

Complete Assignment of the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR Spectra of [1]Benzothieno[2,3-*c*]naphtho[1,2-*h*]quinoline and [1]Benzothieno[2,3-*c*]naphtho[1,2-*h*][1,2,4]triazolo[4,3-*a*]quinoline. Concerted Use of Two-Dimensional NMR Techniques

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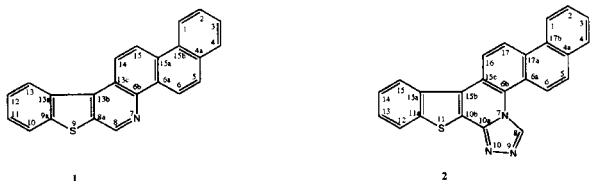
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The  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra of [1]benzothieno[2,3-*c*]naphtho[1,2-*h*]quinoline and [1]benzothieno[2,3-*c*]naphtho[1,2-*h*][1,2,4]triazolo[4,3-*a*]quinoline were totally assigned using a combination of two-dimensional nmr techniques. After correlation of the proton signals by a COSY spectrum and one-bond heteronuclear correlation, complete assignment of the  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra of the novel heterocyclic compounds required the application of long-range CH coupling information particularly for quaternary resonance assignments and the orientations of individual spin systems relative to one another.

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We have been interested in the synthesis of novel polycyclic heterocyclic ring systems *via* photocyclization of the appropriate amides [2a-m] and the study of their spectroscopic properties [3a-e]. In a related paper [2h], we reported the synthesis of [1]benzothieno[2,3-*c*]naphtho[1,2-*h*]quinoline (**1**) and [1]benzothieno[2,3-*c*]naphtho[1,2-*h*][1,2,4]triazolo[4,3-*a*]quinoline (**2**). As an extension of our spectroscopic studies, we now present the complete assignment of  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra of **1** and **2**.

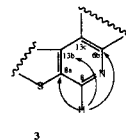
Vicinal proton-proton connectivities were obtained by using the COSY experiment [4]. Direct (one-bond  $^1J_{\text{CH}}$ ) and long-range heteronuclear correlations were established for **1** and **2** using the HMQC and HMBC pulse sequences originally described by Bax *et al.* [5,6].



The COSY spectrum (Figure 1) of **1** showed the expected two-spin systems and two four-spin systems, which cannot be unambiguously assigned from the COSY spectrum. For example, it is difficult to decide whether the proton doublet resonating at 8.81 ppm, which is the terminal proton of one of the four-spin systems, corresponded to H1 or H4. The resonances observed in the  $^{13}\text{C}$ -nmr spectrum are resolved, however, unequivocal assignment of the spectrum is not possible by inspection. Therefore, the concerted use of HMQC and HMBC spectra are necessary to generate a total nmr assignment of **1**.

The singlet resonating at 9.51 ppm is assigned to H8 on the basis of chemical shift and multiplicity. Because this is the only singlet in the  $^1\text{H}$ -nmr spectrum of **1** it serves as the entry point for spectral interpretation. In the HMBC

spectrum (Figure 2), a one-bond correlation is observed between the resonance corresponding to H8 and the carbon resonating at 144.1 ppm, therefore this carbon is assigned to C8. Long-range couplings with H8 are observed at 134.0 ppm, 136.0 ppm, and 142.9 ppm in the HMBC spectrum (Figure 3). From the structure of **1**, H8 should show correlations with the quaternary carbon resonances corresponding to C6b, C8a, and C13b. The correlation at 142.9 ppm is assigned to C6b on the basis of chemical shift. Again, from the structure of **1**, it is expected that the resonance corresponding to C8a can only show a long-range correlation with H8. Therefore, on this basis, the carbon resonating at 134.0 ppm is assigned to C8a. By a process of elimination, the correlation at 136.0 ppm is assigned to C13b. The correlation response of two-bond coupling is generally weaker than that of three-bond coupling, however, the two-bond coupling response between H8 and C8a is stronger than that of the three-bond coupling between H8 and C13b of **1**. These correlation pathways are shown in **3**.



From the structure of **1**, one can see that both C6b and C13b provide a connectivity link *via* long-range correlations between H8 and H14. On this basis the doublet resonating at 9.05 ppm is assigned to H14. With H14 identified, H15 is assigned to the doublet at 8.95 by correlation with H14 on the COSY spectrum. The proton doublet resonance at 9.49 ppm, in the other two-spin system, is assigned to H6 on the basis of chemical shift and from an observed long-range correlation with C6b. Again with H6 assigned, the proton resonance at 8.09 is assigned to H5 from correlation with H6, observed in the COSY spectrum. Finally, C5 (128.0 ppm), C6 (123.1 ppm), C14 (121.1 ppm),

