to H1 resonating at 7.80 ppm and facilitates the assignment of the H1–H4 four spin system. The H14 resonating at 7.78 ppm exhibits an anticipated five-bond epi-zig-zag coupling [16] to H5 and a peri coupling [17] to H13.

Having identified H13, a response correlating H13 with a proton resonating at 8.79 ppm is ascribed to the long-range "bay" coupling through six bonds between H13 and H12 [17-20], which in turn exhibits a long-range correlation to H9 resonating at 7.97 ppm similar to the connectivity between H1 and H4. Two other long-range correla-

tions with H13 are observed. The furthest downfield response is identified as H5 and the upfield response at 7.65 ppm is identified as H15 [17-19] through a five-bond coupling analogous to the correlation between H5 and H7. Given the identity and their orientation of H1, H4, H9 and H12, the assignment of the remaining protons, *e.g.* H2, H3, H10 and H11, may be conveniently elucidated with vicinal couplings as shown in Table 2. Thus, the unusual long-range couplings observed in the COSY spectrum permit an unequivocal assignment of the ^{1}H nmr spectrum of **2** with little assistance from direct heteronuclear correlations.

Given the proton assignment through the COSY spectrum of **2**, the protonated carbons can be immediately identified utilizing proton-carbon direct heteronuclear chemical shift correlation spectrum except C2, C3 and C10 due to the lack of spectral resolution in a very congested area. To accomplish this and complete the total assignment of **2**, a long-range heteronuclear chemical shift correlation spectrum of **2** was employed.

The logical starting point is provided by H7 resonating at 9.27 ppm. Long-range correlation of H7 to four quaternary carbons is observed at 132.81, 134.25, 135.16 and 143.29 ppm. The quaternary carbon resonating furthest upfield of this group is assigned as C7a which exhibits no other long-range coupling as expected. The carbon resonating furthest downfield of this group is assigned as C5a on the basis of chemical shift consideration and past experience [1d]. The C5a exhibits correlations with both H5 *via* a two-bond coupling and to the furthest upfield singlet resonating at 8.98 ppm assigned as H13. The latter response arising from the H13/C5a three-bond couplings reveals a stronger coupling than the former arising from the H5/C5a two-bond coupling [21]. The resonance at 134.25 ppm is assigned as C12b which also exhibits a correlation to H13 *via* a three-bond coupling. The remaining response to the quaternary carbon resonating at 135.16 ppm is of great interest in that it is also coupled with the protons resonating at 7.62, 7.97, 8.79-8.98 and 9.37 ppm. From simple inspection of the structure of the molecule, it should be clear that the resonance at 135.16 ppm must be attributed to C12a. To our surprise, C12a exhibits two rather strong four-bond couplings and one weak five-bond coupling in addition to two usual three-bond couplings arising from H11/C12a and H9/C12a and one weak two-bond coupling arising from H12/C12a. The four-bond coupling [1d,22-24] between H7 and C12a across a W path has been reported previously, but its intensity is unusually strong. The other four-bond coupling resulting from H13 and C12a is rather astonishing. This particular response has not been observed in our analogous ring systems reported previously [1d]. Not only is the intensity of the response comparable to that of the three-bond correlation of H13/C12b, but also the coupling is not through a typical W path as reported [1d,22-24]. The basis for the unexpectedly strong peri (across a U path) coupling between H13 and C12a resonances, however, remains to be accounted for. Very few heteronuclear five-bond correlations have been reported [22]. The five-bond correlation of H5/C12a *via* an epi-zig-zag path is barely visible at the threshold of the contour plot. Differentiation from noise was provided by re-examination of the slice corresponding to this correlation, from the long-range heteronuclear experiment.

Using the location of H13, two more unidentified correlations to carbons resonating at 126.77 and 129.78 ppm are observed. The latter in turn exhibits a weak coupling to H4 and a strong one to H14 and is assigned C4b, while the former is identified as C14 for which no other correlations are observed as anticipated. In a similar fashion using the location of H5, C12c is assigned as the resonance at 123.75 ppm in which no other correlations are found; C4a is assigned at 130.01 ppm *via* correlations to H1, H3 and H15; C13a is assigned at 131.05 ppm through correlation to H15.

