Pergamon

Tetrahedron Letters 40 (1999) 1579–1582

TETRAHEDRON
LETTERS

Unambiguous and Rapid *cis/trans* Assignment of Aryl-carboxy Disubstituted Cyclopropanes Using NMR.

Arlette Solladié-Cavallo* and Thomas Isarno

Laboratoire de Stéréochimie Organométallique associé au CNRS, ECPM/Université L.Pasteur, 1 rue B. Pascal, 67008-Strasbourg.
ascava@chimie.u-strasbg.fr

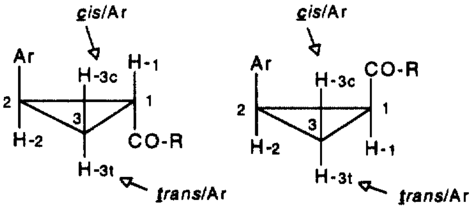
Received 5 October 1998; accepted 14 December 1998

Abstract : *It is shown that cis or trans stuctures of aryl-carboxy disubstituted cyclo propanes can be directly, rapidly and easily determined by ^1H NMR with no need of comparing both cis and trans isomers when vicinal coupling constants are in the range of 8-9 Hz (cis-isomer) or 4-6 Hz (trans-isomer). More, when the precision of the ^1H NMR is ±0.5Hz (the usual conditions), the most deshielded signal is a 'ddd' for the trans isomer and a 'q' (quadruplet) for the cis isomer.*

Polysubstituted cyclopropanes have been extensively studied since the first Simmons-Smith synthesis in 1958.[1] However, during work on enantioselective synthesis of disubstituted aryl-carboxy cyclopropanes[2] **1a-d**, Figure 1, we have been confronted with the difficulty of finding in the literature any examples of NMR determinations of the *cis* and/or *trans* structure of this kind of compound although they had already been synthesized by other methods.[3-6] *Cis/trans* ratios are given without indication of the methods used for the assignment of the structures while the determination of absolute configuration is always described.[7]

We report here a complete study of ^1H and ^{13}C NMR features (chemical shifts, coupling constants and patterns) of these type of cyclopropanes **1** which demonstrate that NMR is a rapid and unambiguous method for *cis/trans* assignment.

Figure 1



I-*trans* II-*cis*

1a Ar = Ph ; R = OEt
1b Ar = Napht ; R = OEt
1c Ar = NC-C_6H_4 ; R = OEt
1d Ar = Ph ; R = Me
1e Ar = Ph ; R = OH (ref. 6)

The ^1H and ^{13}C NMR data are gathered on Tables 1, 2 and 3.

In cyclopropanes **1a**, **1b**, and **1c** the chemical shifts of the ethyl groups are shielded in isomers **II** compared to isomers **I** : the CH_2-quadruplets and the CH_3-triplets are shielded by about 0.2-0.35ppm (Table 1 columns 7 and 8, compare lines 1 and 2, 3 and 4, 5 and 6). In the same way the CH_3-singlet in cyclopropane **1d** is shielded by 0.28ppm in isomer **II** compared to isomer **I**.

These shieldings suggest that the ethyl-groups and the methyl are *cis* to the aromatic-groups in isomers **II**

0040-4039/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)02649-5

and therefore the *cis*-structure can be assigned to these isomers : **II** = ***cis***. However assignment on the basis of chemical shifts needs both isomers for comparison. A complete analysis of the ^{1}H NMR spectra and determination of the vicinal-coupling constants, which could, in principle, be used directly for *trans/cis* assignment, was undertaken.

In cyclopropane **1a-I**-(*trans*) the most deshielded ddd (at 2.51 ppm, Table 1) was assigned to H-2 (C<u>H</u>-Ph) on the basis of the absence of this multiplet in the corresponding 2-deuterated cyclopropane which was prepared from the corresponding deuterated sulfonium salt.[8] This result is in accord with literature results concerning non deuterated and 2,3-dideuterated cyclopropane **1e**.[9] Therefore the most deshielded multiplets (at 2.69, 2.54, 2.53 ppm, Table 1, column 3) were also assigned to the H-2 (C<u>H</u>-Ar) in, respectively, **1b-I**-*(trans)*, **1c-I**-*(trans)* and **1d-I**-*(trans)*.

If one examines the ^{1}H NMR spectra and compare isomers **I**-(*trans)* and **II**-(*cis*) of all cyclopropanes, the most obvious change in pattern is the 'quadruplet' aspect of the most deshielded signal for isomers **II**-(*cis*) in all cases (Table 1, column 3 and Figure 2). Because, in cyclopropane **1e-*cis***[9] the most deshielded signal (at ~2.6ppm) has been also shown to be due to H-2 (C<u>H</u>-Ph), the most deshielded signals (quadruplets at 2.59, 2.74, 2.58 and 2.70ppm, Table 1, column 3) of all the **II**-(*cis*) isomers in cyclopropanes **1a-1d** were assigned to proton H-2.

