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Transmission of Electronic Effects Through 2-[Donor]-1-[Acceptor] Cyclopropanes. Part III. Conformational Studies of 2-(p-x-aryl)-1-cyclopropane Aldehydes with Lanthanide Shift Reagents.

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Abstract: *Substituent mesomeric effects transmitted through cyclopropane have been examined by the influence that a p-x-aryl group (X= OMe, Me, H, Cl) on C2 might have on preferential conformer populations of an aldehyde unit on C1 in solution. The lanthanide induced shift method , which proved to be applicable to this non rigid system by testing the structural self consistency of the model with Ohkata's correlations, was used to determine the preferred C-C=O rotational angle τ relative to the cyclopropane plane. This gave τ around 30°-50° away from the bisected conformation in the direction of the C1-C3 bond, irrespective of the electron withdrawer or donor nature of the arene substituents. This showed that true mesomeric effects do not occur in cyclopropane. Instead, competitive conjugation of substituents for the electron density in the ring is the dominant feature, as predicted by conventional MO theory.*

The complexity of cyclopropane (hereafter cp) goes well beyond its ring strain and reminiscence of the carbon-carbon multiple bond.[1] For one, it is the only alicyclic structure where electron delocalization occurs,[2] and it is the strongest donor of electron density among the hydrocarbon groups.[3] In addition, cyclopropane is capable of σ and π conjugation with vicinal substituents.[4] This peculiar characteristic raises the possibility of mesomeric transmission through the ring of electronic effects between π donors and acceptors of electron density located on vicinal carbons of cp. This subject has been debated for a long time. While various lines of evidence appear to support the conduction of these effects across the ring,[5] others[6] join the theoretical calculations[7] in denying this possibility.

In two past contributions from these laboratories[8,9] that attempted to solve experimentally this dilemma, the ^{1}H NMR spectra of twenty six 2-[donor]-1-[acceptor]-cyclopropanes were analyzed for differential effects of C1 substituents with variable electronic withdrawal potential, on their *cis* protons on the vicinal carbons C2 and C3 (see fig 2 for nomenclature). These results revealed that some 2-donor groups exert a strong modulation effect on the chemical shift of the C2 proton δH2 that depends on the withdrawal power of the C1 substituent,[9] while this modulation is absent in δH3. For example, 2-aryloxy and alkoxy groups make H2 much *less* sensitive than H3 to variations in field anisotropy put forth by the C1 group (COOEt, COOH, CHO and CH_2OH). By contrast, the alkyl groups on C2 do not exert this differential influence on H2 over H3. Only a moderate and progressive effect was found in the p-x-aryl series

This phenomenon is only possible if the extent to which inductive C1-C2 and C1-C3 substituent effects are not equivalent, that is: ***the substituent effects on C1 and C2 must act in combination, one as a function of the other*** but not as a result of conjugation through the ring. The δH2 modulation is probably a response of the C2 group to variations in electron demand by the π electron withdrawer fragment on C1. The larger the demand by C1-R, the lower the electron density on the cp ring and the larger the electron release by the C2-R provided that it is capable of yielding any.

Our ^{13}C NMR data of these models[8] allowed an approximate measurement of this conjugative interaction, using styrene and ethyl benzene, respectively, as extremes of a 100% and 0% conjugation scale.[10] This gave roughly 20-23% conjugative interaction in the cp-ester series whereas the cp aldehyde series predictably was higher (28%). This finding was in line with the high rotational energy barriers that have been recorded for cp aldehydes and amides,[11] and with the known preference of carbonyl groups for a *syn*- bisected conformation like that of fig 1.[12] This conformer preference results from the maximum overlap of the C=O π orbital and the 3e' MO of cp (fig 3) that extends around the C3-C1-C2 domain in a bonding fashion, and between C2 and C3 in an antibonding manner.[13]