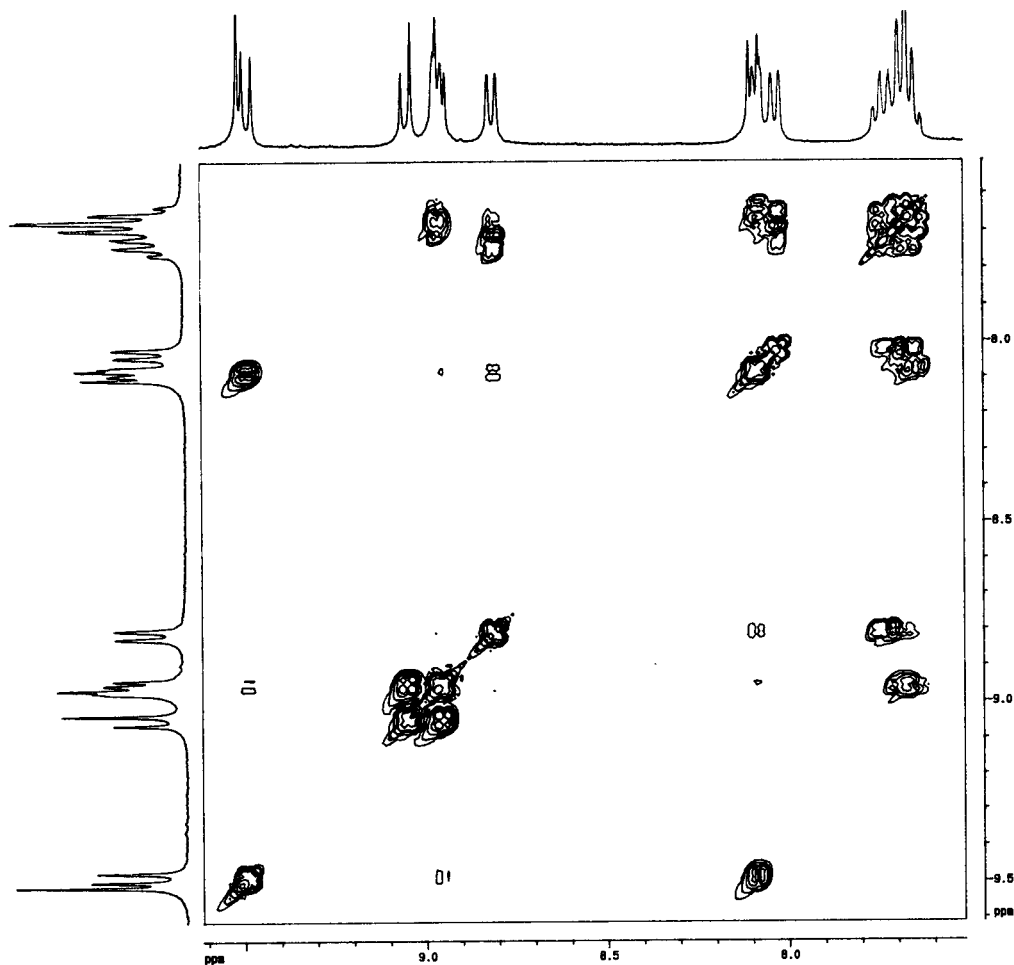


Figure 1. COSY spectrum of **1**. The spectrum was acquired with 256  $t_1$  increments of 540  $\mu\text{sec}$  to encode an  $F_1$  spectral width of 1852 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1852 Hz.

and C15 (123.0 ppm) are easily assigned from one-bond correlations observed on the HMQC spectrum.

From the HMBC spectrum, H5 correlates with three quaternary carbons resonating at 130.6 ppm, 129.9 ppm, and 132.8 ppm (weak response) and one protonated carbon at 128.8 ppm. Inspection of structure **1** reveals that, H5 should show correlations with carbon resonances corresponding to C6a, C15b, C4a and C4. The correlation between C4a and H5 is a two-bond response. Therefore, the protonated carbon resonating at 128.8 ppm is assigned to C4 and from the HMQC spectrum H4 is assigned to the resonance at 8.03 ppm from a one-bond correlation with C4. H4 then gives entry into one of the four-spin systems thus making possible the assignment of H1 (8.81 ppm), H2 (7.71 ppm), and H3 (7.67 ppm), the other members of the spin system, from correlations observed on the COSY spectrum.

The protons in the other four-spin system, H10 (8.08 ppm), H11 (7.66 ppm), H12 (7.67 ppm), and H13 (8.96

ppm) are also assigned from correlations observed on the COSY spectrum. These assignments are based on the assumption that the proton doublet resonating at 8.96 ppm corresponds to H13. H13 is assigned from its chemical shift because it resides at the end of a bay region and should appear further downfield than the other members of the spin system. At this point all of the  $^1\text{H}$  resonances are assigned, and the remaining protonated carbons are easily assigned from correlations observed on the HMQC spectrum.