Assignments of the other ddd to H-1 and to the CH_2 in position 3, were done through ^{1}H-^{13}C-correlation experiments.

Interpretation of the four multiplets, Figure 2, corresponding to the cyclopropyl protons, extraction of all the coupling constants and assignment of H-3*c* and of H-3*t* were then straightforward.

It appeared (Table 2) that, in all cases, the values of the coupling constants between H-1 and H-2 are significantly smaller in isomers **I**, $^3J_{1\text{-}2}$ = 4 Hz, than in isomers **II**, $^3J_{1\text{-}2}$ = 9 Hz. This is in accord with the previous assignment (from chemical shifts) of the *cis* structure to isomers **II**, with known results[10] and with the Karplus-Conroy curves ; *J* values corresponding to dihedral angles close to 0° are larger than those corresponding to diedral angles of 120°.

It can thus be concluded from the values of $^3J_{12}$, which are significantly different in all cases, that isomers **I** are *trans* while isomers **II** are *cis*.

It is worth noting (Table 2, column 7) that while the values of the *cis*-coupling constants between H-2 and H-3t (8.5 to 9 Hz) are identical or close to the values found for H-1/H-2 (9 Hz), the values of the *trans*-coupling constants between H-2 and H-3c are larger (6 to 7.5 Hz, compared to 4 Hz). More the differences ($^3J_{23t}$ - $^3J_{23c}$) are smaller in the *cis*-isomers (ΔJ ~1 Hz) which is responsible (the spectra's resolution being 0.3Hz/pt) for the quadruplet aspect of the signal of H-2 in these *cis*-isomers.

The values of the *cis*-coupling constants linking H-1 and H-3 are smaller (7 to 8.5 Hz) than those found for H-1/H-2 (9 Hz) and the values of the *trans*-coupling constants larger (5 to 5.5 Hz compared to 4 Hz).

However, apart for cyclopropane **1d** where J_{13t}*cis* = 7 Hz and J_{23c}*trans* = 7.5 Hz, the values of the *cis*-coupling constants (9 -7.5 Hz) are larger than the values of the *trans*-coupling constants (7.5-4 Hz).

Most interesting is the ~6 ppm shielding of carbon-3 on passing from the *trans*-isomer to the *cis*-isomer (Table 3, column 5) while the shielding of carbon-1, carbon-2 and other carbons are very small, if not nil (Table 3).

Table 1 : ^{1}H NMR of compounds **1a-1d** (δ in ppm, CDCl$_3$/TMS)

Compd	isomer	Cyclopropyl protons				R group	
		H-2	H-1	H-3c	H-3t		
1a	**I**-*trans*	2.51 ddd	1.90 ddd	1.32 ddd	1.61 ddd	4.17 q	1.28 t
1a	**II**-*cis*	2.59 ~q	2.09 ddd	1.71 ddd	1.32 ddd	3.85 q	0.95 t
1b	**I**-*trans*	2.69 ddd	2.00 ddd	1.43 ddd	1.67 ddd	4.21 q	1.30 t
1b	**II**-*cis*	2.74 ~q	2.17 ddd	1.86 ddd	1.42 ddd	3.87 q	0.95 t
1c	**I**-*trans*	2.54 ddd	1.95 ddd	1.33 ddd	1.68 ddd	4.18 q	1.20 t
1c	**II**-*cis*	2.58 ~q	2.15 ddd	1.71 ddd	1.40 ddd	3.87 q	1.00 t
1d	**I**-*trans*	2.53 ddd	2.23 ddd	1.39 ddd	1.69 ddd	2.30 s	
1d	**II**-*cis*	2.70 ~q	2.42 ddd	1.82 ddd	1.30 ddd	2.02 s	

Table 2 : Coupling constants (in Hz) within the cyclopropyl ring for **1a-1d** *

Compd	isomer	J_{12}	J_{13c}	J_{13t}	J_{23c}	J_{23t}	J_{gem}
1a	**I**-*trans*	4 (t)	8.5 (c)	5 (t)	6.5 (t)	9 (c)	4
1a	**II**-*cis*	9 (c)	5.5 (t)	8 (c)	7.5 (t)	8.5 (c)	5
1b	**I**-*trans*	4 (t)	8.5 (c)	5 (t)	6.5 (t)	9.5 (c)	4
1b	**II**-*cis*	9 (c)	5.5 (t)	8 (c)	7.5 (t)	8.5 (c)	5
1c	**I**-*trans*	4 (t)	8.5 (c)	5 (t)	6 (t)	9 (c)	4
1c	**II**-*cis*	9 (c)	5.5 (t)	8 (c)	7.5 (t)	8.5 (c)	5.5
1d	**I**-*trans*	4 (t)	8 (c)	5 (t)	6.5 (t)	9 (c)	4
1d	**II**-*cis*	9 (c)	5.5 (t)	7 (c)	7.5 (t)	8.5 (c)	5

* (c) and (t) after the *J* values mean that the corresponding *J* is *cis* and *trans* respectively.

