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Benchtop NMR Spectroscopy and Spectral Analysis of the *cis*- and *trans*-Stilbene Products of the Wittig Reaction

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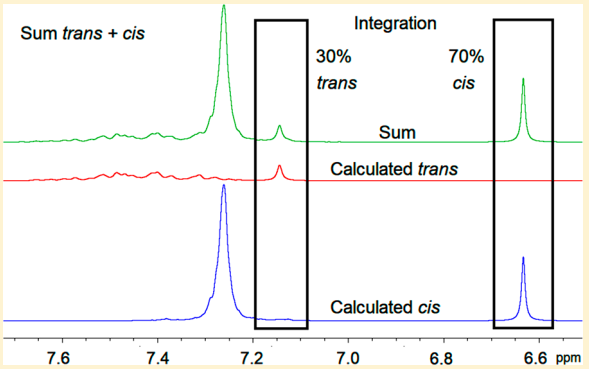
Supporting Information

ABSTRACT: Benchtop NMR spectrometers are now becoming more widely employed in university teaching laboratories. These low-field instruments are increasingly used in reaction monitoring and product purity applications. NMR spectra obtained using these spectrometers (40−80 MHz) tend to suffer from significant overlap of signals when compared to those obtained at 300−400 MHz or above, and therefore, some reactions may be less suited to analysis using such benchtop systems. While some reactions can be modified to make them more amenable to analysis on low-field benchtop spectrometers, the fact remains that many common undergraduate laboratory chemistry reactions remain as a stalwart of the university education system. Therefore, there is currently a major requirement for benchtop NMR analysis to improve in order to facilitate student understanding. Herein, it is demonstrated that a combination of spectral analysis and simulation at low-fields (40−80 MHz) allows the fine structure of second-order effects and overlapping spectra to be deduced, enabling an improved understanding of the low-field benchtop NMR technique within undergraduate student cohorts. The evolution of well-resolved and distinct multiplets at 400 MHz to complex, overlapping multiplets at 40−80 MHz also serves as a useful guide for laboratory demonstrators and academic staff when explaining the advantages of such benchtop systems. The Wittig reaction has been a standard reaction practical session in many university teaching laboratories since the 1980s, the products of which are a mixture of *cis*- and *trans*-stilbenes. This reaction serves as an ideal example of how benchtop NMR spectrometers and analysis can support chemistry teaching laboratories.



KEYWORDS: *Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry, Inquiry-Based/Discovery Learning, NMR Spectroscopy, Conformational Analysis*

INTRODUCTION

The Wittig reaction[1] was first published in 1953, and this synthetic route has since become a significant economic and educational success, earning Wittig a Nobel Prize in Chemistry in 1979. In 1973, Markl and Merz[2] reported the simultaneous preparation of *cis*- and *trans*-stilbenes from the Wittig condensation of benzaldehyde with benzyltriphenylphosphonium chloride (Scheme 1). This method was eminently applicable to undergraduate teaching laboratories and has been widely adopted in this context globally.[3]

In principle, it is possible to separate the *cis*- and *trans*-stilbene regioisomers for their analytical characterization using techniques such as melting point, FTIR spectroscopy, or electronic absorption spectrophotometry. However, high-field ^{1}H NMR spectroscopy removes the requirement for prior purification of the products arising, since the relative yields of the *cis*- and *trans*-regioisomers can be determined simply by integrating the alkene signals located at 6.63 and 7.13 ppm, respectively, with triphenylphospine oxide not appearing in this part of the NMR spectrum. In addition, the cost savings on equipment, chemicals, and laboratory time by the omission of a time-consuming purification step is very attractive to many teaching laboratories.

The requirement of having access to high-field NMR spectrometers (typically 300−400 MHz operating frequencies)[4] is, of course, a significant consideration since these generally range between $100K and $300 K, and while these instruments may be financed as a research instrument on which undergraduate teaching time can be hired on an hourly rate basis, the full economic cost per laboratory experiment and per student can be substantial. Currently, many novel applications are being explored for NMR spectroscopy, particularly with regard to the miniaturization of "state-of-the-art" rapid analytical monitoring technologies.[5−8] Indeed,

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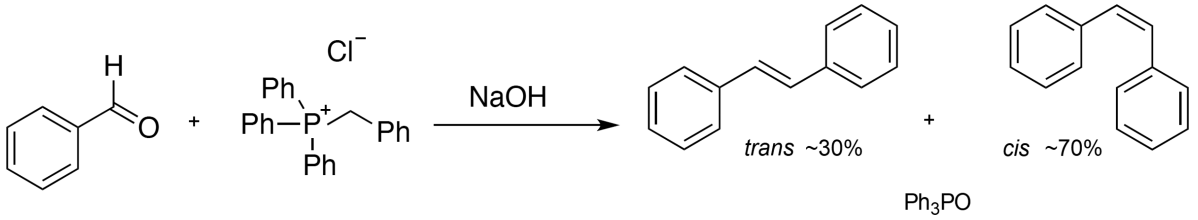
Scheme 1. Reaction of Benzaldehyde with Benzyltriphenylphosphonium Chloride To Form a Mixture of *cis*-Stilbene (Major Product), *trans*-Stilbene (Minor Product), and By-product Triphenylphosphine Oxide



many universities have now invested in low-field, benchtop NMR spectrometers and utilize them in chemistry undergraduate teaching experiments[9−11] in order to determine reaction progress and product purities, for example. The value of the student experience that comes with direct access to a benchtop NMR instrument, however, must be considered when the purchase price is discussed; the cost of these facilities lies between $20K and $70K. Also, tangible and intangible savings of staff time and sample transport to available high-field NMR instruments support a stronger financial case to invest in benchtop NMR systems within the teaching laboratory. Herein, the advantages offered to a potentially wide range of undergraduate laboratory experiments by the application of benchtop NMR spectrometers are highlighted, as well as the benefits of supporting low-field spectral computations in tandem.