The remaining quaternary carbons then are assigned from long-range correlations observed on the HMBC spectrum. Long-range couplings to H3 are observed at 123.0 ppm and 132.8 ppm. The carbon resonating at 123.0 ppm is already assigned to C1 and therefore the other corresponds to C4a. This correlation confirms the two-bond response between H5 and C4a. Similarly, C15b (129.9 ppm) is assigned from correlation with H2. The remaining quaternary carbons are assigned in a similar fashion. These correlation pathways are shown in **4**, **5**, and **6**. The

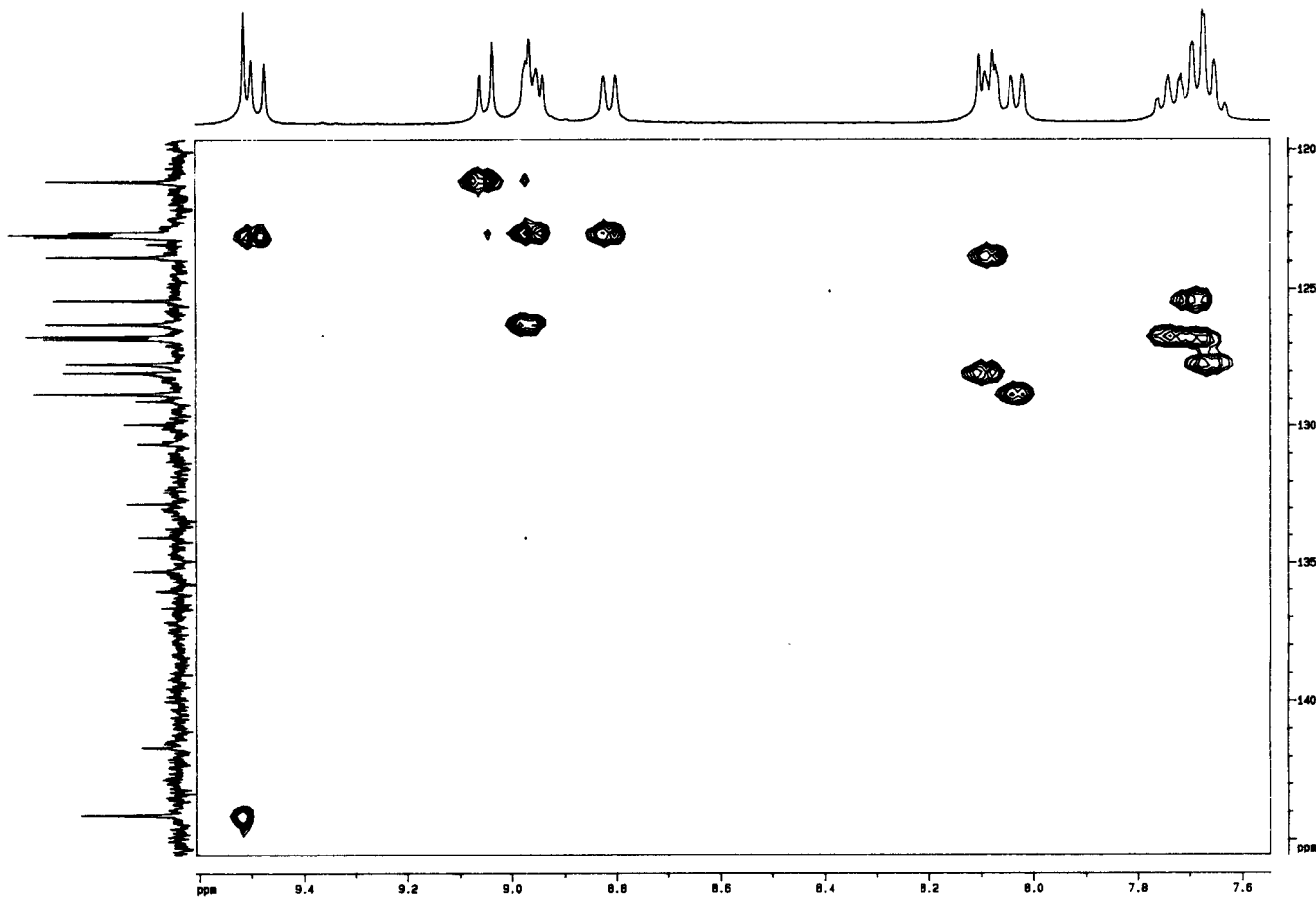
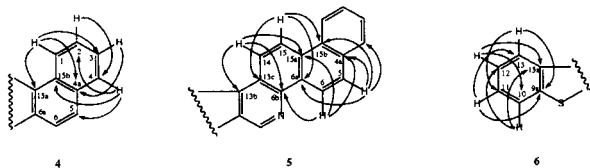


Figure 2. HMQC spectrum of **1**. The spectrum was acquired with 256  $t_1$  increments of 51.5  $\mu\text{sec}$  to encode a spectral width of 4854 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1852 Hz.

$^1\text{H}$ - and  $^{13}\text{C}$ -nmr chemical shifts of **1** are recorded in Table 1.



