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THE APPLICATION OF ^{13}C-N.M.R. SPECTROSCOPY TO THE DETERMINATION OF THE STEREOCHEMISTRY OF DIELS-ALDER ADDUCTS

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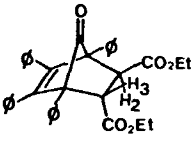
ABSTRACT. *Long-range (^{3}J) ^{13}C-H coupling is a reliable probe to evaluate the stereochemistry of cycloaddition products. The method is best applied to carbonyl containing adducts but not restricted to them. Several structures have been revised and new ones evaluated.*

A key feature of the widely used Diels-Alder reaction is the degree of stereochemical control it affords to the newly formed tetrahedral centres. The stereochemical outcome of such a reaction is of paramount importance, particularly if the adduct is to be further elaborated in a synthesis, but the results are difficult to predict. Consequently numerous chemical[1] and physical methods[2] have been used to determine the stereochemistry of Diels-Alder adducts, but in practice all these methods suffer from limitations. This communication reports a new stereochemical probe which compliments existing methods and is extremely useful for application to adducts derived from tetra-substituted cyclopentadienones. These latter compounds are widely used as dienes and whilst the substituents aid stability and reactivity, adducts derived from these dienones cannot be readily assigned a stereochemistry by current N.M.R. methods. In particular the lack of vicinally coupling protons[2a] and the often weak co-ordinating ability of the carbonyl group to Lanthanide Shift Reagents[2b] has hampered previous stereochemical studies. However such adducts do possess a well isolated carbonyl group resonance in their ^{13}C-N.M.R. spectra and it is upon the multiplicity of this signal that attention is now focussed.

The current method correlates the stereochemistry of Diels-Alder adducts with a ^{3}J ^{13}C-H coupling, the magnitude of which is known to be dependent upon the angular relationship between the coupling nuclei.[3] Thus an *endo* bridge junction proton (Fig. 1a) is unfavorably aligned with carbonyl carbon and essentially no coupling is observed. In contrast the *exo* bridge junction proton is favorably aligned (Fig. 1b) and couplings of the range 5-9 Hz are observed.



(1)

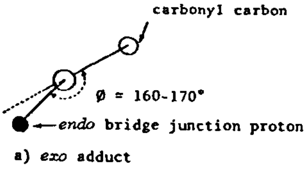


FIG. 1a

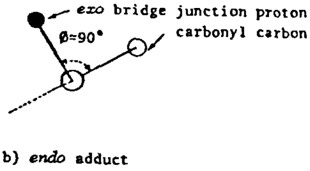


FIG. 1b

Consider the adduct (1) derived from tetracyclone and diethyl fumarate.[4] Here the coupled ^{13}C-N.M.R. spectrum[5] displays a doublet resonance at 196.1 p.p.m. (J = 7.1 Hz) for the C7-carbonyl carbon which is due to long-range coupling with one of the methine protons (H2 or H3). That coupling was due to the *endo*-bridge junction proton (H2) was established by reference to the isomeric *cis*-3,4-dichlorocyclobutene-phencyclone adducts (2) and (3) which are compounds of firmly established structure.[6] The *exo*-adduct (2), which contains a pair of *endo*-protons, displayed a triplet (^3J = 7.4 Hz) for the carbonyl carbon resonance, while the *endo*-adduct which lacks *endo*-bridgehead protons, yielded a singlet resonance.

This technique has been applied to a variety of adducts. A selection of these is included in the following tables which are divided into three groups. In the first table compounds of firmly established structure are considered. There are no cases where the results of this technique fail to agree with the reported structure.

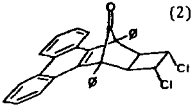
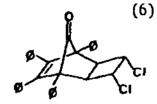
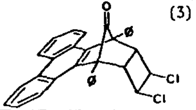
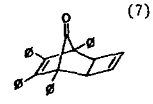
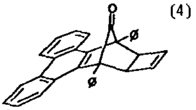
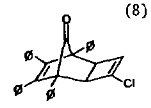
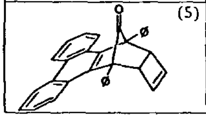
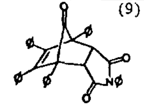
ADDUCT	CARBONYL MULTIPLICITY	PREPn.	ADDUCT	CARBONYL MULTIPLICITY	PREPn.
(2) 	triplet (*J* 7.4 Hz)	Ref.6	(6) 	triplet (*J* 7.4 Hz)	Ref.6
(3) 	singlet	Ref.6	(7) 	triplet (*J* 7.0 Hz)	Ref.6
(4) 	triplet (*J* 7.4 Hz)	Ref.6	(8) 	triplet (*J* 6.3 Hz)	Ref.7
(5) 	singlet	Ref.6	(9) 	singlet	Ref.7

TABLE 1
Compounds of Previously Established Stereochemistry

In the second group new compounds are collected to which structural assignments are made for the first time. Compound (10) represents an interesting case since neither thermal Cope rearrangement[1b,8] nor photocyclisation techniques[1a] are applicable to this adduct.

