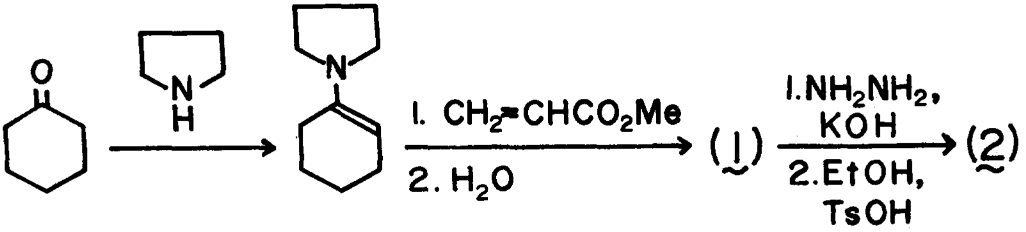
Tetrahedron Letters No. 42, pp 3643 - 3646, 1975. Pergamon Press. Printed in Great Britain.

C-13 NMR STUDY ON CONFIGURATIONS OF DISUBSTITUTED CYCLOHEXANONE AND CYCLOHEXANE DERIVED THEREFROM BY THE HUANG-MINLON PROCESS

Naoji Matsumoto and Ju Kumanotani
The Institute of Industrial Science, the University of Tokyo
22-1, Roppongi 7 Chome, Minato-ku, Tokyo 106, Japan

(Received in Japan 18th August 1975; received in UK for publication 8th September 1975)

During a study of the motion of rings involved in polymer main chains, we were forced to reveal the configurations of dimethyl cyclohexanone-2,6-dipropionate (1) and diethyl cyclohexane-1,3-dipropionate (2). According to the method of Stork et al.[1)] (1) was prepared, from which (2) was derived by the Huang-Minlon process[2)] and subsequent alcoholysis with ethanol. We wish to report here the stereochemistry of (1) and (2) determined by ^{13}C NMR spectroscopy.[3)]

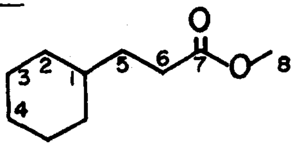


The ^{13}C signals were assigned for methyl 3-cyclohexylpropionate (3) and ethyl 3-(2-oxocyclohexyl)-propionate (4) (see Table 1) by an application of the additivity principle of substituent effects,[4)] using the chemical shifts of related compounds[5-7)] such as n-butylcyclohexane, 2-methylcyclohexanone, methyl n-hexanoate, n-heptane, and so on.

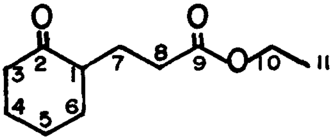
The chemical shifts of the cis-isomer of (1) and (2) were predicted easily with the aid of the substituent shift parameters of $-CH_2CH_2CO_2R$ (R= Me or Et) which had been determined from the chemical shift differences between (3) and cyclohexane[6)] and those between (4) and cyclohexanone.[7)]

Table 1. ^{13}C Chemical Shifts of (3) and (4), δ in $CDCl_3$

Carbon	(3)		(4)	
No.	Observed	(Predicted)	Observed	(Predicted)
1	37.1	(36.9)	49.1	(49.5)
2	32.9	(33.6)	209.7	(212.5)
3	26.3	(26.6)	41.5	(41.8)
4	26.3	(26.9)	27.8	(28.0)
5	32.2	(32.4)	24.9	(25.2)
6	31.4	(30.9)	33.8	(33.1)
7	170.9	(174.0)	24.9	(23.4)
8	50.6	(51.2)	31.5	(31.4)
9			169.7	(173.5)
10			59.1	(60.0)
11			14.0	(13.9)



(3)



(4)

In trans-isomers, steric effects should be taken into consideration for C-1, -2, -4, and -5.[6] Comparison of cis- and trans-3,5-dimethylcyclohexanones gave steric shifts of 1.5-3.6 ppm.[7] The trans-isomer of (1) may exhibit a similar magnitude of steric shifts. The observed spectrum of (1), however, agreed well with that predicted for the cis-isomer.