The COSY spectrum of **2** shows the expected pattern for the two two-spin systems and the two four-systems (Figure 4). However, it is difficult to distinguish between the two four-systems. On the other hand the two two-spin systems are quite different from one another. Of the four protons composing the two two-spin systems, the proton doublet resonating at 8.09 ppm appears upfield from the other three protons and is assigned to H5 by comparison with **1**. Furthermore, the proton doublet resonating at 8.77 ppm is assigned to H6 from a COSY correlation with H5. However at this point, it is difficult to distinguish between the members of the other two-spin system (H16 and H17). As with **1**, unequivocal assignment of the  $^{13}\text{C}$ -nmr spectrum of **2** is also impossible by inspection, and again a con-

certed use of the HMQC (Figure 5) and HMBC (Figure 6) spectra are necessary to obtain a total nmr assignment of **2**.

The proton singlet resonating at 10.36 ppm is easily assigned to H8 on the basis of the chemical shift and multiplicity and is used as the spectral entry point. The HMQC spectrum shows that H8 correlates with the carbon resonating at 139.6 ppm corresponding to C8. Long-range couplings with H8 are observed at 126.5 ppm (weak response) and 145.2 ppm (strong response) in the HMBC spectrum. From the structure of **2**, H8 should correlate with C6b and C10a. C6b then should also correlate with H6 and H16 whereas C10a should only correlate with H8. Therefore, the carbon resonating at 145.2 ppm is assigned to C10a, and the carbon resonating at 126.5 ppm is assigned to C6b. Also, the proton doublet resonating at 9.08 ppm is assigned to H16. From a COSY correlation between the resonances corresponding to H16 and H17, the doublet resonating at 9.01 ppm is assigned to H17. From the HMQC spectrum, C5 (128.5 ppm), C6 (120.8 ppm), C16