Few undergraduates have access to "hands-on" training on large, high-field NMR spectrometers, with many analyses taking place as a remote service with the students receiving their NMR spectrum and associated data, or even a generic handout containing this information recorded some years prior. Unfortunately, this process, which disconnects key linkages between students and their institutional NMR spectrometer(s), strongly impacts the educational value of such laboratory classes; i.e., pedagogically important synchronous connections between NMR lecture materials and the on-site practical assessment of reaction products using this technique are broken (Figure 1). Therefore, this represents one of the most compelling reasons for inclusion of benchtop NMR spectrometers within undergraduate laboratories, in order to allow students to have a "hands-on", real-time access to a means of analysis which provides substantial information on their analyte samples during laboratory classes. Recent advances in pedagogical analytical chemistry[12] have highlighted the importance of pooling novel and well-established teaching techniques to a course where the practical and theoretical components are intrinsically interlinked.

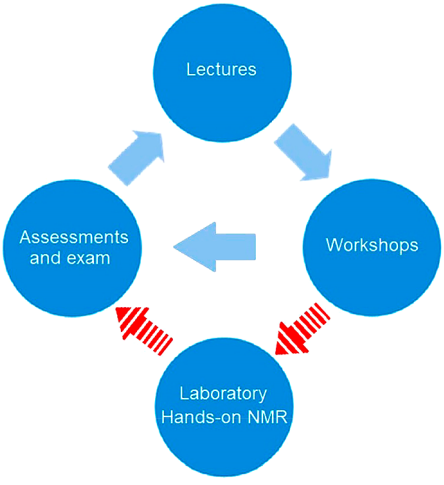


Figure 1. Disconnect in pedagogy (shown in red) caused by the removal of "hands-on" NMR spectroscopy in teaching laboratories during a typical higher education institute academic year.

Several universities have had success using benchtop NMR spectrometers at an operating frequency of 45 MHz, and these low-field systems have been used to analyze Fischer esterification products,[13] and the free-radical-mediated bromination of ethylbenzene.[14] Moreover, the portability of these systems also permits them to be used in university−high school partnership programs in the USA,[15] and university outreach strategies in the UK.[16]

The teaching of NMR theory that is offered at the undergraduate level is focused on high-field magnets (300−400 MHz and beyond); however, the rules and principles do not strictly apply to low-field benchtop NMR spectrometers in the same manner.[17,18] In recent decades, many NMR courses and textbooks have evolved to the point where low-field NMR magnets are no longer mentioned, and the influences of first- and second-order effects are no longer covered in significant detail. The term "roofing" for the slight distortion away from the classic 1:1, 1:2:1, and 1:3:3:1 Pascal's triangle intensities of simple multiplet resonances is insufficient to analyze a closely coupled ABX spin-system. Hence, both undergraduates and university academic staff should develop the ability to appreciate modifications to the appearance of NMR spectra as a function of magnetic field strength.

As early as the middle of the 20th century it was reasoned that the direct (through-space) dipole−dipole coupling between two hydrogen nuclei would average to zero in view of random isotropic motion in the liquid state which is indeed correct (*J*-coupling tensor 3 × 3 matrix averages to zero). However, small couplings of a few Hz in magnitude were routinely observed. This was the subject of much debate but rationalized by the influence of the bonding electrons between the hydrogen atoms (H−C−H or H−C−C−H, etc.) and is therefore referred to as the *indirect* (through-bond) dipole−dipole coupling. This interaction can be defined as the average of the diagonal of the elements of the *J*-coupling tensor, which is scalar, indicating that the isotropic component of the *J*-coupling Hamiltonian is independent of molecular motion.[19] Now more commonly referred to as the *J*-coupling in undergraduate chemistry lectures and textbooks, the size of this interaction between neighboring hydrogen atoms is the same at 40 MHz as at 400 MHz; it is field independent, and thus, a typical $^3J_{HH}$ coupling in an aromatic group will correspond to 7.7 Hz at 40 MHz as well as at 400 MHz. As the magnitude of the *J*-coupling remains the same size in different magnetic fields, this has a significant influence on the

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appearance of NMR spectra recorded at different magnetic fields since the chemical shifts involved are field independent of the ppm scale, but are field dependent on the Hz scale. Consequently, by inspection, a doublet may appear to be "larger" at 40 MHz (40 Hz per ppm) than at 400 MHz (400 Hz per ppm). This, in turn, leads to the second-order nature of the spectra being more pronounced at low-field than at high-field, in which a doublet can appear to be distorted and no longer adhere to a 1:1 intensity ratio. This distortion arises from the quantized energy levels that exist for the spin-system and the transition probabilities between each level therein. Undergraduates are taught that allowed transitions by established selection rules appear as resonances in the spectra, whereas forbidden transitions by the selection rules do not appear to be present therein. Thus, for a first-order spectrum both transitions that create a doublet are equally probable, hence producing the 1:1 doublet intensity ratio (H_AH_X). When the chemical shift difference between the coupling pair of hydrogens (in Hz) approaches approximately 10 times the *J*-coupling between them, one of the transitions becomes less probable (less allowed), leading to a distorted doublet as indicated by the term "roofing" (H_AH_B). For a strongly second-order system in which the chemical shift difference between the coupling pair of hydrogen nuclei (in Hz) approaches approximately 5 times the *J*-coupling between them, then the transition probability decreases significantly for one signal in the doublet, leading to a steeply roofed doublet ($H_AH_{A'}$). The natural end point occurs when the chemical shifts of the two hydrogen nuclei are equivalent (i.e., they have the same chemical shift value), and in this model the transition probability of one signal in the doublet is zero, therefore giving rise to a signal that appears to be a singlet.