In the third table two examples are reported where the stereochemistry is in need of revision. The *exo* structure of (16) follows directly from the ^{13}C-N.M.R. method whilst that

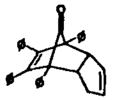
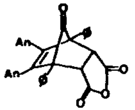
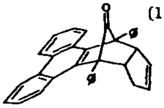
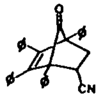
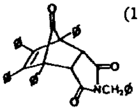
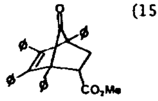
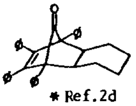
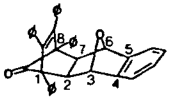
ADDUCT	CARBONYL MULTIPLICITY	PREPn.	ADDUCT	CARBONYL MULTIPLICITY	PREPn.
 (10)	Singlet	Ref.1b,9	 (13)	Singlet	Ref.7
 (11)	Singlet	Ref.4	 (14)	Doublet (*J* 7.6 Hz)	Ref.7
 (12)	Singlet	Ref.8	 (15)	Doublet (*J* 6.8 Hz)	Ref.7

TABLE 2
New stereochemical assignments

In the third table two examples are reported where the stereochemistry is in need of revision. The *exo* structure of (16) follows directly from the ^{13}C-N.M.R. method whilst that of (17) is fully defined by a combination of the new method and the lack of vicinal coupling between the protons H2 and H3 (H6 and H7) in the ^{1}H-N.M.R. spectrum. It is pertinent here to point out that the new assignments further highlight the inadequacy of two previously reported ^{1}H-N.M.R. stereochemical probes, namely, the Coxon-Battiste 'Phenyl Multiplicity' technique[2d] and the Haywood-Farmer 'Solvent induced proton shift' method.[2c]

TABLE 3
Compounds of revised Stereochemistry

ADDUCT*	CARBONYL MULTIPLICITY	ADDUCT*	CARBONYL MULTIPLICITY
 * Ref.2d (16)	Triplet (*J* 5.9 Hz)		Singlet

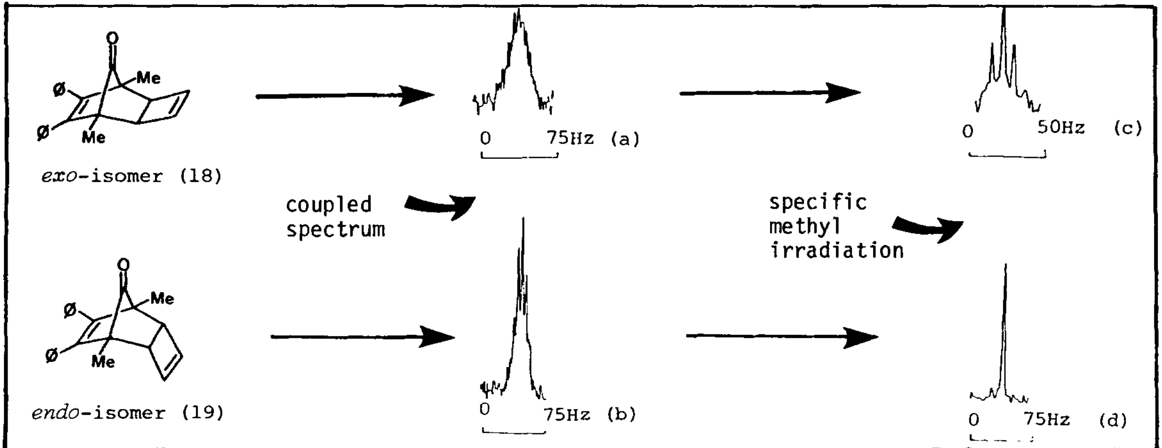
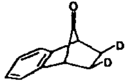
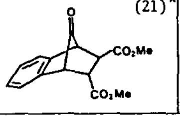
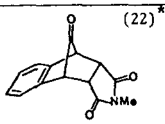


FIG. 2. Carbonyl Region of ^{13}C-n.m.r. Spectra of (18) and (19) at 67.89 MHz.

Comment is required regarding other factors which cause splitting of the carbonyl carbon resonance. Naturally adducts containing other protons in a β-relationship to the carbon probe (^{3}J) can cause increased splittings. This is illustrated by adducts containing bridgehead methyl groups such as (18) and (19)[10], the carbonyl carbon resonances of which are shown in fig. 2. Stereochemical assignments can still be made in the coupled spectrum, since comparison of the *exo*-isomer resonance [fig. 2a] and the *endo*-isomer resonance [fig. 2b] clearly shows the increased multiplicity present, as anticipated, in isomer (18) which contains *endo*-protons. Interpretation can be simplified, in this case, by selective methyl proton irradiation which collapses the carbonyl resonance for the *exo*-adduct (18)[fig. 2c] to a triplet and that of the *endo*-adduct (19)[fig. 2d] to a singlet.

Compounds containing protons with an α-relationship to the carbon probe also cause additional splitting (^2J). Thus the carbonyl carbon resonance of adduct (20) shows splitting due to both the protons on the α-carbons (^2J) as well as the *endo*-protons at the β-carbons (^3J) However in the three cases examined (Table 4) the magnitude of the ^2J coupling is smaller than that of the ^3J coupling, and the two are readily distinguished.

TABLE 4
^{13}C-H coupling constants in related bicyclic systems

ADDUCT	^2J (Hz)	^3J (Hz)	ADDUCT	^2J (Hz)	^3J (Hz)	ADDUCT	^2J (Hz)	^3J (Hz)
(20)* 	2.7	7.6	(21)* 	2.8 2.8	7.4	(22)* 	2.8	-

* for preparation see ref. 11.

Preliminary work has shown that the method is not restricted to carbonyl compounds, and its extension to non-carbonyl bridges will be reported separately.

ACKNOWLEDGEMENTS

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