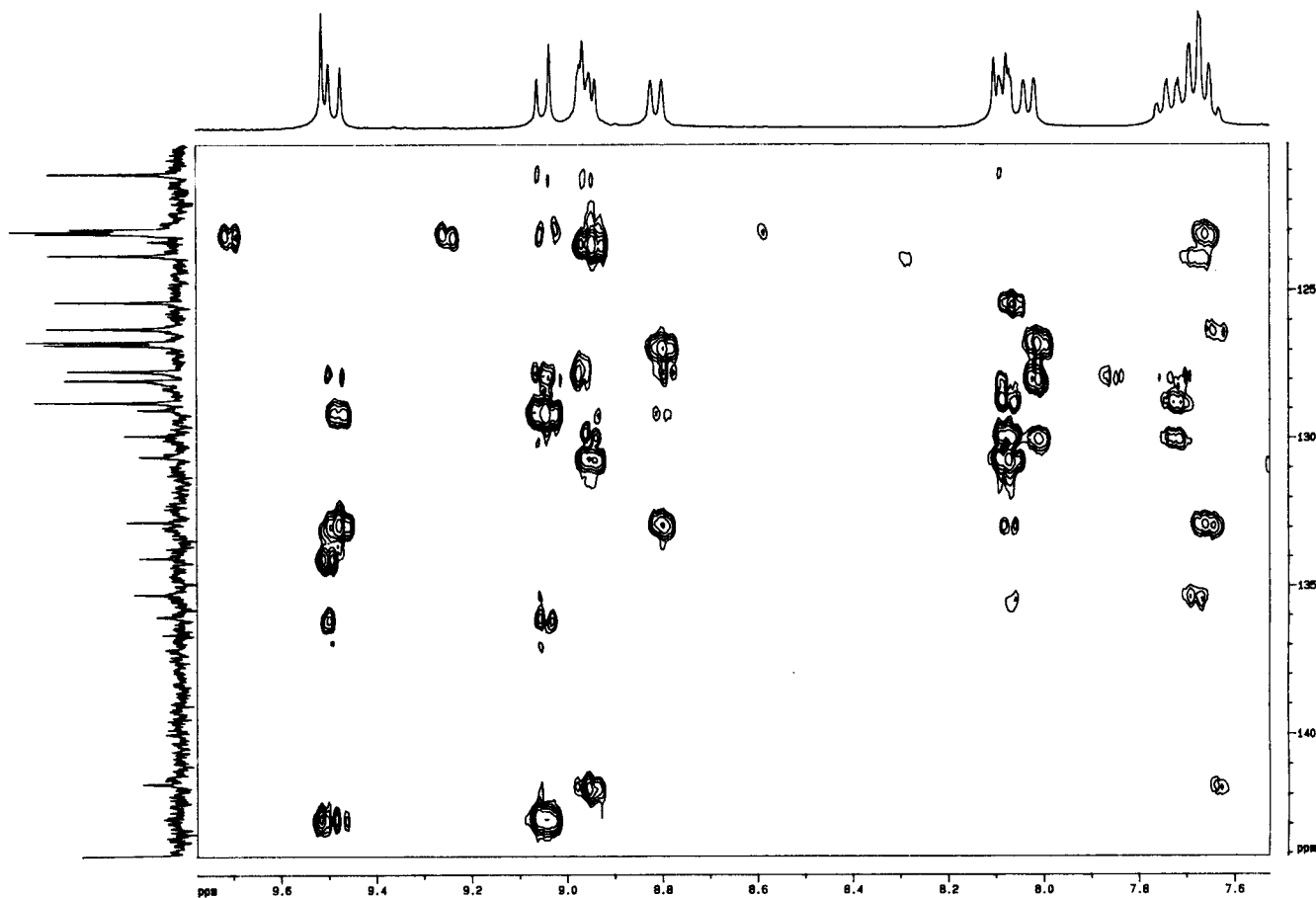


Figure 3. HMBC spectrum of **1**. The spectrum was acquired with 128  $t_1$  increments of 103  $\mu\text{sec}$  to encode a spectral width of 4854 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1852 Hz.

Table 1  
 $^1\text{H}$  and  $^{13}\text{C}$  Chemical Shifts and Long-range Correlations Observed for Compound **1**

Position	$\delta$ $^1\text{H}$	Carbons to which Long-Range Correlations are Observed	$\delta$ $^{13}\text{C}$
1	8.81	C3, C15a, C4a	123.0
2	7.71 [a]	C4, C15b	126.7
3	7.76 [a]	C1, C4a	126.8
4	8.03	C2, C5, C15b	128.0
4a			132.8
5	8.09 [a]	C4, C4a, C6a, C15b	128.0
6	9.49	C4a, C6b, C15a	123.1
6a			130.6
6b			142.8 [b]
8	9.51	C6b, C8a, C13b	144.1
8a			134.0
9a			141.7
10	8.08	C12, C13a	123.8
11	7.66 [a]	C13, C9a	127.7
12	7.67 [a]	C10, C13a	125.4
13	8.96	C11, C9a	126.3
13a			135.3

13b			136.0
13c			123.4
14	9.05	C6b, C13b, C15a	121.1
15	8.95	C6a, C9a, C15b	123.0
15a			129.0
15b			129.9

[a] Exact chemical shifts were obtained from 1D-slices of the HMQC spectrum. [b] This resonance was not observed in the 1D  $^{13}\text{C}$  spectrum and was identified from the contour plot of the HMBC spectrum *via* long-range correlations with H6 and H14.

(122.0 ppm), and C17 (121.9 ppm) are all assigned from one-bond correlations with H5, H6, H16, and H17, respectively.

From the structure of **2**, only one long-range correlation should be observed with C5, that with H4. Thus, the proton doublet resonating at 8.06 ppm, which correlates with C5, is assigned to H4. H4 then is the terminal proton in a four-spin system and the entry point needed to assign the other members of the spin system, from the COSY spectrum. Hence, H1, H2, and H3 are assigned to the proton resonances at 8.87 ppm, 7.76 ppm, and 7.73 ppm, respec-

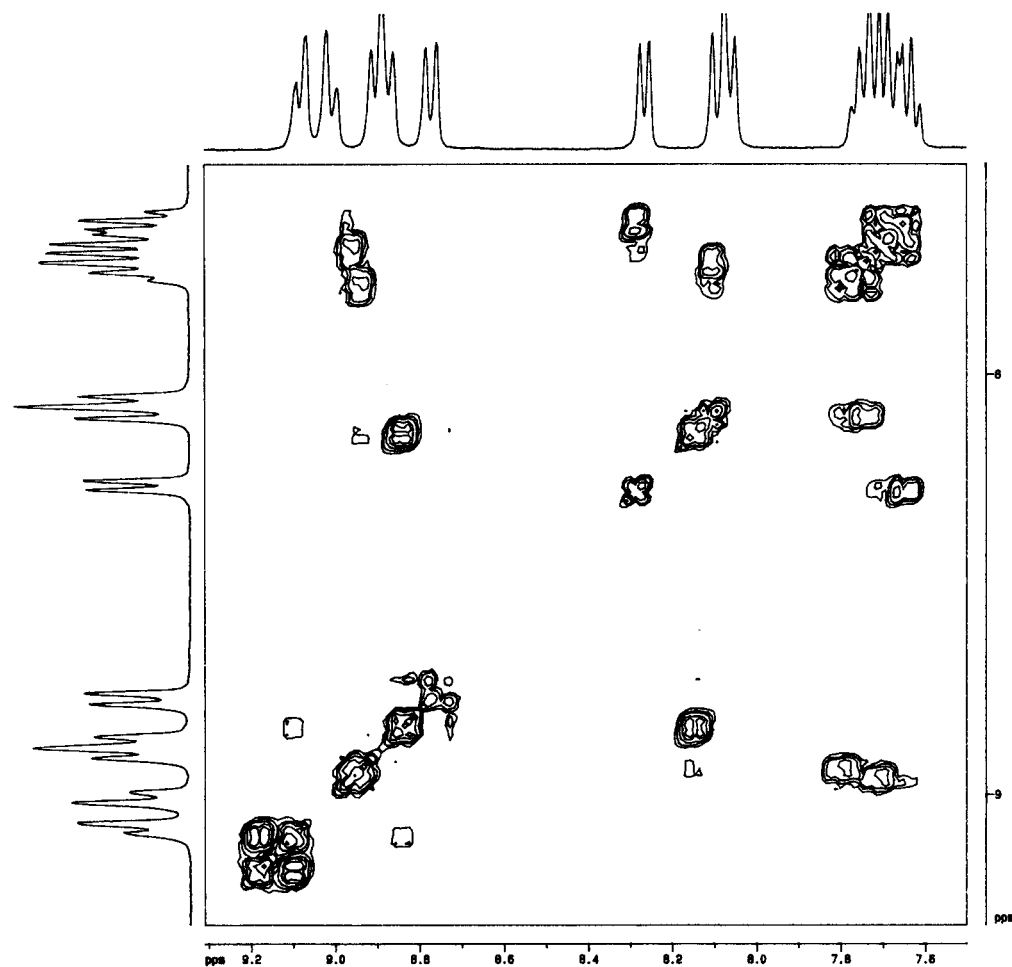
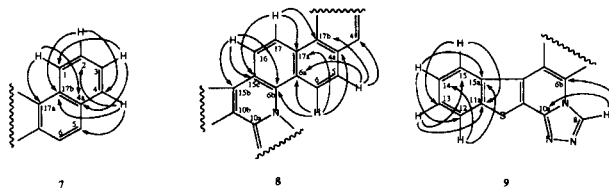