Herein, the high- and low-field NMR spectra of *cis*- and *trans*-stilbenes serve as an illustrative example to highlight these changes. In particular, the computationally simulated spectra decrementing from 400 → 300 → 200 → 80 → 60 → 40 MHz, allow students to follow the evolution of multiplets from prominent and clearly distinct signals at the higher operating frequencies to those affected by lower resolution, with an increasing level of spectral overlap and significant second-order effects.

CHEMICAL SHIFTS AND COUPLING CONSTANTS

Analysis of NMR multiplets to extract chemical shift and coupling constant values has been a central part of NMR spectroscopy since the 1950s,[20,21] when the AA′BB′ spin-systems[22] of thiophene,[23] furan and pyrrole,[24] and substituted fluoro-aromatics[25] were recorded at 30, 40, and 60 MHz, and analyzed using pencil and paper calculations. Since that time, detailed theoretical[26−28] and computational progress has vastly improved solutions to such NMR problems. This resulted in the employment of computational methods such as Laocoon,[29] and PANIC,[30] and in more recent decades, by graphic-based calculations such as those featured in WinDNMR,[31] Louiville calculations employing the experimental pulse-programs within NMR-SIM,[32] iterative methods such as SpinWorks,[33,34] and line-shape algorithm approaches, i.e., ANATOLIA in 2018 (S1 and S2 in Supporting Information),[35] such that it has never been easier to analyze experimental NMR spectra. In addition, the theoretical chemistry community has developed spectral prediction routines for common electronic structure codes such as Gaussian,[36] allowing for the calculation of NMR shielding tensors and coupling from *ab initio* methodologies as well as semiempirical methods.[37,38]

Mnova[39] is a popular suit of commercial software that can process, predict, and analyze NMR spectra from all NMR vendors. One module allows extraction of first-order coupling constants but does not allow iterative analysis of second-order spin-systems. The chemical shift and coupling data extracted from highly second-order spectra using other methods can be input manually to generate simulated spectra. Spin Works is a popular spectral analysis program that employs an assign−iterate method to optimize spectral parameters, and this works very well; however, the assign process can be slow and time-consuming even when the "automatic assign" feature is employed. Thus, multiple attempts to extract parameters can be time-consuming, especially when input parameters produce a calculated spectrum that is very different to the experimental spectrum. WinDNMR is a graphical program that used chemical shift and coupling values to generate a spectrum; a significant advantage of this program is that a chemical shift and/or coupling constant value can be incremented with the resulting spectrum updated in real time, which allows an intuitive visual comparison to be made regarding the influence of parameters on the appearance of the spectrum. Bruker TopSpin4.0 is free for academic use and contains a line-shape analysis module, DAISY,[40] that can analyze first-order and some second-order spin-systems. TopSpin can import experimental data sets from benchtop spectrometers (JCAMP-DX), and from JEOL and Varian spectrometers ready for analysis using ANATOLIA.

It is prudent to consider chemical shift and scalar coupling constant values at an operating frequency of 400 MHz (S3 and S4 in Supporting Information) before moving on to spectra recorded at only 60 MHz. The literature values for the AA′BB′C spin-system of the aromatic protons in stilbene are an excellent starting point for analysis, and the SpinWorks module[30,31] and ANATOLIA generated excellent fits to the 400 MHz ^{1}H NMR spectra of the *trans*-regioisomer, which displayed small second-order effects within the clearly defined doublets and triplets. However, the ^{1}H NMR spectrum of *cis*-stilbene was more complex, since the doublet and triplet patterns overlap significantly, even at an operating frequency of 400 MHz, and the second-order effects are significant ($\Delta\delta/J <$ 5) for all coupling nuclei. In this instance, the iterative line-shape analysis program ANATOLIA proved to be more user-friendly and a faster analysis method than the traditional assign−iterate methods and achieved an excellent match with experimental results. The results are shown in Tables 1 and 2. t1 t2

The ^{1}H NMR spectrum of *trans*-stilbene is composed of three magnetically distinct sets of aromatic hydrogen nuclei, together with the vinylic hydrogen, which are labeled AA′, BB′, C (aromatics), and D (vinylic), as shown in Figure 2. If the $^3J_{HH}$ couplings are considered (∼8.0 Hz), then the expected multiplet patterns would be AA′, doublet; BB′, triplet; and C, triplet, with the integration ratio of 2:2:1, respectively, for the *ortho*-, *meta*-, and *para*-position hydrogens (2,6-, 3,5-, and 4-positions). However, it is important to include additional coupling constant parameters in such evaluations, since the magnetic inequivalence of the A and A′, and B and B′, nuclei gives rise to significant couplings between them, i.e., on the order of approximately 1−2 Hz. Once the long-range $^4J_{AC}$, $^4J_{A'C}$ couplings of ∼1.22 Hz and $^5J_{AB'}$, $^5J_{A'B}$ couplings ∼0.6 Hz are included, then the ^{1}H NMR spectrum can be accurately calculated and predicted at any magnetic field. The chemical

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Table 1. Chemical Shift and Coupling Constant Values for *cis*- and *trans*-Stilbenes[a]

	cis-Stilbene	*trans*-Stilbene
$\delta A = \delta A'$	7.285 ppm	7.550 ppm
$\delta B = \delta B'$	7.259 ppm	7.391 ppm
δC	7.225 ppm	7.292 ppm
δD	6.633 ppm	7.150 ppm
$^3J_{AB} = {}^3J_{A'B'}$	7.92 Hz	7.92 Hz
$^3J_{BC} = {}^3J_{B'C}$	7.47 Hz	7.47 Hz
$^4J_{AA'}$	2.05 Hz	2.05 Hz
$^4J_{BB'}$	1.42 Hz	1.42 Hz
$^4J_{AC} = {}^4J_{A'C}$	1.22 Hz	1.22 Hz
$^5J_{AB'} = {}^5J_{A'B}$	0.60 Hz	0.60 Hz

