MAGNETIC RESONANCE IN CHEMISTRY, VOL. 25, 981-984 (1987)

Application of the XCORFE Long Range Heteronuclear Correlation Sequence to Several Biphenyls and *m*-Quaterphenyls

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A series of highly substituted biphenyls and *m*-quaterphenyls have been synthesized and carbon and proton NMR spectra have been assigned by a combination of 1D and 2D techniques. The XCORFE variation of the long range heteronuclear correlation experiment was found to be particularly valuable in making assignments via H-C-C-^{13}C correlations.

KEY WORDS XCORFE Long Range Heteronuclear Correlation ^{13}C NMR ^{1}H NMR Biphenyls *m*-quaterphenyls

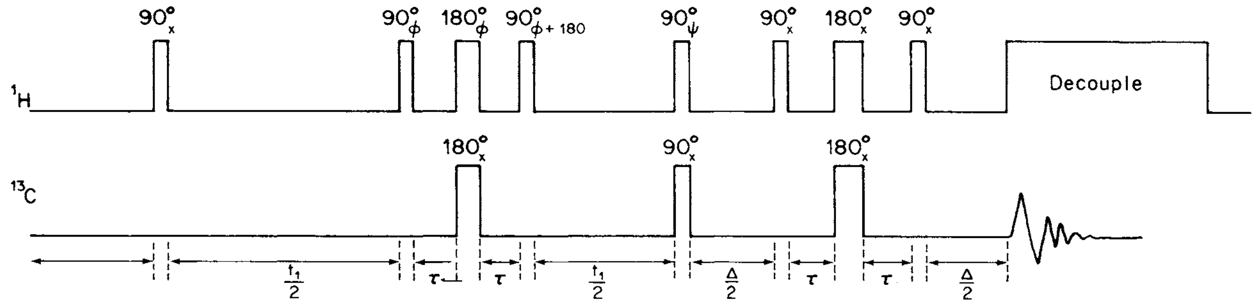
INTRODUCTION

Organic chemists have found the 2D heteronuclear chemical shift correlation experiment (HETCOR) to be of particular utility in tying together proton and carbon chemical shifts for structure assignment purposes. The extention of this experiment to two and three bond couplings, potentially of equal or greater utility in the assessment of the carbon framework, has proven more challenging. The conventional HETCOR sequence suffers in that the final pair of 90° pulses is bracketed by delay periods which become long as the couplings between protons and carbon become smaller. Compounded by signal losses due to multiple homonuclear proton couplings, T_2 losses can greatly reduce the sensitivity of the experiment. One solution to this problem has been offered by Kessler, *et al.*[1] who have produced a pulse sequence, COLOC, which cuts the T_2 losses by placing the evolution period inside the delay preceeding the final pair of 90° pulses.

Recently, Reynolds, *et al.*[2] have described another approach (XCORFE, *X*-nucleus-proton *COR*relation with *F*ixed *E*volution time) to this problem which seems to offer some attractive features. Reproduced here for discussion purposes, the details of the sequence including the phase cycling are given in their article. As can be seen, simultaneous 180° pulses on ^{1}H and ^{13}C are stepped incrementally through a fixed evolution period. The sequence includes two bilinear rotations (BIRD pulses), the first of which has the effect of decoupling protons which are not directly bonded to ^{13}C but which leave vicinal proton couplings intact for two bond J(^{1}HC^{13} C) correlations. This allows one to differentiate such two bond from three bond couplings in the long range HETCOR experiment. The BIRD Sequence, originally described by Garbow, Weitekamp and Pines[3] was applied by Bax to the conventional one bond HETCOR experiment to produce broad band homonuclear decoupling.[4]

The second BIRD pulse addresses another problem encountered in heteronuclear correlation spectroscopy involving transfer of magnetization via long range couplings. Bauer, Freeman and Wimperis[5] first pointed out that large one bond J(CH) couplings may complicate such spectra and interfere with the detection of signals transferred through the long range couplings. Subsequently, this effect has been observed.[6] Operationally, the second BIRD pulse in the XCORFE sequence provides for the decoupling of this one bond modulation of the long range response intensity.

Recently, during the course of certain synthetic studies it became desirable to produce and characterize by NMR a number of known highly substituted biphenyls and *m*-quaterphenyls. Substituent additivity rules are only approximate for quaternary aromatic carbons and become even more uncertain when multiple substituents are present. While the conventional HETCOR experi-



0749-1581/87/110981-04$05.00

Received 6 May 1987
Accepted (revised) 30 June 1987

ment is useful for carbon assignments when the immediately attached proton assignments are secure, the XCORFE experiment offered a potentially useful aid for the assignment of more remote carbons, particularly those without attached protons. The results of these studies are reported here.