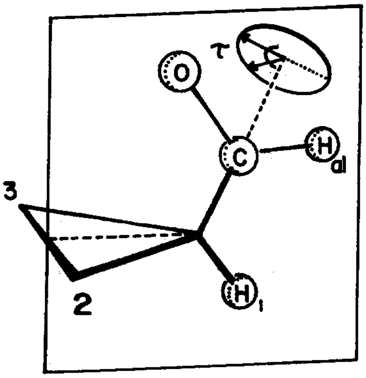
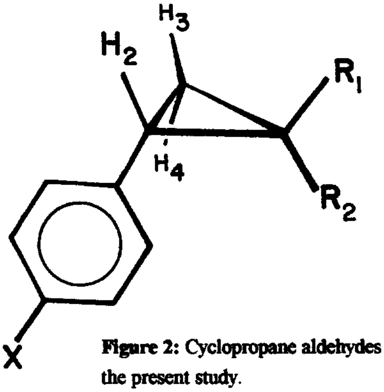


Figure 1: Drawing of the *syn* bisected conformation of a cyclopropyl carbaldehyde illustrating the definition of τ that is used in this work.



a: X= OMe
b: X= Me
c: X= H
d: X= Cl

Figure 2: Cyclopropane aldehydes used in the present study.

1: R1= CHO; R2=H. 2: R1= H; R2= CHO

It was thought that, if the δH2 modulation is a symptom of the donation of electron density to the cp ring by C2-R donors as described above, it should affect the conformer population of a carbonyl group, *e.g.* an aldehyde on C1, owing to the redistribution of that electron density in the ring. Namely, the torsional angle τ of the C(H)O group of atoms relative to the cp plane as defined in figure 1 should change according to the aforementioned combination of electron demand-release. Within this context, substituent mesomeric phenomena and competitive conjugation for cp electron density should have opposite effects on τ and consequently should be capable to distinguish these two distinct processes. This paper reports on the development of evidence sustaining this hypothesis.

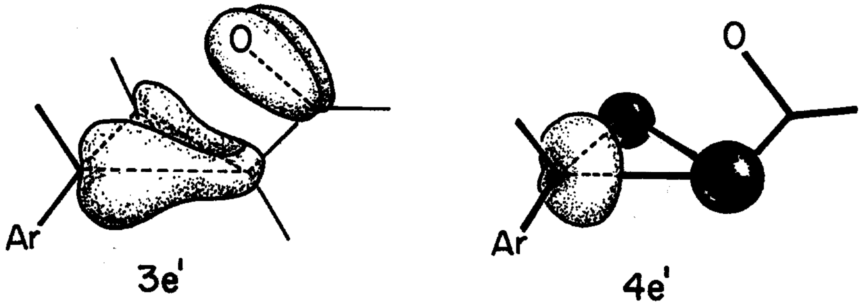


Figure 3: Drawing of the 3e' and 4e' MO's of cp that interact with π electron attractor and σ donor/attractor substituents. Clear and dark MO's have opposite signs.

RESULTS AND DISCUSSION:

The model compounds chosen for this investigation are represented by the series **1a-d** /**2a-d** that comprises electron donor and moderately electron withdrawer groups on C2 and a strong π attractor C(H)=O on C1 in the *cis* and *trans* configurations.

At the outset the O=C(H)-C1-H coupling constant $J_{\text{Hald-H1}}$ was examined as a first approximation. It was found that it remained constant within experimental error (0.3 Hz) around 4.2 Hz in the 34 to -80°C range. This result suggested that at room temperature the conformational preferences of these aldehydes were representative of a particular conformation whose stability stemmed from the carbonyl-cp conjugation. This allowed the ensuing NMR studies to be made at the normal magnet temperature (34°). Also, $J_{\text{Hald-H1}}$ remained constant within each of the **1a-c** and **2a-c** series, only showing a smaller value in the **1d**/**2d** compounds that contained the electron attractor p-Cl-aryl group on C2 (see Table 4 in experimental part). However, $J_{\text{Hald-H1}}$ alone is not a sufficiently solid criterion to assess τ because it is not only a function of the dihedral angle and other factors influence its value.[14]

$$\Delta Eu_i = [K\,(3\mathrm{Cos}^2\theta_i - 1)]\,/\,d^3 \qquad \text{The McConnell-Robertson equation}$$