[a]Recorded and analyzed at 400 MHz in $CDCl_3$, but the same data set can be used to calculate spectra at any magnetic field strength.

shift (ppm) of the AA′, BB′, and C nuclei remains the same at both 400 and 60 MHz magnetic fields (indeed at any magnetic field). However, the chemical shift differences $\Delta\delta$ in Hz are significant at 400 and 60 MHz operating frequencies (400 Hz per ppm vs 60 Hz per ppm, respectively), and hence, spectra recorded at low-field display significant second-order effects, when $\delta\Delta/J < 5$. It is important to note that undergraduates should not be expected to analyze and obtain these values themselves but employ these data to generate spectra at a variety of magnetic fields in order to observe changes in their appearance and configuration. Analysis of such ^{1}H NMR spectra acquired at ≥400 MHz provides a data set of chemical shift and coupling constant values that can then be used for predictively calculating the corresponding 60 MHz spectral profile.

By calculating NMR spectra at a variety of different magnetic field strengths, and comparing these to experimental spectra, it is clear that some of the signals that could easily be assigned to "impurities" are actually part of the NMR spectrum. This is clear in Figures 3 and 4, in which the classic doublet-triplet−triplet system is clearly visible in *trans*-stilbene at 400 MHz, but more difficult to visualize for the *cis*-isomer since the chemical shift values of these aromatic ^{1}H nuclei are very similar and the second-order effects are significant. The calculated NMR spectra for 400−45 MHz of *trans*-stilbene serve as a useful illustration to students to guide them from familiar high-field NMR spectra to less familiar low-field NMR spectra. In Figure 5, the *trans*-stilbene spectrum obtained at only 60 MHz displays low-intensity signals both upfield and downfield of the aromatic signal envelope, which may erroneously be attributed to impurities, and the asymmetry of the main aromatic resonance may be explained as "poor shimming". Only by a comparison of the calculated spectrum

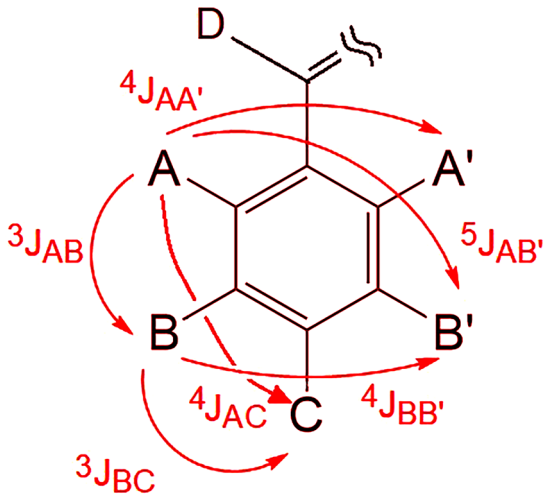

Figure 2. Phenyl moiety and alkene, with the AA′BB′CD labeling and scalar coupling interactions.

to the experimental spectrum can these signals be rationalized unequivocally.

The Wittig reaction typically yields ∼60−70% of the *cis*-stilbene product, and 30−40% of the *trans*-product (S5, S6, and S7 in Supporting Information), and these two isomers are readily distinguishable in the 60 MHz ^{1}H NMR spectrum via their vinylic proton signals located at δ = 6.63 and 7.15 ppm, respectively. For this experiment, ∼100 mM solutions were used (∼20 mg of total stilbene in 0.70 mL of $CDCl_3$) which provided an excellent signal-to-noise (SNR) ratio of 208 (Bruker TOPSPIN-4.0.3 "sinocal" command) with only 16 scans completed on the benchtop system. Determination of the exact *cis*:*trans* ratio of stilbenes synthesized by each student during a practical laboratory class can be readily obtained by integrating the vinylic proton resonances; an example of the appearance of the calculated spectrum for a 70:30 mol % mixture of these isomers is shown in Figure 6. It is important to highlight that the SNR is of such a high level that an acceptable spectrum can be obtained using a single scan using a ∼100 mM solution and still provides a reliable estimate of the *cis*:*trans* ratios of stilbene product analytes. Therefore, solutions of ∼10 mM (∼2 mg sample in 0.70 mL $CDCl_3$) could be used with a larger number of scans.

With regard to Wittig reaction chemistry, it is clear from these studies that using ∼2 g of the benzaldehyde starting material for this purpose is excessive, and that much smaller amounts could be used. The cost of benzaldehyde is ∼$35 for 100 g, and that of benzyltriphenylphosphonium chloride is ∼$60 for 100 g of material. Moreover, there are significant cost savings achievable via reductions in the amounts and volumes

Table 2. Chemical Shift Difference ($\Delta\delta$) in Hz and Ratio with Coupling Constants[a]

	cis-Stilbene	*trans*-Stilbene	*cis*-Stilbene	*trans*-Stilbene
Field strength	400 MHz	400 MHz	60 MHz	60 MHz
$\Delta\delta$(A − B)	10.51 Hz	63.42 Hz	1.58 Hz	9.51 Hz
$\Delta\delta$(B − C)	13.74 Hz	39.57 Hz	2.06 Hz	5.94 Hz
$\Delta\delta$(A − B)/$^3J_{AB}$	10.51/7.92 = 1.33	63.42/7.92 = 8.00	1.577/7.92 = 0.20	9.513/7.92 = 1.20
$\Delta\delta$(B − C)/$^3J_{BC}$	13.74/7.47 = 1.84	39.57/7.47 = 5.29	2.061/7.47 = 0.28	5.936/7.47 = 0.80
$\Delta\delta$(A − C)/$^4J_{AC}$	24.25/1.22 = 19.88	102.99/1.22 = 84.42	3.64/1.22 = 2.98	15.45/1.22 = 12.66
$\Delta\delta$(A − B′)/$^5J_{AB'}$	10.51/0.60 = 17.52	63.42/0.60 = 105.7	1.58/0.6 = 2.63	9.51/0.6 = 15.86

[a]Recorded and analyzed at 400 and 60 MHz in $CDCl_3$. For $\Delta\delta/J < 5$, then second-order coupling effects are expected.