Figure 4. COSY spectrum of **2**. The spectrum was acquired with 256  $t_1$  increments of 500  $\mu\text{sec}$  to encode an  $F_1$  spectral width of 1984 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1984 Hz.

tively. By the same process, the four protons in the other four-spin system are assigned by assuming that H15 corresponds to the doublet resonating at 8.90 ppm. H15 is assigned because it resides at the end of the bay-region and thus appears farther downfield than the other members of the spin system. Therefore, H12, H13, and H14 correspond to the proton resonances at 8.26 ppm, 7.63 ppm, and 7.69 ppm respectively. At this point, all the proton resonances are identified and the remaining protonated carbons are easily assigned using the HMQC spectrum.

In the  $^{13}\text{C}$ -nmr spectrum, the resonances corresponding to C2 and C3 are completely overlapped. Long-range couplings with H2 are observed at 128.1 ppm, which has already been assigned to C4, at 128.8 ppm. Because H2

should correlate with C4 and C17b, the carbon at 128.8 ppm is assigned to C17b. Similarly, C4a (131.0 ppm) is assigned from a long-range correlation with H3. The remainder of the quaternary carbons are assigned in similar fashion. Possibly because of a zig-zag relationship between H4 and C17a, a correlation through four bonds ( $^4J_{\text{CH}}$ ) is observed. These correlation pathways are shown in **7**, **8**, and **9**. The  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr chemical shifts of **2** are recorded in Table 2.