EXPERIMENTAL

Compounds. 2,6-Dinitrobiphenyl (**3**) was prepared by a modification of the procedure of Cornforth, Sierakowski and Wallace.[7] Dimethoxyethane (DME, 50 ml) was distilled from lithium aluminum hydride into a 250 ml three-necked flask which had been flame dried under an argon purge. Potassium hydride (4.6 g, 35% in oil) was added, and a solution of 3.0 g (41 mmol) of *tert*-butyl alcohol in 10 ml of DME was added dropwise with stirring. After fifteen minutes, the mixture was cooled to 0°, and 7.9 g of copper (I) iodide (41 mmol) was added. After coming to room temperature, stirring was continued for one hour. A solution of 5.8 g (35 mmol) of *m*-dinitrobenzene in 8 ml of dry pyridine was added followed immediately by the addition of 7.4 g (35 mmol) of iodobenzene. The mixture was stirred and heated to reflux overnight. After cooling, the contents of the flask were poured into 300 ml of water which was then made acidic with hydrochloric acid. The crude reaction product was collected by filtration and air dried. The crude product was slurried with low boiling light petroleum and again filtered. The filter cake was broken up and placed in Soxhlet extractor. Extraction was carried out with 200 ml of ethyl acetate. During this process 0.5 g of very pure 2,6-dinitrobiphenyl, mp 191-192° (lit[5] 191-192°) precipitated out. Evaporation of the solvent gave 7.2 g of light brown solid, mp 188-191°. The proton NMR for this material was identical with that of the pure sample. Crystallization was from a minimum of hot ethyl acetate, yield 6.3 g, mp 191-192°.

Conversion of 2,6-dinitrobiphenyl to the 2-nitro-6-methoxybiphenyl (**4**) was by treatment with sodium methoxide in HMPT as per the route of Cornforth, Sierakowski and Wallace.[7] This, in turn, was converted to 2-nitro-3-iodo-6-methoxybiphenyl (**5**) and by coupling with copper triflate[8] to 4″, 6′-dimethoxy-2′,2″-dinitro-*m*-quaterphenyl (**7**). Compound **7** (300 mg) was dissolved in 60 ml of acetic acid and catalytically hydrogenated over 100 mg of palladium (5 per cent) on carbon. Hydrogen uptake was slow, requiring three days for completion. Workup consisted of filtration to remove the catalyst, removal of the bulk of the solvent by rotary evaporation, and precipitation of the product by the addition to 100 ml of water. The melting points of all compounds were in agreement with the reported values.[7,8]

Biphenyl was nitrated to form 2,2′,4,4′-tetranitrobiphenyl (**2**).[7] Copper *tert*-butoxide was prepared by the method given above, and the tetranitrobiphenyl was coupled with iodobenzene following the published procedure[7] yielding 2′, 2″, 4″, 6′-tetranitro-*m*-quaterphenyl (**6**).

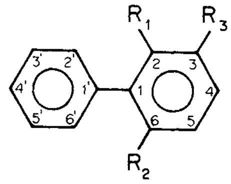
NMR Determinations. All spectra were determined on a Varian XL-300 NMR Spectrometer operating at 300 MHz for protons and 75 MHz for carbon. A 5 mm switchable probe was used throughout. The 90° pulse widths for this probe were 20 μs for protons, 23.5 μs for carbon. Decoupling was carried out using the instrument's low power decoupler. Calibration of the proton 90° pulse on the decoupler coil using a sample of menthol and the DEPT sequence gave a value of 89 μs with a low power coupler attenuation of 1. All experiments were run on 30-50 mg samples made up to 0.7-1.0 ml in deuterochloroform. Chemical shifts are reported with respect to internal TMS. Varian version 6.1 software was used throughout.

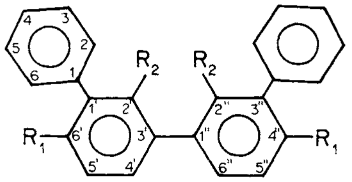
Heteronuclear chemical shift correlation spectra (HETCOR) were acquired with 128 time increments zero filled to give a final 1024 by 1024 data matrix. The minimum sweep width required to cover the proton spectrum in the aromatic region was used. The Varian software uses the pulse sequence of Bax[4] for H-H decoupled spectra.

The XCORFE spectra were acquired similarly. The delay Δ (D3 in the Varian software) was set at 0.05 s. The number of increments was determined by the relationship NI = 2 · SW2 · T, where SW2 is the width of the proton spectrum and T is defined by the pulse sequence already given. An average value of $^1J(CH)$ of 165 Hz was used. The most generally useful value for T was 0.128, but trial experiments with T = 0.07 or 0.04 were essayed in some instances.