Among the available techniques to evaluate τ in solution, the lanthanide induced shift (LIS) method[15] using the McConnell-Robertson (M-R) equation[16] shown above (see fig 4 for definition of parameters) was chosen. The three cp nuclear proton positions relative to the lanthanide (L) would provide three converging sources of information to locate with certainty the emplacement of L relative to the carbonyl oxygen to which it would be associated in the pseudo contact complex. Variations in τ would cause L to be displaced accordingly, thus changing sensibly its position (angle θ_i and distance $d_{L\cdots H_i}$) relative to the three cp protons as fig 4 illustrates. The M-R expression relates the induced shift ΔEu_i with distance $d_{L\cdots H_i}$ to the third power so it is a sensitive tool to locate L. To the advantage of this application in the present case, compounds **1a-d** contain a proton (H_{ald})-C=O rigidly held to the rotating molecular fragment to which L becomes associated. As a consequence, the $H_{ald}\ldots L$ distance and the H_{ald}–C=O—L dihedral angle θ_i will remain constant *independently of* τ. This allowed to determine the proportionality constant K of the M-R expression while it gave additional data to confirm the location of L relative to the C=O with reasonable confidence.

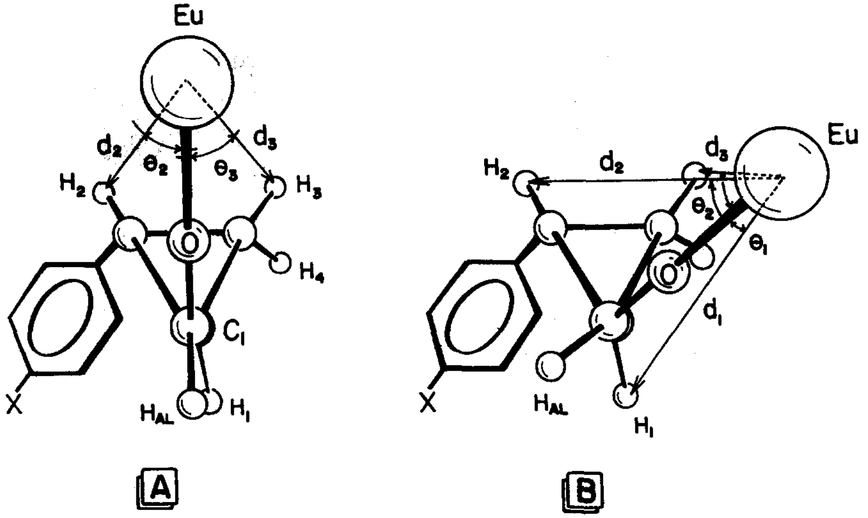


Figure 4: Perspective View of the Presumed Pseudo Contact Complex between a Cyclopropane Aldehyde and $Eu(fod)_3$ showing the basic parameters of the McConnell-Robertson equation. **A:** a bisected conformation ($\tau = 0°$) and **B:** a skewed conformation with $\tau = 30°$.

Before giving credit to any LIS inspection[17] it was necessary to first ascertain the conformational consistency of the series of model compounds. Ohkata and coworkers[18] offered a simple answer to this problem by establishing a proton-proton correlation of their ΔEu_i by way of their individual *relative* LIS that was defined as:

$$RLIS_i = (\Delta Eu)_i / (\Delta Eu)_{std}$$

for the ith proton relative to an arbitrary standard proton in the molecule. The $RLIS_i$ values of a reference compound, *e.g.* **1c**, are plotted against the $RLIS_i$ of each compound of the **1a-d** series. A linear correlation with a slope *m*=1 will result if the configuration and conformation of the pair are similar. Different conformations will lead to no correlation at all.

To this end, ΔEu_i of **1a-d/2a-d** were obtained using $Eu(fod)_3$ as lanthanide, in carbon tetrachloride to bring to a minimum the effect of the solvent on the natural conformer population of these aldehydes. Extrapolation of a plot of δH_i vs the concentration ratio of $[Eu(fod)_3]$ relative to [aldehyde] when the latter equals one gave ΔEu_i. As table 1 shows, the LIS follows the order $H_{ald} > H_1 > H_2 > H_3 > H_4$ in the *trans* series, whereas this was $H_{ald} > H_1 > H_4 > H_2 > H_3$ in the *cis* series. This order is the same recorded for 2-aryl-cyclopropane carboxylates.[19] Figure 5 shows a typical Ohkata plot obtained from the RLIS data of compound **1a** relative to **1c** that was used as standard because its aryl group lays between the electron donor and attractor extremes of the series. The highly linear correlation obtained there was also observed in similar plots of the *trans* series of compounds among themselves as well as between those of the *cis* series (see Table 2) but predictably, scattered points resulted when RLIS of any *trans* derivative was plotted against any RLIS of the *cis* epimers. The high correlation coefficients were interpreted in terms of enough structural self consistency of the model compounds to proceed with the attempt to unveil the most stable carbonyl conformer by LIS studies.