Table 1

Resonance Assignments of [1]Benzothieno[2,3-*c*]-naphtho[1,2-*f*]quinoline (1) in Deuterochloroform [a]

Position	Chemical Shift Proton	ppm Carbon	Long Range Couplings of Labeled Resonance to Other Resonances
H12	7.87	128.78	C14, C15a, C11d
H13	7.08	125.86	C15, C11e
H14	7.49	126.25	C12, C15a
H15	8.02	128.07	C11e
C15a		131.64	H12, H14, H2
H1	8.05	128.70 [b]	
H2	7.97	125.99	
C2a		132.08	H1, H2, H4
H3	8.07	128.69 [b]	
H4	8.25	128.74	
C4a		145.70	H3, H6
H6	9.47	144.51	C15a, C2a, C11b
C6a		133.53	H2
C7a		140.26	H9, H11
H8	7.94	122.74	
H9	7.37	127.56	
H10	8.02	128.07	
H11	7.01	127.74	
C11a		134.67	H8, H10
C11b		137.47	H6, H11
C11c		119.50	H4
C11d		125.39	H12, H2, H3
C11e		130.13	H13, H15, H1

[a] Data were recorded at observation frequencies of 499.84 and 125.697 MHz for proton and carbon observation, respectively. [b] Assignments for the resonances noted may be interchanged. Unequivocal assignment could not be made with the digital resolution available.

Table 2

Resonance Assignments of [1]Benzothieno[2,3-*c*]-naphtho[2,1-*g*]quinoline (**2**) in Deuteriochloroform

Position	Chemical Shift (ppm) Proton	Carbon	Longe-range Correlation
H1	7.80	128.51	C3, C15, C4a, C15a
H2	7.62	127.34	C4, C15a
H3	7.64	127.12	C1, C4a
H4	8.71	123.06	C2, C4b, C15a
C4a		130.01	H5, H1, H15, H3
C4b		129.78	H13, H4, H14
H5	9.37	124.07	C12c, C4a, C13a, C12a, C5a
C5a		143.29	H5, H7, H13
H7	9.27	145.96	C7a, C12b, C12a, C5a
C7a		132.81	H7
H9	7.97	123.63	C11, C12a
H10	7.58	127.20	C12, C8a
H11	7.62	125.36	C9, C12a
H12	8.79	125.76	C10, C12a, C8a
C12a		135.16	H5, H7, H13, H12, H9, H11
C12b		134.25	H7, H13
C12c		123.75	H5
H13	8.98	121.71	C14, C4b, C12b, C12a, C5a
C13a		131.05	H5, H15
H14	7.78	126.77	C13, C4b, C15a
H15	7.65	128.19	C1, C4a, C13a
C15a		131.71	H4, H1, H14, H2

[a] Data were recorded at observation frequencies of 360.13 and 90.56 MHz for proton and carbon observations, respectively

Given the location of H12, we note that H12 exhibits correlations to carbons resonating at 127.20, 135.16 and 141.23 ppm. The response at 141.23 ppm is assigned as C8a through chemical shift consideration and correlation to H10, ultimately leading to the assignment of C12 resonating at 125.76 ppm. Thus, the resonance at 127.20 ppm is assigned as C10 through elimination and the possibility of other responses. The weak resonance at 135.16 ppm assigned as C12a is described as above. Continuing to H9 resonating at 7.97 ppm, C11 is assigned as the resonance at 125.36 ppm, and exhibits no other correlations as predicted.

To this point the remaining unassigned carbon resonances are C2, C3 and C15a. Given H4 resonating at 8.71 ppm, C15a is immediately assigned as the resonance at 131.71 ppm by correlations to H1, H2 and H14; C2 is then assigned at 127.34 ppm and shows no other possibility of coupling. The remaining unidentified carbon resonance at 127.12 ppm is therefore assigned as C3 which displays one and the only one correlation with H1 as expected. There are, in addition, numerous other connectivities that link the structural network further serving to confirm the assignment of the ^1H and ^{13}C nmr spectra shown in Table 2.

Thus, we are assured that the structures of compounds **1** and **2** have been correctly determined and the proton and carbon nmr spectra unequivocally and totally assigned.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The ir spectra were recorded on a Beckman FT 1100 spectrometer as potassium bromide pellets and frequencies are expressed in cm^{-1}. The ^1H nmr spectra were obtained on a JEOL FX-90Q spectrometer in the solvent indicated with TMS as the internal standard and chemical shifts are reported in ppm (δ) and J values are in Hz. Analyses (tlc) were performed on Whatman precoated silica gel plates containing a fluorescent indicator. Column chromatography was performed with Aldrich silica gel, 70-230 mesh, 60 Å. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

3-Chloro-*N*-(3-phenanthryl)benzo[*b*]thiophene-2-carboxamide (**5**).