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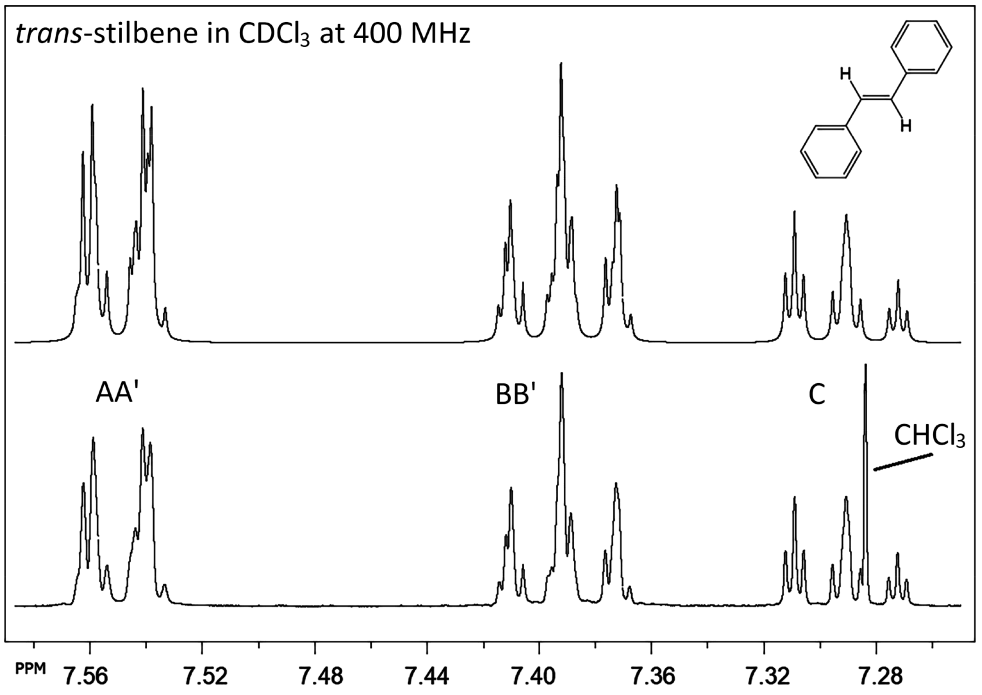

Figure 3. ^{1}H NMR spectrum of *trans*-stilbene in $CDCl_3$ at 400 MHz, displaying the classic double-triplet−triplet patterns. This analysis was performed using ANATOLIA and SpinWorks software programs to yield accurate chemical shift and coupling constants (top, calculated; bottom, experimental).

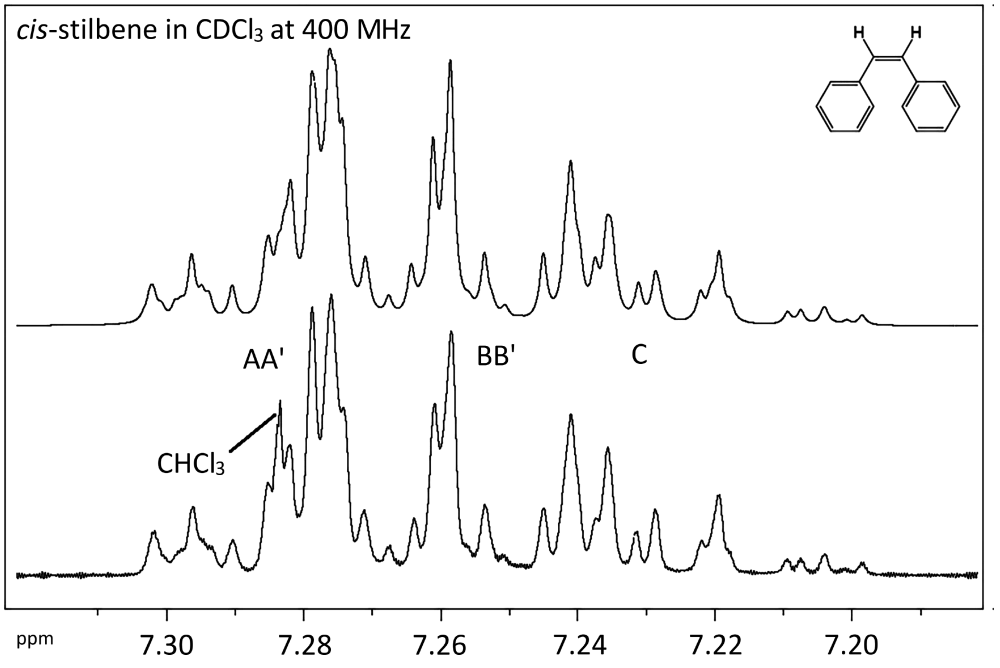

Figure 4. ^{1}H NMR spectrum of *cis*-stilbene in $CDCl_3$ at 400 MHz. Here, second-order effects are significant, and signal overlap and distorted intensities prevent the classic doublet-triplet−triplet patterns from being observed. Nevertheless, computational analysis using ANATOLIA and SpinWorks software programs allowed accurate chemical shift and coupling constant values to be extracted from the profile (top, calculated; bottom, experimental).