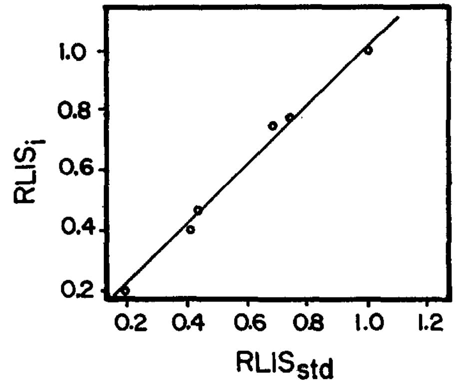


Figure 5: Correlation of Relative Lanthanide Induced Shifts (RLIS) of Protons of Compound **1a** relative to the reference cyclopropane **1c**.

Table 1. (ΔEu)$_i$ Values of Compounds **1a-d/2a-d** using Eu(fod)$_3$ in CCl$_4$. $r^2 = 0.98$ in all the correlations.

				(Eu)$_i$		
Compound	**X**	**H_1**	**H_2**	**H_3**	**H_4**	**Hald**
1a	OMe	933	940	909	607	1410
1b	Me	1022	936	940	574	1430
1c	H	991	914	994	608	1465
1d	Cl	1101	1000	1006	641	1635
2a	OMe	993	425	412	537	960
2b	Me	1022	**nd**	492	573	957
2c	H	991	430	426	560	965
2d	Cl	1101	476	487	635	1144

nd: Proton H2 could not be resolved in the nmr spectrum of the *cis* aldehyde **2b**

Then the LIS method in combination with the McConnell-Robertson equation[15] was applied to determine the geometry of the most favorable C=O rotamers of **1a-d** in solution. This was restricted to the *trans* epimers because in the *cis* epimers the steric interaction of the phenyl group appears to be a dominant factor in yielding preferred carbonyl conformations.[12] The method is based on the comparison of $\Delta Eu_i(e)$ that is the induced shift determined experimentally for each proton (see table 1) with $\Delta Eu_i(c)$ that is calculated by the M-R expression.

To determine $\Delta Eu_i(c)$ an initial captodative cyclopropane structure was required in which bond and dihedral angle dimensions were well established. The x-ray crystallographic data of the closely related *trans*-2-tolyl-1-cyclopropyl carboxylate in which $\tau=0°$ was used[20] since there are no cp aldehydes with known detailed structures.

Table 2. Ohkata Type Correlations of Relative Lanthanide Shifts RLIS of Compounds **1a-d/2a-d.**

	***Trans* Series 1a-d**		***Cis* Series 2a-d**	
X	*m*	r^2	*m*	r^2
OMe	0.93±0.07	0.99	1.1±0.2	0.93
Me	0.96±0.05	0.98	1.1±0.2	0.96
H	1.00	-----	1.0	-----
Cl	1.04±0.06	0.99	1.1±0.2	0.93

m: Slope, r^2 : Correlation coefficient

The position of H_{ald} was artificially located at its usual distance of 1.07 Å from the carbonyl carbon along the C-O bond of the carboxylate to represent the aldehydes of type **1** while the OH was removed. The lanthanide atom was placed arbitrarily at a distance of 2.0 Å from the carbonyl oxygen on the C=O axis and moved away along this line at 0.05 Å intervals while the angle θ_i and distance $d_{Eu\text{-}Hi}$ (fig 4) to each proton on the cp ring were calculated by vectorial analysis with the aid of a computer (see experimental part). Each of the four $\Delta Eu_i(c)$ corresponding to each proton was then determined by substitution of θ_i and $d_{Eu\text{-}Hi}$ in the M-R equation for each position of the lanthanide relative to O=C and compared proton by proton with the $\Delta Eu_i(e)$ that was determined experimentally from the values of Table 1.