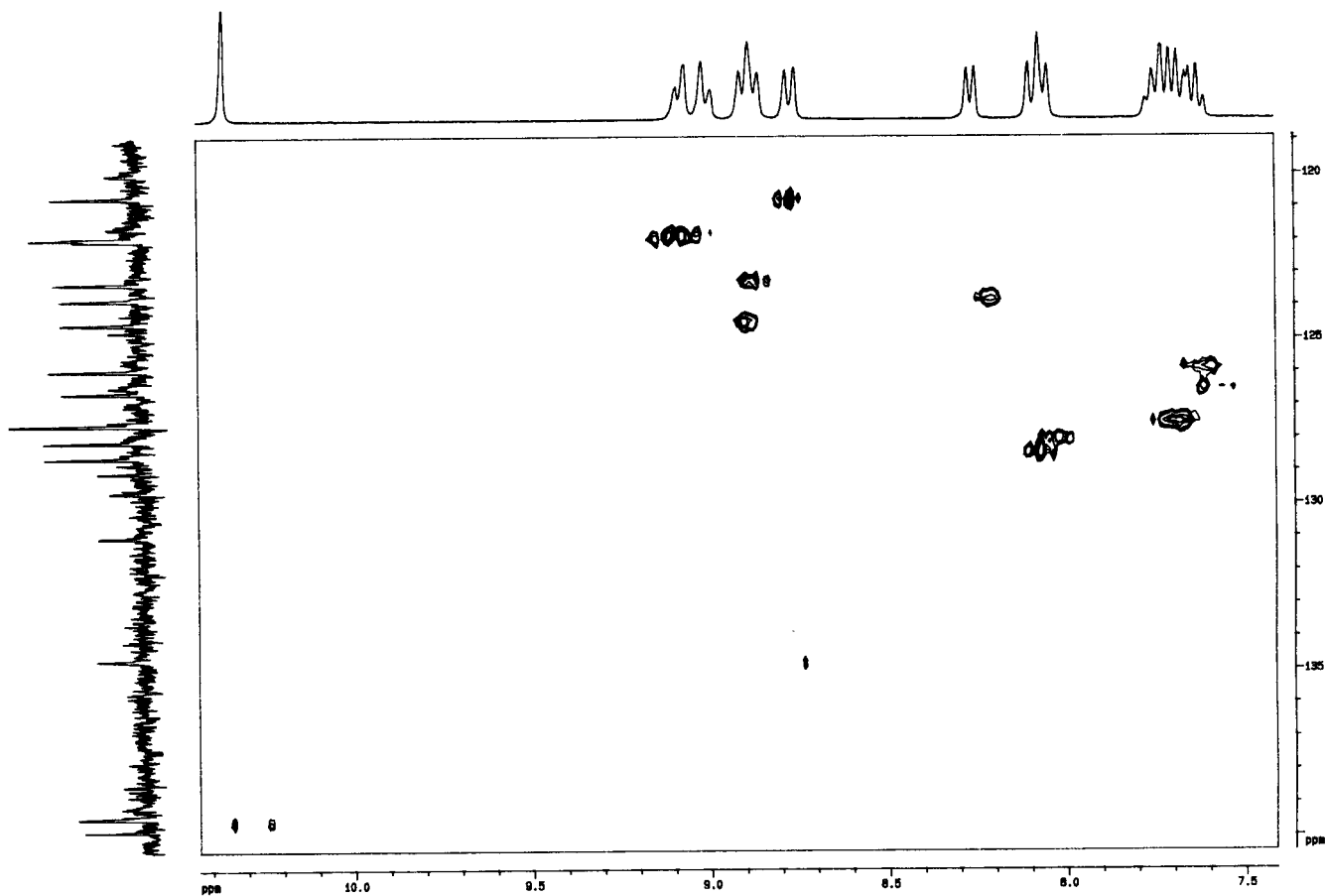


Figure 5. HMQC spectrum of **2**. The spectrum was acquired with 256  $t_1$  increments of 52.5  $\mu$ sec to encode a spectral width of 4762 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1984 Hz.

Table 2				8	10.36	C10a, C6b	139.6
$^1\text{H}$ and $^{13}\text{C}$ Chemical Shifts and Long-range Correlations Observed for Compound <b>2</b>				10a			145.2
Position	$\delta$ $^1\text{H}$	Carbons to which Long-Range Correlations are Observed	$\delta$ $^{13}\text{C}$	10b			124.8
				11a			139.8
				12	8.26	C14, C15a	123.9
				13	7.63 [a]	C15, C11a	126.6
				14	7.69 [a]	C12, C15a	126.0
				15	8.90	C13, C11a	124.6
				15a			134.7
1	8.87	C3, C4a, C17a	123.3	15b			128.7
2	7.76 [a]	C4, C17b	127.6	15c			120.0
3	7.73 [a]	C1, C4a	127.6	16	9.08	C6a, C15b, C17a	122.0
4	8.06	C2, C17b, C5	128.1	17	9.01	C6a, C15c, C17b	121.9
4a			131.0	17a			129.6
5	8.09	C4, C6a, C17b	128.5	17b			128.8
6	8.77	C4a, C17a	120.8				
6a			121.6				
6b			126.5				

[a] Exact chemical shifts were obtained from 1D-slices of the HMQC spectrum.