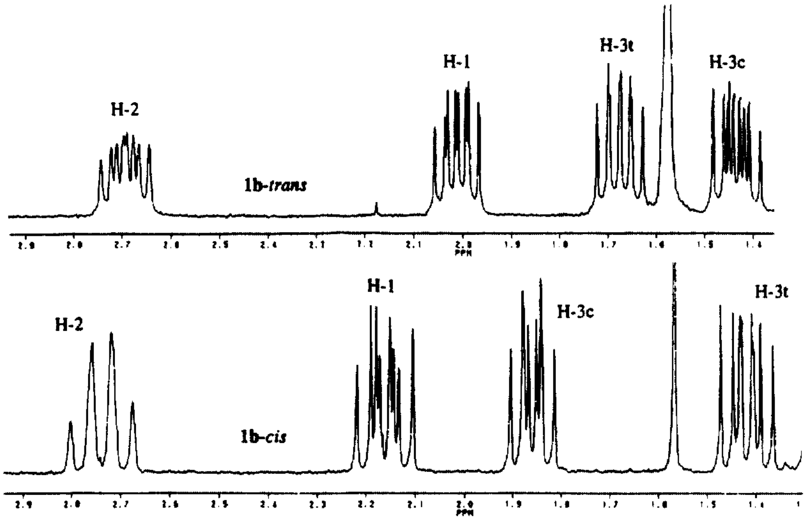
Table 3 : ^{13}C NMR of compounds **1a-1d** (δ in ppm, CDCl$_3$/TMS)

Compd	Isomer	cyclopropyl ring			R group	
		C-1	C-2	C-3		
1a	**I**-*trans*	23.5	26.0	17.0	61.0	14.5
1a	**II**-*cis*	21.9	25.5	11.2	60.2	14.1
1b	**I**-*trans*	24.3	26.5	17.1	60.7	14.4
1b	**II**-*cis*	22.2	25.8	11.5	60.3	14.2
1c	**I**-*trans*	24.9	25.8	17.6	60.8	14.2
1c	**II**-*cis*	22.4	25.4	11.6	60.6	14.2
1d	**I**-*trans*	28.4	32.0	19.0	30.0	
1d	**II**-*cis*	28.0	31.3	11.7	30.4	

Therefore values in the range 8-9 Hz (4-6 Hz) are directly indicative of a *cis*-relationship (*trans*-relationship), while, of course, for intermediate values (6.5-7.5 Hz) both isomers and comparison will be necessary for a *trans/cis* assignment.

More, for *trans*-isomers the most deshielded signal (corresponding to H-2) is a 'ddd' while it is a 'q' (quadruplet) for the *cis*-isomers.

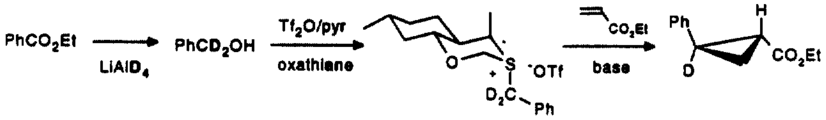
Figure 2



Acknowledgement : M. Schmitt (CNRS engineer at DCOF) is strongly acknowledged for all the 2D NMR spectra.

References.

1. Simmons H.E., Smith R.D. *J. Am. Chem. Soc.* **1958**, *80*, 5323.
2. Solladie-Cavallo A., Diep-Vohuule A., Isarno T. *Angw. Chem., Int. Ed.* **1998**, *37*, 1689.
3. Nozaki H., Moriuti S., Takaya H., Noyori K. *Tetrahedron Lett.* **1966**, 5239.
4. Fritschi H., Leutenegger U., Pfaltz A. *Helv. Chim. Acta* **1988**, *71*, 1553.
5. Evans D.A., Woerpel K.A., Hinman M.M., Faul M.M. *J. Am. Chem. Soc.* **1991**, *113*, 726.
6. Denmark S.C., O'Connor S.P. *J. Org. Chem.* **1997**, *62*, 584.
7. Determinations of absolute configurations refer to the pioneering work of Walborsky (Inouye Y., Sugita T., Walborsky H.M. *Tetrahedron* **1964**, 1695.)
8. Cyclopropane **1a** deuterated in position 2 has been obtained in the following way :



9. Nakamura A., Konishi A., Tatsuno Y., Otsuka S. *J. Am. Chem. Soc.* **1978**, *100*, 3443.
10. Graham J.D., Rogers M.T. *J. Am. Chem. Soc.* **1962**, *84*, 2249 and included references. Bednar R., Herzig U., Schuster I., Schuster P., Wolschann P. *Org. Magnet. Reson.* **1976**, *8*, 301 and included references.