Table 3. Optimal Distances $d_{Eu\text{-}O}$ and Rotational Angles τ Calculated for Compounds **1a-d** according to the Application of the McConnell-Robertson Equation and the Curves of Figure 6.

Compound	τ °	$d_{Eu\text{-}O}$ (Å)
1a	30	2.63
1b	30	2.63
1c	40	2.63
1d	50	2.48

Then the accumulated differences between $\Delta Eu_i(e)$ and $\Delta Eu_i(c)$ of all four protons were assessed by the conventional standard deviation SD. The minimum value of SD would correspond to the best adjustment calculated and experimental values of induced shifts, $\Delta Eu_i(c)$ and $\Delta Eu_i(e)$, respectively. In turn the optimal $\Delta Eu_i(c)$ thus obtained would convey that structure with the most favorable C=O- - - lanthanide distance d_{Eu-O} in the pseudo contact lanthanide-substrate complex for each fixed τ. The procedure was repeated changing τ at 5° increments in the 0 to 355° range. The end result was a paired collection of values of standard deviation and torsional angles τ which in graphical form acquired the shape of the family of curves that is depicted in Figure 6. Each curve corresponds to each one of the compounds of the **1a-d** series. The structure of the most likely conformer for each compound will be that at which τ possesses the lowest SD.

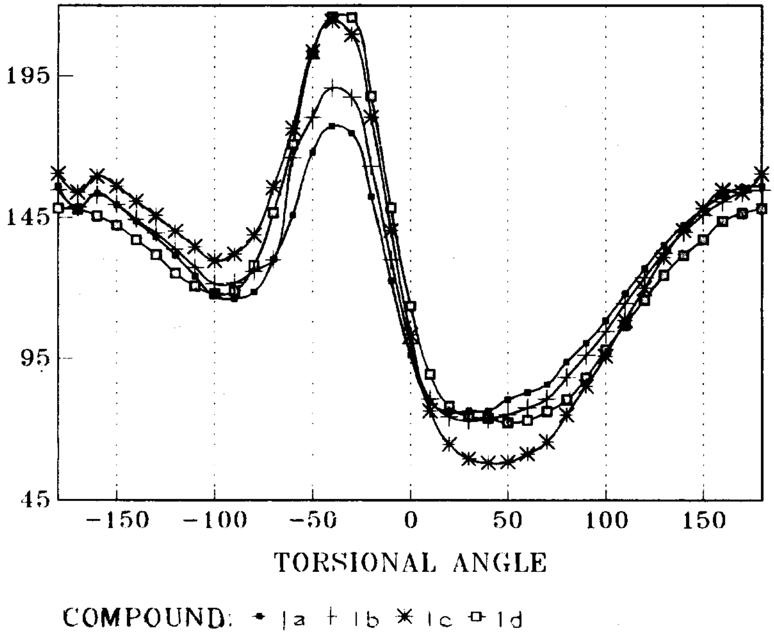


Figure 6: Plot of the Standard Deviation (SD) Calculated from $\Delta Eu_i(e)$ *vs* $\Delta Eu_i(c)$ Differences against τ for Compounds **1a-d.**

From these curves it is evident that none of the compounds examined here show τ = 0°. This means that the plane of the aldehyde unit that contains the C_1-C(H)=O elements does not lay bisecting the cp ring. This is likely to be due to an *uneven* distribution of electron density in the cp ring caused necessarily by the perturbation of the aryl substituent. This in turn must be affecting the carbonyl-cp conjugation. Figure 6 also shows that the C_1-C(H)=O plane appears tilted by approx. 30° away from the bisected conformation, so the C=O is situated right over the C1-C3 bond much in the way represented by part B of figure 4. This strongly suggests that there is a higher electron density along this particular linkage.

