^{1}H Nuclear Magnetic Resonance Contact Shifts of Some Tropanes

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Summary Application of ^{1}H n m r contact shifts, using nickel and cobalt diacetylacetonates, to tropanes demonstrates that the six-membered ring of tropanes is in a nearly semiplanar form

RECENTLY the ^{1}H n m r contact shift has received considerable attention[1] We have discussed[2] the proton paramagnetic shifts of piperidines, using nickel and cobalt diacetylacetonates, and suggested the usefulness of those phenomena for determining the orientation of the nitrogen lone-pair electrons We now report the application of this technique to the stereochemical analysis of some tropanes

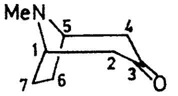
The Table summerizes the relative paramagnetic shifts of each proton of tropinone (I) tropine benzoate (II), and homatropine (III) measured with a Varian HR-220 MHz instrument. This high-frequency ^{1}H n.m.r. technique demonstrated that all eleven protons attached to the tropane skeleton in (III) are magnetically different, on account of the presence of an asymmetric centre.[3] The spectra were analysed on the basis of the coupling features[4] and with the double resonance technique.

Chemical shifts and relative paramagnetic shifts of proton resonances of tropanes (*in* $CDCl_3$, *internal ref.* Me_4Si, *at* 220 *MHz*: + *and* − *mean up- and down-field shifts, respectively*)

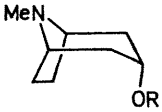
		1-H 5-H	6-H *endo*	7-H *exo*	2-H and 4-H ax.	 eq.	3-H	N-CH_3
	δ (p.p.m.)	3·46	1·63	2·13	2·21	2·71		2·50
(I)	Ni	−0·14	−0·06	+0·11	+0·05	+0·05		−1·00
	Co	+0·23	−0·07	+0·08	+0·04	−0·07		−1·00
	δ (p.p.m.)	3·22	2·14		1·87	2·28	5·27	2·35
(II)	Ni	−0·15	−[a]	+[a]	+0·20	+0·20	+1·10	−1·00
	Co	+0·20	−0·05	0	0	−0·07	−0·17	−1·00
	δ (p.p.m.)	2·91 3·07	0·98 1·72	1·65 1·88	1·42 1·72	2·05 2·16	5·04	2·20
(III)	Ni	−0·10	−0·10	+[a]	+0·10	+0·07	+0·10	−1·00
	Co	+0·13	−0·13	0	0	−0·11	−0·15	−1·00

[a] Up- (+) and down-field (−) shifts; relative values were not determined because of the signals' overlapping.

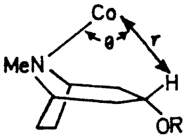
On addition of Ni(acac)$_2$ the paramagnetic up- and downfield shifts for *exo*- and *endo*-protons at C-6 and C-7 are accounted for in terms of "folded" or "zig-zag" route based on the axial nitrogen lone-pair conformation.[2,4,5] The six-membered ring in the tropane skeleton is in the deformed chair form.[4–6] A comparison of the paramagnetic shifts of proton resonance of (I), (II), and (III) with those of 1,4-dimethylpiperidine will illustrate this point. With Ni(acac)$_2$ the signals of both axial and equatorial protons at C-2 and C-4 shifted up-field in the spectra of the tropanes, while in the case of 1,4-dimethylpiperidine those of axial and equatorial protons at C-2 and C-4 moved up- and down-field, respectively. This difference in behaviour suggests that the six-membered ring of the tropanes is somewhat different in conformation from the normal chair form. On addition of Co(acac)$_2$ large downfield shifts of the C-3 proton resonances of (II) and (III) occurred. It is known that in the Co(acac)$_2$ complex systems the observed paramagnetic shift is the sum of a contact shift and an anisotropic pseudo-contact shift which is proportional to the geometric factor,[7] $(3\cos^2\theta - 1)/r^3$ where r is the distance between the resonating proton and the Co atom and θ is the angle between Co–N axis and the r vector. Assuming that the nitrogen lone-pair is axial and the Co–N distance is 2 Å,[2] the calculated geometric factor for the C-3 equatorial hydrogen of *N*-methylpiperidine is nearly zero (−0·003) for the normal chair form but strongly negative (−0·17) for the boat form. The observed downfield shift of the C-3 proton resonance, comparable with that of C-2 equatorial protons in (II) and (III), is in accord with the calculated values based on a semi-planar form (IV; C-3 H, —0·030; C-2 eq. H, −0·023). Taking into account the coupling of the C-3 proton (triplet *J* 5 Hz) we conclude that the nearly semiplanar form (IV) must predominate over the normal chair form.



(I)



(II) R=COPh
(III) R=CO·CHOH·Ph



(IV)

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