of reagents and solvents required, i.e., dichloromethane (20 mL), aqueous NaOH solution (20 mL), distilled water (30 mL), saturated aqueous sodium bisulfite solution (50 mL), anhydrous sodium sulfate (~5 g), absolute ethanol (30 mL), low-boiling-point (30−60 °C) petroleum ether (30 mL), etc.; typical current standard undergraduate laboratory requirement values are provided in parentheses. One salient point to highlight is that benchtop NMR spectrometers do not necessitate the use of deuterated solvents, which therefore offers a wider choice of low-cost solvents and a significant financial savings. Thus, a judicious selection of a solvent that has signals in a different part of the spectrum from the signals of interest can yield perfectly acceptable spectra, particularly if solvent suppression methods are employed. Therefore, this

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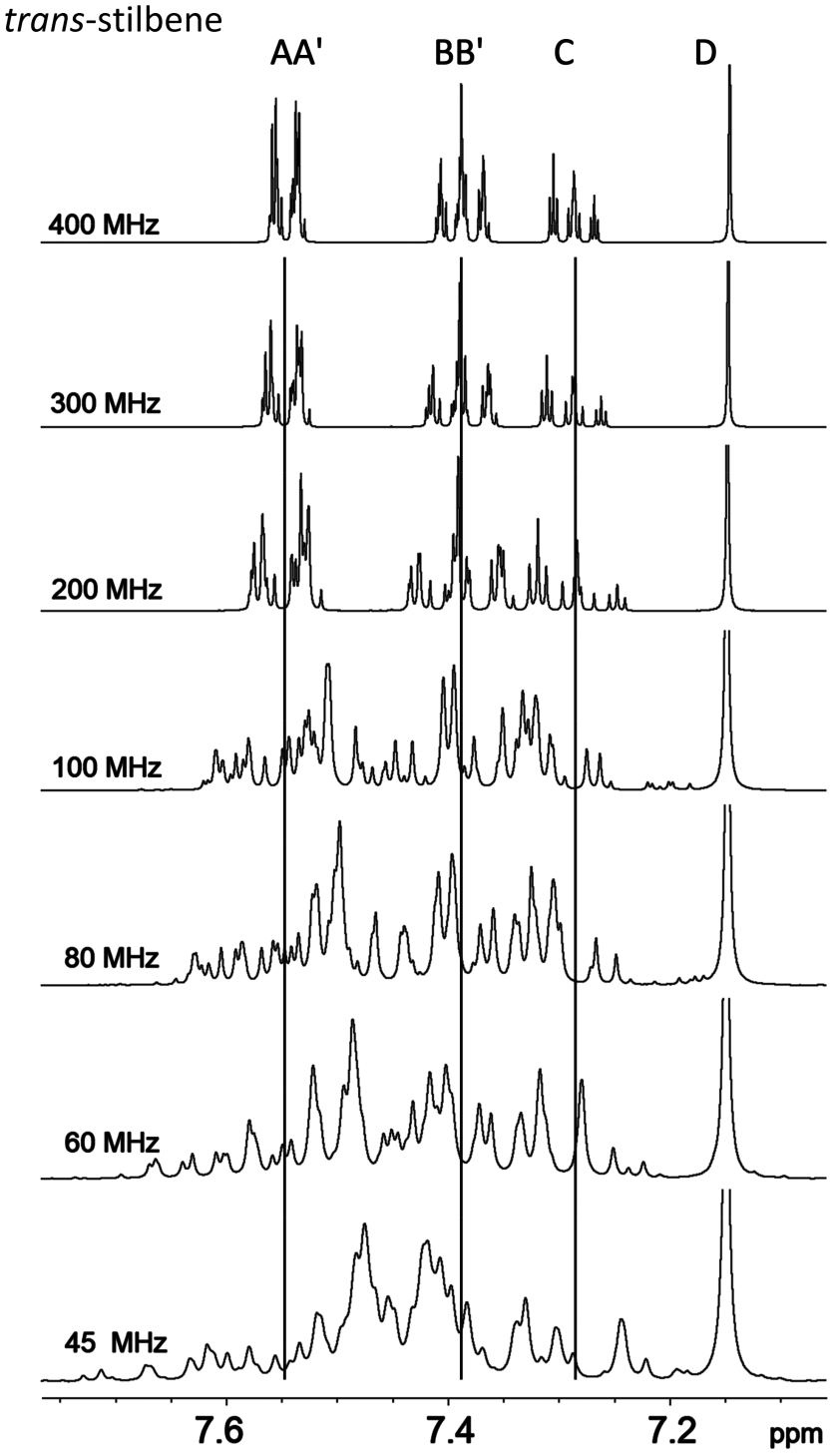

Figure 5. Calculated ^{1}H NMR spectrum of *trans*-stilbene in $CDCl_3$ at 400, 300, 200, 100, 80, 60, and 45 MHz using NMR-SIM software and accurate chemical shift and coupling constant values. Line widths were kept to a minimum in order to show as much detail as possible. The experimental spectrum at an operating frequency of 60 MHz shows an excellent fit to the calculated profile.

novel low-field benchtop NMR analysis approach offers major economic budgetary advantages to undergraduate teaching laboratory activities.

EXPERIMENTAL SECTION

The lab experiment is part of the second-year undergraduate practical chemistry class and is set up for ∼110 students each year, with the benchtop NMR aspect of the stilbene experiment being present for the past four years. The undergraduates have access to the lab for 4 h at a time with up to a maximum of 20 h available for the experiment; however, this is very rarely required. A single lab session is sufficient for most students to complete the chemistry. Academics create the lab classes. Technical tutors (with degree and PhD level qualifications) run the lab class, and postdocs and PhD students monitor the lab classes. Group demonstrations are provided for "tricky" chemistry at the start of the class; thereafter, the students follow a detailed lab script.