The additivity rule of cp bonds[21,22] and the frontier MO theory[13] state that π attractors, in withdrawing electron density from the 3e' HOMO of cp, procure the lengthening of vicinal bonds while the distal linkage is shortened roughly by two times the lengthening of the former. In the cp aldehyde this means that bonds C1-C2 and C1-C3 become *longer* while C2-C3 gets *shorter* relative to unsubstituted cp. Conversely, π donors such as the aryl group in **1a-c** interact only with the 4a' LUMO of cp that is antibonding along the vicinal bonds and bonding in the distal link (see fig 3). Therefore, the 2-aryl substitution brings about the *lengthening* of the C2-C1 and C2-C3 bonds while C1-C3 *becomes shorter.* The sum of the C1-C=O and C2-aryl effects in **1a-c** both point in the same direction: that of increasing the C1-C2 distance, and therefore the electron density along this axis is decreased, while by comparison the bonds between C1-C3 and C2-C3 appear shortened and therefore strengthened. This is consistent with x-ray crystallographic data of 2-tolyl-1-cyclopropane carboxylate[20] where the C1-C2, C1-C3 and C2-C3 distances are 1.513, 1.499, and 1.474 Å, respectively, in spite of the low electron withdrawer ability of the COOH group relative to aldehyde. As a result, the C=O group of aldehydes **1a-d** should prefer the skewed conformation of figure 4B. Consequently, the experimental data here confirm the predictions of the frontier MO theory.

The 2-p-chloro-aryl substituent in **1d** appears to exert a more pronounced effect on τ This group is a σ attractor so it withdraws electron density from the 3e' orbital and consequently, the net effect on bond length *follows the same direction as above.* Again structural crystallographic data bring support to this because *trans*-2-p-nitrophenyl-1-cyclopropyl methyl ketone has a similar asymmetry pattern (1.51, 1.49, and 1.48 Å, respectively).[23] If there were true mesomeric effects through the cp ring in the way they occur in acetylenes, arene electron donors and attractors on C2 would have had *opposite effects* on τ , but our data indicate that the carbonyl is tilted in the *same direction in all cases,* hence showing clearly that through the ring, alkene/alkyne like electronic transmission phenomena do no occur in cyclopropane. Rather, a strong and competitive conjugation with substituents appear to be the dominant feature.

EXPERIMENTAL

NMR spectra were obtained from a Varian Associates CFT-80 and EM-390 spectrometers operating at 80 and 90 MHz, respectively. The reported chemical shifts are in ppm downfield from TMS in carbon tetrachloride solutions. LIS studies were performed at 34° in this solvent with 0.1 M substrate concentration and a $Eu(fod)_3$/substrate ratio between 0 and 0.13 in six different concentrations. All proton frequencies were resolved except for H2 of compound **2b** (see table 1). Compounds **1a-d/2a-d** were synthesized from ethyl diazoacetate and the corresponding p-x-styrene by known procedures.[8] Molecular Graphics[24] and Alchemy II (Tripos Associates) computer programs running on a 386/387 based computer were used to locate artificially the L and Hald atoms and obtain the Cartesian coordinates of each atom in the molecule. The (o,o,o) point was located at the center of the C1 atom. A Quattro Pro (Borland) spreadsheet program was used for the vectorial calculations to determine $\mathbf{d}_{Eu-Hi}$, θ_i and τ, and from these the value of $\Delta Eu_i(c)$ and SD.

Table 4: Chemical Shifts (ppm) of Pertinent Protons and Hald-H1 Coupling Constants of **1a-d/2a-d.**

Compound	X	δH_1	δH_2	δH_3	δH_4	δH_{al}	$J_{H_{ald}\text{-}H_1}$ (Hz)
1a	OMe	2.00	2.45	1.67	1.35	9.20	4.2
1b	Me	2.02	2.45	1.70	1.35	9.35	4.2
1c	H	2.05	2.52	1.62	1.34	9.25	4.2
1d	Cl	2.10	2.50	1.70	1.40	9.42	3.3
2a	OMe	2.00	2.67	1.35	1.67	8.60	6.3
2b	Me	2.02	2.45	1.35	1.70	8.62	6.3
2c	H	2.05	2.70	1.38	1.67	8.63	6.3
2d	Cl	2.10	2.50	1.40	1.70	8.73	5.7

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