RESULTS AND DISCUSSION

The compounds utilized in this study consisted of biphenyl (**1**), included for comparison purposes, 2, 2′, 4, 4′-tetranitro-biphenyl (**2**) and the three biphenyls **3**, **4** and **5** below, as well as the three indicated *m*-quaterphenyls. The assigned carbon and proton chemical shifts are given in Tables 1 and 2, respectively. The values for biphenyl were also determined and are included for comparison purposes.





R = H if not specified

3 $R_1 = R_2 = NO_2$
4 $R_1 = NO_2, R_2 = OCH_3$
5 $R_1 = NO_2, R_2 = OCH_3, R_3 = I$

6 $R_1 = R_2 = NO_2$
7 $R_1 = OCH_3, R_2 = NO_2$
8 $R_1 = OCH_3, R_2 = NH_2$

The assignment techniques used throughout may be exemplified by the case of 2′, 2″-diamino-4″, 6′-dimethoxy-*m*-quaterphenyl (**8**). The 1D proton and ^{13}C NMR Spectra are shown along with the XCORFE spectrum in Figure 1. The upfield proton doublet at 6.55 ppm can be assigned to protons 5′ and 5″ since these are *ortho* to the methoxyl groups and *para* to the amino groups. It follows that protons 4′ and 6″ are to be assigned as the doublet at 7.15 ppm. The associated carbons were deduced from the HETCOR spectrum. The XCORFE

Table 1. Carbon chemical Shifts (Deuterochloroform).[a]

Compound Carbon	1	2	3	4	5	6	7	8
1	141.2	138.4	129.7	125.0	125.4	130.2	131.6	135.0
2	127.1	146.9	150.9	151.0	155.5	128.3	129.6	130.6
3	128.7	120.9	127.1	115.4	73.0	129.0	128.3	128.9
4	127.2	148.4	130.3	128.0	139.4	130.1	128.5	127.3
5		128.1		114.5	114.2			
6		131.7		157.5	157.6			
1′			131.3	132.6	131.2	129.9	123.8	117.1
2′			128.4	129.2	129.3	150.9	151.5	143.0
3′			128.9	128.2	128.2	129.3	119.9	118.4
4′			129.5	128.5	128.6	130.5	130.8	130.9
5′						125.2	112.2	102.0
6′						150.6	157.4	157.0
OCH_3				56.0	56.4		56.7	55.7

[a] The chemical shifts for carbons identified by symmetry are not given

Table 2. Proton Chemical Shifts (Deuterochloroform)[a]

Compound C-H	1	2	3	4	5	6	7	8
2	7.53					7.31	7.32	7.35
3	7.37	9.15	8.00	7.38		7.45	7.39	7.30
4	7.28		7.66	7.37	7.78	7.42	7.37	7.30
5		8.62		7.15	6.84			
6		7.56						
2′			7.26	7.26	7.24			
3′			7.44	7.41	7.38			
4′			7.44	7.37	7.38	7.58	7.34	7.15
5′						8.00	7.04	6.55

[a] The chemical shifts for protons that are identical by symmetry are not given.

[b] Not clearly resolved.

spectrum shows H-5′ to be correlated with the carbons at 1′ and 3′ (both three bond correlations). The H-4′ is correlated with C-2′ and C-6′. At first glance there appears to be a two bond correlation between H-4′ and C-3′ but this is, in fact, a three bond correlation to C-1″. Consistently it was found that T values of 0.128 showed these three bond couplings. Correlations which crossed the essential single bond between aromatic rings were observed in every case. This observation was of considerable value as it allows one to differentiate C-1′ from C-3′. The ortho protons on the terminal phenyls are correlated with C-1′ as well as with the *ortho* and *para* carbons in their respective rings. In similar fashion, *meta* proton and carbon assignments are given by the observation in the XCORFE spectrum that the meta protons are correlated with the quaternary carbon at C-1 as well as with the opposing *meta* carbon through the three bond H-C-^{13}C magnetization transfer. The combination of HETCOR and XCORFE data provides nearly all the needed assignments for both carbons and protons in these compounds. They do not, however, allow a unique decision on the assignments of the two carbons bearing nitro groups in **2** and **6**, and proton coupled ^{13}C NMR spectra were obtained for both. The splitting patterns were readily interpreted to yield the assignments in Table 1.