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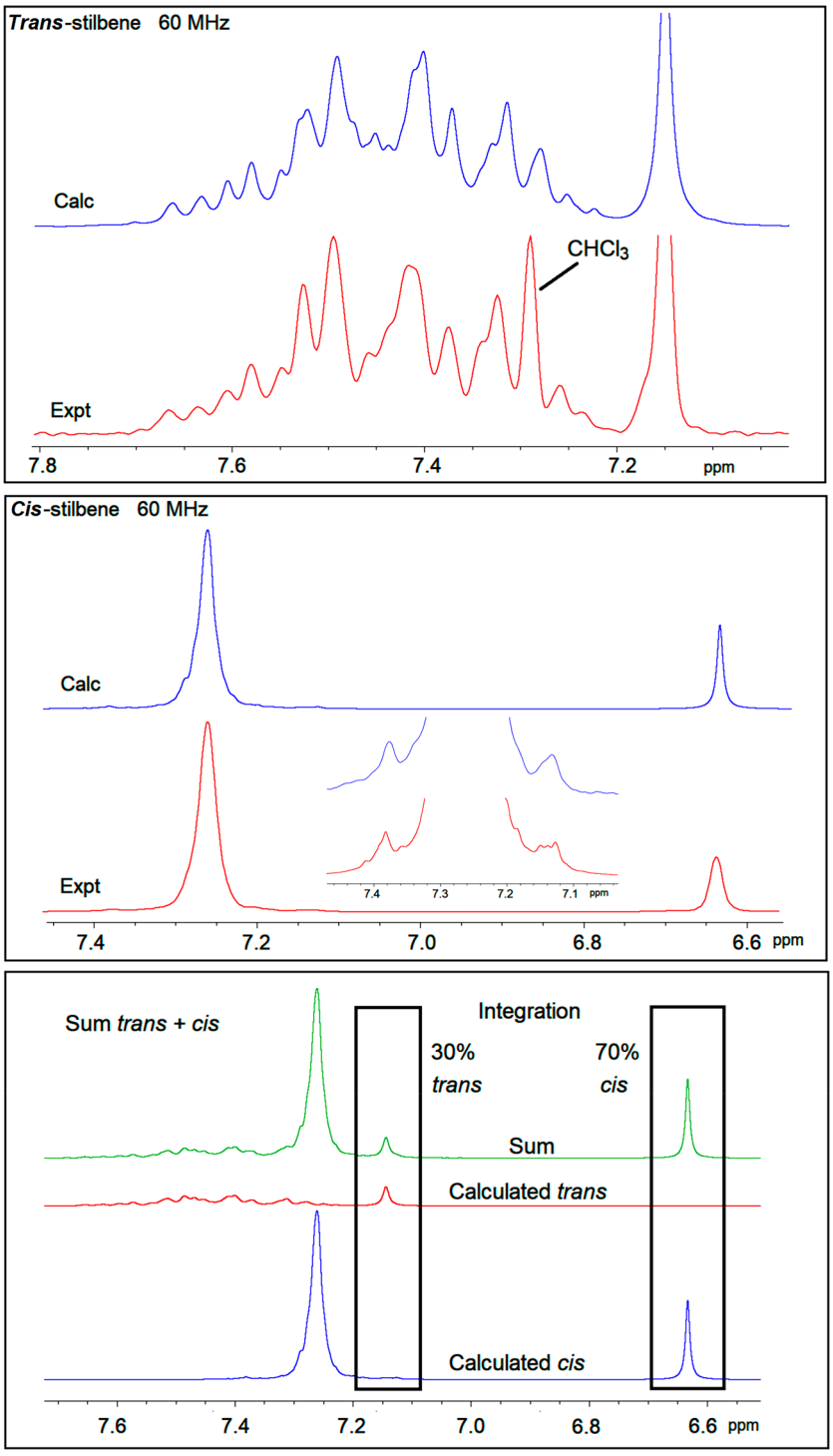

Figure 6. Calculated and experimental ^{1}H NMR spectra of *trans*-stilbene in $CDCl_3$ at 60 MHz (upper); calculated and experimental ^{1}H NMR spectra of *cis*-stilbene in $CDCl_3$ at 60 MHz (center); and calculated ^{1}H NMR spectra of a 70:30 *cis*:*trans* mixture of stilbene at 60 MHz (lower). Computational analysis was performed using ANATOLIA, WinDNMR, NMR-SIM, and/or SpinWorks software modules to yield accurate chemical shift and coupling constant values.

Careful reagent handling is required throughout the lab class, particularly for the handling of NaOH solution and starting materials. The lab capacity of ∼60 requires that the class be split into two groups and the experiment is run twice. The students are not expected to use the ANATOLIA software but have access to benchtop NMR spectrometers and handouts of 400 MHz NMR spectra which connect the 400 MHz result to the 40−80 MHz results.

The second-year students have 12 NMR lectures very early in the term, covering spin, chemical shift, couplings, ^{13}C-DEPT, COSY, and HMQC, NOE, T_1 and T_2, solvent and temperature effects, inorganic NMR, and solid-state NMR. The second-year students have an assessed NMR workshop question (H, C, DEPT, COSY, HMQC, and NOE) in term 1 where they need to assign ^{1}H and ^{13}C signals; this year, they

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have cinnamyl acetate and construct multiplets and the contributing $^1H-^1H$ interactions from neighbors.