A mixture of 1.93 g (8.35 mmoles) of 3-chlorobenzo[*b*]thiophene-2-carboxoyl chloride (**3**) [2-4], 1.62 g (8.38 mmoles) of 3-aminophenanthrene (**4**) [5] and 80 ml of benzene was heated under reflux for 4 hours. After cooling to room temperature the precipitate was collected by filtration and recrystallized from benzene to yield 3.04 g (7.84 mmoles, 94%) of **5** as colorless crystals, mp 220-221°; tlc (cyclohexane:benzene, 1:4) R_f 0.56; ir (potassium bromide): 3312 (NH stretching), 3050 (aromatic CH stretching), 1640 (>C=O stretching); ^1H nmr (deuteriochloroform and 3 drops of DMSO-d_6): 50° δ 7.45-7.99 (m, 11H), 8.62-8.73 (m, 1H), 9.19 (s with shoulder, 1H, H-4'), 9.48 (br s, 1H, NH).

Anal. Calcd. for $C_{23}H_{14}ClNOS$: C, 71.22; H, 3.64; N, 3.61; S, 8.27. Found: C, 71.39; H, 3.76; N, 3.63; S, 8.22.

[1]Benzothieno[2,3-*c*]naphtho[1,2-*f*]quinolin-6(5*H*)-one (**6**) and [1]-Benzothieno[2,3-*c*]naphtho[2,1-*g*]quinolin-7(6*H*)-one (**7**).

A mixture of 0.5 g (1.29 mmoles) of **5**, 0.13 g (1.29 mmoles) of triethylamine and 500 ml of cyclohexane was irradiated with a 450 watt Hanovia medium pressure mercury lamp for 5 hours. A slow stream of air was passed through the solution during the course of the irradiation. The precipitate was collected by filtration and washed with water to afford a 0.40 g (1.14 mmoles, 88%) of a mixture of **6** and **7** as a yellow product, mp >280°; ir (potassium bromide): 3032 (aromatic CH stretching), 1643 (>C=O stretching); ^1H nmr (DMSO-d_6): 120° δ 6.80-7.09 (m, 4H, ArH), 7.29-9.25 (m, 20H, ArH). These two compounds were utilized as a mixture in the next reaction without further purification.

6-Chloro[1]benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**8**) and 7-Chloro[1]benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**9**).

A mixture of 1.83 g (5.21 mmoles) of **6** and **7**, and 50 ml of phosphorus oxychloride was heated at 110-120° for 5 hours. After cooling in an ice bath, the mixture was poured into 450 ml of ice water very slowly with vigorous stirring. The precipitate was collected by filtration and recrystallized from benzene to give 0.20 g (0.54 mmole, 10%) of **9** as yellow needles, mp 265-266°; tlc (cyclohexane:benzene, 1:4) R_f 0.59; ir (potassium bromide): 3060, 3034 (aromatic CH stretching); ^1H nmr (deuteriochloroform): 55° δ 7.54-8.10 (m, 8H), 8.71-8.97 (m, 2H), 9.16 (s, 1H, H13), 9.40 (s, 1H, H-5).

Anal. Calcd. for $C_{23}H_{12}ClNS$: C, 74.69; H, 3.27; N, 3.79; S, 8.67. Found: C, 74.90; H, 3.54; N, 3.89; S, 8.32.

The filtrate from the above crystallization was evaporated to dryness *in vacuo* and the solid residue was recrystallized from cyclohexane to give 1.10 g (2.97 mmoles, 57%) of **8** as yellow clus-

ters, mp 231-233°; tlc (cyclohexane:benzene, 1:4) R_f 0.59; ir (potassium bromide): 3052 (aromatic CH stretching); ^1H nmr (deuteriochloroform): δ 6.69-7.54 (m, 5H), 7.71-8.18 (m, 7H).

Anal. Calcd. for $C_{23}H_{12}ClNS$: C, 74.69; H, 3.27; N, 3.79; S, 8.67. Found: C, 74.79; H, 3.38; N, 3.57; S, 8.51.

[1]Benzothieno[2,3-*c*]naphtho[1,2-*f*]quinoline (**1**).