Substituent effects on chemical shifts for this series of aromatics will reflect the usual inductive and field effects compounded by the complexities of multiple

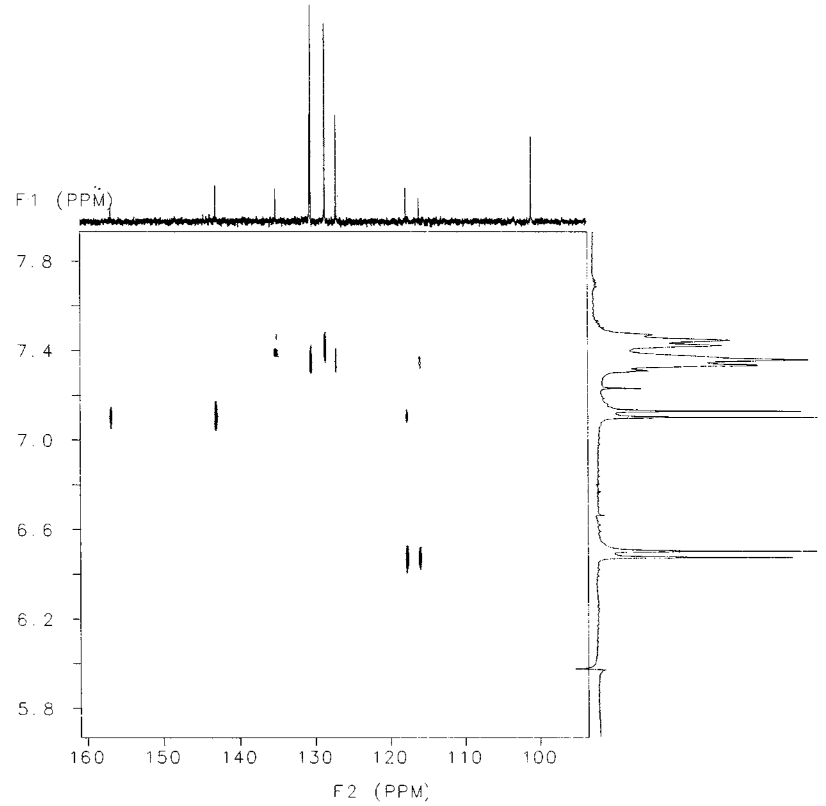


Figure 1. The XCORFE spectrum of 2′,2″-diamino-4″,6′-dimethoxy-*m*-quaterphenyl.

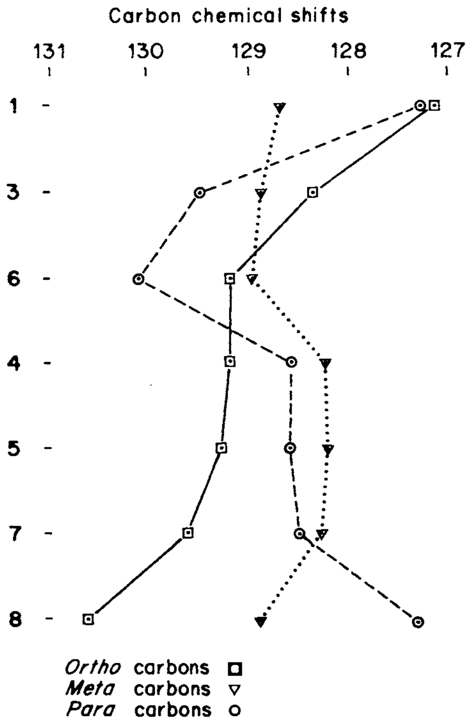


Figure 2. Schematic of the variation in phenyl carbon chemical shifts for differing structures in this study.

substitution and transmission through the biaryl framework. Schulman, *et al*[9] have reported the long range substituent effects for a series of 4-substituted biphenyls systems which may approach planarity of the aromatic rings allowing substantial conjugative interaction. By comparing substituent effects in a series of substituted fluorenes and biphenyls, Roberts[10] has devised a scheme for calculating the degree of non-planarity in several 2,2'-biphenyls.

Figure 2 shows the variations in chemical shifts for the ^{13}C nuclei of the unsubstituted phenyl groups in the present series of compounds. The vertical ordering is by increasing substitutional complexity and electron donating power. Excepting biphenyl, these phenyls must be oriented at substantial twist angles to their adjacent, substituent-bearing aryl rings. Conjugative transmission of substituent effects (resonance) must be minimal in such systems. Not unexpectedly, *meta*-carbon chemical shifts show a small range of chemical shifts (128–129 ppm). Introduction of two nitro groups at the *ortho* positions (**3** and **6**) produces a marked deshielding in the unsubstituted ring at the *ortho* and *para* carbons. The union of **3** to form **6** augments this deshielding slightly.

Replacement of the nitro group in **3** by a methoxy group causes a perceptible shielding increase for the *para* carbon which persists upon iodination to **5** and subsequent coupling to form **7**. Reduction of the nitro group in **7** to **8** produces a further shielding of the *para* carbon. However, both the *ortho* carbons and C-1 exhibit downfield shifts. These observations imply the operation of a multiplicity of substituent effects and reemphasize our deficiencies in understanding the details of their operation.

Acknowledgement

Grateful acknowledgement is hereby extended to The Robert A. Welch Foundation for their support of this work.

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