High-field ^1H spectra were recorded using JEOL ECS-400 MHz or Bruker Avance-I 400 MHz NMR spectrometers, using an autotune probe and 5 mm NMR tubes. Samples were prepared using ∼20 mg of stilbene dissolved in a 0.70 mL volume of $CDCl_3$ obtained from Apollo-UK, i.e., ∼100 mM solutions. High-quality 5 mm diameter NMR tubes purchased from Norell were used at both 400 and 60 MHz operating frequencies. ^1H NMR spectra were recorded using the small flip-angle pulse program with P_{90} = 15.25 μs covering a sweep-width of 12.0 ppm (4,789 Hz) with 64K time domain data points giving an acquisition time of 685 s, with a relaxation delay of 5 s, Fourier-transformed using 128 K data points and referenced to an internal TMS standard at 0.00 ppm.

Benchtop ^1H NMR spectra were acquired on a Magritek-Ultra 60 MHz NMR spectrometer, with 16 scans, covering a sweep-width of 81 ppm with 64K data points in the FID, and providing an acquisition time of 6.55 s and a digital resolution of 0.059 Hz (pulse angle was 90° with a pulse length of 12.8 μs). The FID was Fourier transformed using zero-filling to 128k data points providing a spectrum with 0.038 Hz resolution. The T_1 relaxation time was measured and found to be under 2 s for each signal, and therefore, a repetition time of 10 s between scans was sufficient to allow relaxation of the ^1H nuclei to equilibrium subsequent to each scan. The total experimental time required to record the ^1H NMR spectrum was 2 min and 40 s. The temperature of the sample at both 400 and 60 MHz was 20 °C (the magnet temperature was 26.5 °C for the latter spectrometer).

Following the reaction of benzaldehyde with benzyltriphenylphosphonium chloride (typically 2.0 and 7.4 g, respectively, equivalent to a 1:1 molar ratio) in dichloromethane (20 mL), products form on addition of 20 mL of aqueous NaOH solution (50% w/w), with the mixture being stirred for 30 min. Subsequently, the organic phase was separated and washed with a 30 mL volume of distilled water, and then, 50 mL of a saturated solution of sodium bisulfite was added until the solution was neutralized. The organic phase was then dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. Finally, 30 mL of absolute ethanol was added to the thick cloudy residue, and the mixture then cooled in an ice bath for 15 min. The primary precipitate obtained was *trans*-stilbene (yield ca. 1.0 g), mp 122−123 °C. The filtrate was then evaporated, and a 40 mL volume of low-boiling-point petroleum ether (30−60 °C) was added to precipitate triphenylphosphine oxide (∼5 g), mp 146−147 °C. The filtrate arising following removal of triphenylphosphine oxide was then evaporated, yielding a liquid, *cis*-stilbene (yield ∼1.5 g).

HAZARDS

Benzyltriphenylphosphonium chloride (CAS 1100-88-5) can be fatal if swallowed or if inhaled. It is toxic in contact with skin, causes skin irritation, causes serious eye irritation, may cause respiratory irritation, and is toxic to aquatic life with long lasting effects. Dispose of in halogen waste.

Benzaldehyde (CAS 100-52-7) is harmful if swallowed, harmful in contact with skin, and causes skin irritation. Dispose of in hydrophilic waste.

Sodium hydroxide (CAS 1310-73-2) may be corrosive to metals, causes severe skin burns and eye damage, and is neutralized with 5 M HCl.

Magnesium sulfate (CAS 7487-88-9) has no hazard statements applicable; dispose of in waste bin.

Dichloromethane (CAS 75-09-2) causes skin irritation, causes serious eye irritation, may cause respiratory irritation, may cause drowsiness or dizziness, is suspected of causing cancer, and may cause damage to organs. Dispose of in halogenated waste.

Sodium bisulfite saturated solution (CAS 7631-90-5) is harmful if swallowed, causes serious eye damage, and when in contact with acids liberates toxic gas. Provide bisulfite waste bottle.

Ethanol (CAS 64-17-5) is a highly flammable liquid and vapor and causes serious eye irritation. Dispose of in hydrophilic waste. Light petroleum ether is a highly flammable liquid and vapor, is harmful if swallowed, may be fatal if swallowed and enters airways, causes skin irritation, may cause drowsiness or dizziness, and is toxic to aquatic life with long lasting effects. Dispose of in hydrophobic waste.

(*E*)-Stilbene and (*Z*)-stilbene products (*trans*, CAS 103-30-0; *cis*, CAS 645-49-8) are harmful if swallowed, cause serious eye irritation, and are toxic to aquatic life with long lasting effects.

Triphenylphosphine oxide (CAS 791-28-6) product is harmful if swallowed, causes skin irritation, causes serious eye irritation, and may cause respiratory irritation.

CONCLUSIONS

A combination of "state-of-the-art" spectral analysis and experimental benchtop NMR methods provides valuable information which helps to explain the overlapping features that are common in low-field NMR spectra. This renders benchtop NMR spectrometer systems much more applicable and accessible to undergraduate teaching laboratories. One significant advantage of calculating low-field NMR spectra is that commonly employed undergraduate laboratory experiments in synthetic organic chemistry or other areas, which may be dismissed as being "too complicated" or "lacking sufficient analytical information", can now be understood and used, without recourse to wholesale changes in methods or reagents that may have unwanted cost and safety implications. In conclusion, ANATOLIA software is an effective and robust tool which markedly facilitated the extraction of chemical shift and scalar coupling constant values from second-order overlapping spectra.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.8b00657.

Introduction to help install the ANATOLIA program, ABX spin-system example, description of the ANATOLIA input data files, ABX output file, input data files for stilbene, 400 MHz ^1H NMR spectrum of *trans*-stilbene, 400 MHz ^1H NMR spectrum of *cis*-stilbene, and 60, 80 and 400 MHz ^1H NMR spectra of crude reaction mixture (triphenylphosphine oxide, *trans*-stilbene, and *cis*-stilbene (PDF, DOCX)

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Notes

The authors declare no competing financial interest.

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