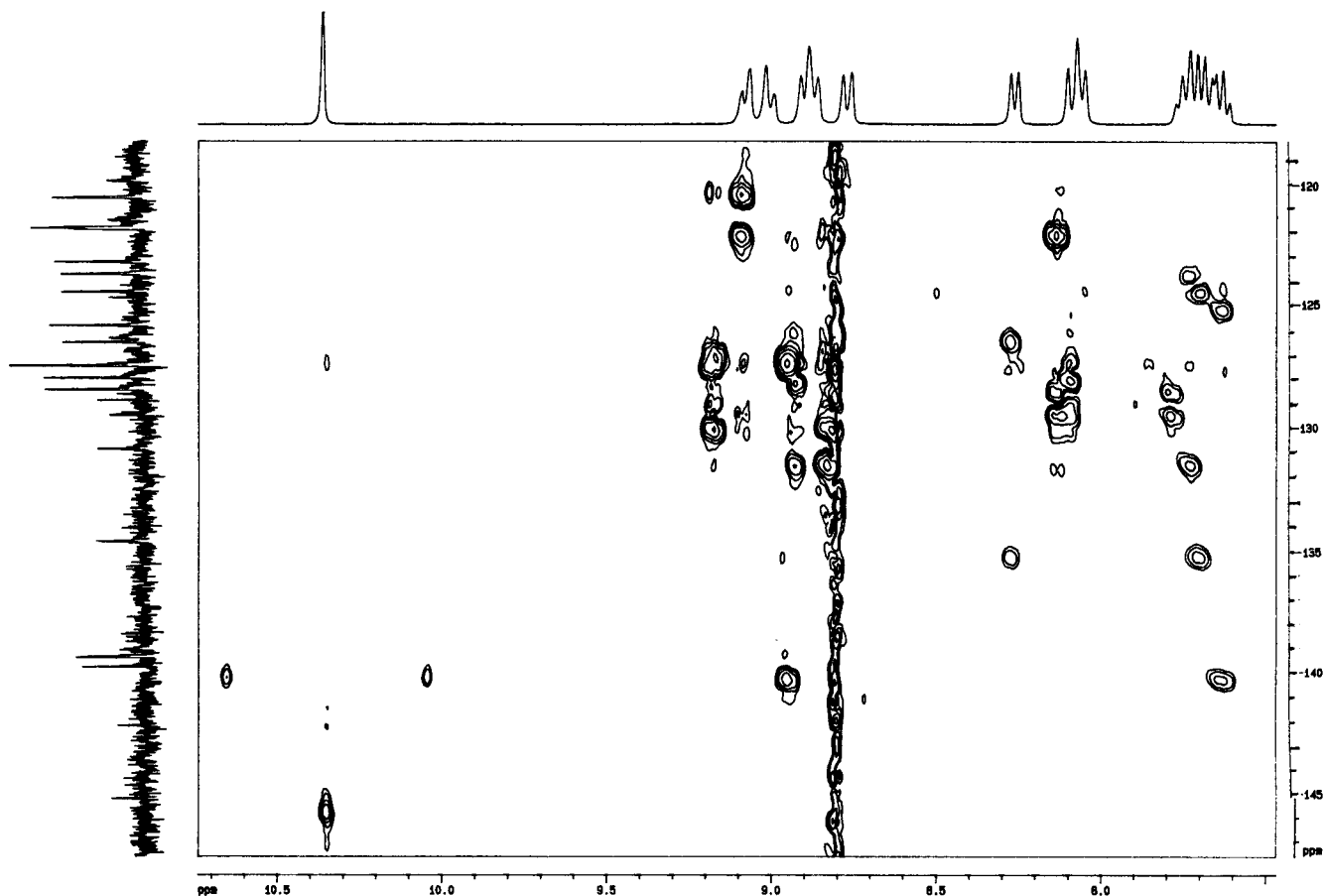


Figure 6. HMBC spectrum of **2**. The spectrum was acquired with 128  $t_1$  increments of 105  $\mu\text{sec}$  to encode a spectral width of 4762 Hz. The  $F_2$  dimension was acquired at 1024 data points for a spectral width of 1984 Hz.

## EXPERIMENTAL

Proton and carbon nmr spectra of **1** and **2** were acquired using a Bruker AMX 360 MHz spectrometer operating at a proton frequency of 360.13 MHz and a carbon frequency of 90.56 MHz. The proton spectra were obtained using a 4  $\mu\text{sec}$  ( $50.0^\circ$ ) pulse and a 5 second acquisition time to ensure accurate integrals. All two-dimensional experiments were acquired with a Bruker inverse geometry probe where the proton and carbon  $90^\circ$  pulses were calibrated and values of 7.2 and 14.5  $\mu\text{sec}$ , respectively, were obtained. A simple COSY [4] was used for the proton correlation experiment. The COSY spectrum was acquired at 1024 by 256 points and upon processing was zero-filled to a final real data matrix of 512 by 512 points. Proton-carbon correlation experiments (HMQC and HMBC) were acquired using the inverse-detection techniques described by Bax [5,6]. Fixed delay times of 3.0 msec and 47 msec (165 Hz and 10 Hz) were used for direct and long-range methods, respectively.

## REFERENCES AND NOTES

- [1] To whom correspondence should be directed at the Department of Chemistry, University of South Florida, Tampa, FL 33620-5260, USA.
- [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).
- [3a] J. P. Shockcor, R. C. Crouch, G. E. Martin, A. Cherif, J.-K. Luo and R. N. Castle, *J. Heterocyclic Chem.*, **27**, 455 (1990); [b] R. C. Crouch, C. W. Andrews, G. E. Martin, J.-K. Luo and R. N. Castle, *Magn. Reson. Chem.*, **28**, 774 (1990); [c] M. J. Musmar and R. N. Castle, *J. Heterocyclic Chem.*, **28**, 1533 (1991).
- [4] K. Nagayama, A. Kumar, K. Wüthrich and R. R. Ernst, *J. Magn. Reson.*, **40**, 321 (1980).
- [5] A. Bax and S. Subramanian, *J. Magn. Reson.*, **67**, 565 (1986).
- [6] A. Bax and M. F. Summers, *J. Am. Chem. Soc.*, **108**, 2093 (1986).