A mixture of 0.44 g (1.19 mmoles) of **8**, 67 mg (1.19 mmoles) of potassium hydroxide, 100 ml of benzene, 100 ml of methanol and 0.1 g of 10% palladium on carbon was hydrogenated at atmospheric pressure at room temperature until the uptake of hydrogen ceased. The catalyst was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. The solid was recrystallized from cyclohexane to give a 0.20 g (0.6 mmole, 50%) of **1** as brown crystals, mp 243-245°; tlc (cyclohexane:benzene, 1:4) R_f 0.15; ir (potassium bromide): 3052 (aromatic CH stretching).

Anal. Calcd. for $C_{23}H_{13}NS$: C, 82.36; H, 3.91; N, 4.18. Found: C, 82.27; H, 4.01; N, 3.91.

[1]Benzothieno[2,3-*c*]naphtho[2,1-*g*]quinoline (**2**).

A mixture of 0.14 g (0.38 mmole) of **9**, 21.5 mg (0.38 mmole) of potassium hydroxide, 120 ml of benzene, 80 ml of methanol, and 0.1 g of 10% palladium on carbon was hydrogenated at 45 psi at room temperature in a Parr hydrogenation apparatus until the uptake of hydrogen ceased. The catalyst was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. The solid was taken up in 10 ml of chloroform and chromatographed on a silica gel column eluting with a 1:1 mixture of cyclohexane and chloroform. The eluate containing the product was evaporated to dryness *in vacuo* and the residue was recrystallized from a cyclohexane-benzene mixture to yield 0.056 g (0.17 mmole, 44%) of **2** as short yellow needles, mp 225-227°; tlc (cyclohexane:benzene, 1:4) R_f 0.15; ir (potassium bromide): 3050, 3019 (aromatic CH stretching).

Anal. Calcd. for $C_{23}H_{13}NS$: C, 82.36; H, 3.91; N, 4.18. Found: C, 82.32; H, 4.08; N, 4.31.

NMR Spectroscopy of **1**.

All of the nmr experiments described in this work were performed on an analytically pure 10 mg sample of the title compound dissolved in 0.8 ml of deuteriochloroform. Data were acquired using a Varian VXR500-S spectrometer equipped with a 5 mm inverse geometry probe operating at observation frequencies of 499.84 and 125.697 MHz for ^1H and ^{13}C, respectively. Pulse widths (90°) were 15.5 and 23 μsec, respectively. Spectral widths for the proton were 1672.5 Hz for all experiments performed. Carbon spectral widths for the HMQC and HMQC-TOCSY experiments were 3393.8 Hz. The carbon spectral width for the HMBC experiment was 4399.4 Hz to accomodate the chemical shift range of the quaternary carbons.

Heteronuclear Multiple Quantum Coherence (HMQC).

The HMQC experiment was performed using the pulse sequence described by Bax and Subramanian [11]. The data were recorded as 96 x 1K complex points with 8 transients/increment of the evolution time with a 1.6 sec interpulse delay giving a total accumulation time of approximately 30 minutes. Data were processed to give a final matrix consisting of 512 x 1K real points.

HMQC-TOCSY.

The HMQC-TOCSY experiment was performed using the pulse sequence of Lerner and Bax [9]. Three experiments were performed with isotropic mixing times of 12, 24 and 36 msec. Data were taken as 128 x 1K complex points with 8 transients/increment of the evolution time with a 1.6 sec interpulse delay giving an accumulation time of approximately 2 hours/mixing time. Data were processed to give final data matrices consisting of 512 x 1K real points.

Heteronuclear Multiple Bond Correlation (HMBC).

The HMBC experiment was performed using the HMBC pulse sequence as described by Bax and Summers [25]. Two experiments were performed, both optimized for a 10 Hz long-range coupling (50 msec). Data were taken for one experiment with a full proton spectral width as 256 x 2K complex points. The other experiment was recorded using 96 x 1K complex points concentrated in the proton spectral region from 7.83 to 8.31 ppm (241 Hz) with the full carbon spectral width. Interpulse delays of 2.7 sec were uniformly employed for these experiments giving data aquisition times of yyy and yyy hours, respectively.

Recently we have published a detailed paper using HMBC and HMQC-TOCSY experiments to establish connectivity networks in three different ring systems of six and seven rings [26]. Reported are HMBC contour plots of all three heterocyclic ring systems as well as contour plots and interpretation thereof of the HMQC-TOCSY experiments complete with multiple mixing times to observe longer range couplings.

NMR Spectroscopy of **2**.

The proton and carbon nmr spectra of **2** were acquired using a Bruker AMX360 spectrometer operating at a proton frequency of 360.13 MHz and a carbon frequency of 90.56 MHz. The experimental details were described in the previous paper [1d].

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REFERENCES AND NOTES

[1a] 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] 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).

[2] A. J. Krusback and T. Higa, *Tetrahedron Letters*, 5149 (1968).

[3] S. Nakagawa, J. Okumura, S. Sakai, H. Hoshi and T. Naito, *Tetrahedron Letters*, 3719 (1970).

[4] W. B. Wright, Jr. and H. J. Brabander, *J. Heterocyclic Chem.*, **8**, 711 (1971).

[5] W. E. Bachman and C. H. Boatner, *J. Am. Chem. Soc.*, **58**, 2097 (1936).

[6] M. J. Quast, G. E. Martin, V. M. Lynch, S. H. Simonsen, M. L. Tedjamulia, J. G. Stuart, R. N. Castle and M. L. Lee, *J. Heterocyclic Chem.*, **23**, 1115 (1986).

[7] M. J. Quast, E. L. Ezell, M. L. Lee, M. L. Tedjamulia, J. G. Stuart

and R. N. Castle, *J. Heterocyclic Chem.*, **23**, 1453 (1985).

[8] R. C. Crouch, C. W. Andrews, G. E. Martin, J.-K. Luo and R. N. Castle, *Magn. Reson. Chem.*, **28**, 774 (1990).

[9] L. Lerner and A. Bax, *J. Magn. Reson.*, **69**, 375 (1986).

[10] K. Sohn and S. J. Opella, *J. Magn. Reson.*, **82**, 193 (1989).

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

[12] H. Kessler, M. Ernst, M. Bernd, H. Kogler, O. W. Sørensen, G. Bodenhausen and R. R. Ernst, *J. Am. Chem. Soc.*, **105**, 6944 (1983).

[13] A. Bax, *J. Magn. Reson.*, **53**, 149 (1983).

[14] M. J. Musmar, G. E. Martin, M. L. Tedjamulia, H. Kudo, R. N. Castle and M. L. Lee, *J. Heterocyclic Chem.*, **21**, 929 (1984); M. J. Musmar, G. E. Martin, R. T. Gampe, Jr., M. L. Lee, R. E. Hurd, M. L. Tedjamulia, H. Kudo and R. N. Castle, *J. Heterocyclic Chem.*, **22**, 219 (1985).

[15] G. E. Martin and A. S. Zektzer, Two-Dimensional NMR Methods for Establishing Molecular Connectivity, VCH Publishers, Inc., New York, 1988, p 319.

[16] K. D. Bartle, D. W. Jones and R. S. Matthews, *Rev. Pure Appl. Chem.*, **19**, 191 (1969).

[17] M. W. Jarvis and A. G. Moritz, *Aust. J. Chem.*, **21**, 2445 (1968).

[18] M. W. Jarvis and A. G. Moritz, *Aust. J. Chem.*, **24**, 89 (1971).

[19] M. J. Musmar, M. R. Willcott, III, G. E. Martin, R. T. Gampe, Jr., M. Iwao, M. L. Lee, R. E. Hurd, L. R. Johnson and R. N. Castle, *J. Heterocyclic Chem.*, **20**, 1661 (1983).

[20] J. P. Shockcor, R. C. Crouch, G. E. Martin, A. Cherif, J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **27**, 455 (1990).

[21] Ref [15], p 445.

[22] P. E. Hanson, *Org. Magn. Reson.*, **12**, 109 (1979) and references cited therein.

[23] Atta-ur-Rahman, One and Two Dimensional NMR Spectroscopy, Elsevier Sciences Publishers, Amsterdam, 1989, pp 396, 505-507.

[24] Atta-ur-Rahman, M. S. Shekhari, S. Perveen, Habib-ur-Rahman, A. Yasmin, A. Zia-ul-Haque and D. Shaileh, *J. Chem. Res. (M)*, 501 (1989).

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

[26] L. W. Castle, M. D. Johnston, Jr., Ch. L. Camoutsis and R. N. Castle, *J. Heterocyclic Chem.*, **29**, 1805 (1992).