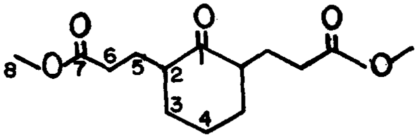
Chemical shifts of trans-isomer of (2) were predicted by applying the steric shifts observed in trans-1,3-dimethylcyclohexane[6] to the predicted chemical shifts of cis-isomer of (2). Both of the predicted and observed chemical shifts are listed in Table 2. It is concluded that (1) has cis-configuration and (2) consists of both cis- and trans-isomers with a molar ratio of cis/trans = 1/3 which was determined approximately from the relative peak heights of ^{13}C signals of both C-4 and -5.[8]

Predominant formation of the thermodynamically less stable trans-isomer over the cis-isomer is explainable as follows.[9.10] Under alkaline reducing conditions, trans-isomer (1C) as well as cis-isomers, (1A) and (1B) (see Scheme), could participate in the reduction. However, the cis-isomer (1A) with the most stable chair conformation would be least susceptible to the reduction since the carbonyl group is crowded by the neighbouring $-CH_2CH_2CO_2Me$ groups. The cis-isomer of (2), therefore, was likely produced through the flexible conformer (1B), which is sterically less stable and may exist in a smaller amount than the trans-isomer (1A) does.[11,12]

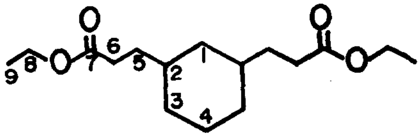
Table 2. ^{13}C Chemical Shifts of (1) and (2), δ in CDCl$_3$

Carbon No.	cis-(1) Observed	cis-(1) (Predicted)	cis-(2) Observed	cis-(2) (Predicted)	trans-(2) Observed	trans-(2) (Predicted)
1	207.7	(208.1)	39.4	(38.9)	36.4	(35.6)
2	49.7	(49.1)	37.0	(37.1)	(*)	(31.3)
3	35.2	(33.8)	(*)	(32.9)	(*)	(31.4)
4	25.3	(24.7)	25.9	(26.3)	20.7	(20.6)
5	24.5	(24.9)	(*)	(32.2)	29.6	(29.9)
6	31.3	(31.5)	(*)	(31.4)	(*)	(31.4)
7	170.6	(174.0)	171.2	(173.5)	171.2	(173.5)
8	50.7	(51.2)	59.7	(60.0)	59.7	(60.0)
9			14.3	(13.9)	14.3	(13.9)

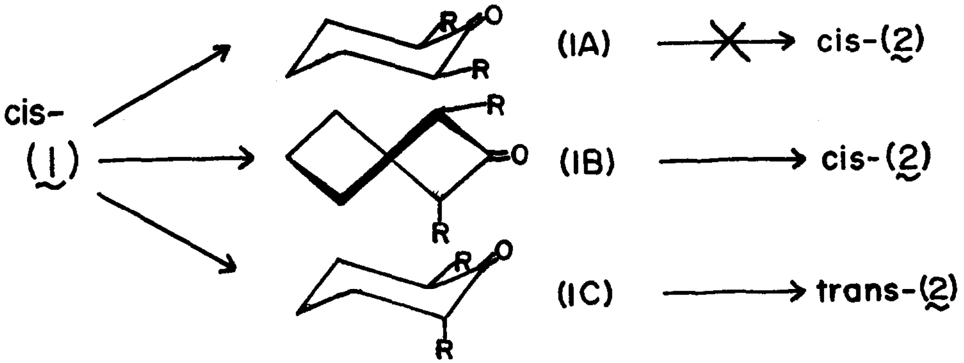
(*) Two peaks with a shoulder appeared in the region of δ31.4-32.6, which might correspond to C-3, -5, and -6 of cis-isomer and C-2, -3, and -6 of trans-isomer of (2).



(1)



(2)



Scheme. Steric Relationship in Huang-Minlon Process

REFERENCES

1) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, J. Amer. Chem. Soc. **85**, 207 (1963).

2) Huang-Minlon, ibid. **68**, 2487 (1946).

3) ^{13}C NMR spectra in $CDCl_3$ were run on a Hitachi R-26 FT NMR spectrometer operating at 10.0 MHz. The chemical shifts are expressed by δ. FT NMR measurement conditions were as follows: concentrations: ca.500mg/cm^3, spectral width: 3000 Hz, pulse angle: 30° or 45°, acquisition time: 0.2 sec, pulse intervals: 1 or 2 sec, no. of transients: 4000, no. of data points: 2048, lock: internal deuterium, and sample tube o. d.: 10 mm.

4) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, New York (1972).

5) L. F. Johnson and W. C. Jankawski, "Carbon-13 NMR Spectra," Wiley-Interscience, New York (1972).

6) D. K. Dalling and D. M. Grant, J. Amer. Chem. Soc. **89**, 6612 (1967).

7) F. J. Weigert and J. D. Roberts, ibid. **92**, 1347 (1970).

8) Integrated peak areas or peak heighs in a ^{13}C NMR spectrum cannot be exactly correlated to the number of carbons. The observed ratio, however, may be reasonable because nuclear Overhauser effects and relaxation times are considered to be almost equal for the corresponding carbons of cis- and trans-isomers.

9) R. L. Clarke, J. Amer. Chem. Soc. **83**, 965 (1961).

10) C. Djerassi, T. T. Grossnickle, and L. B. High, ibid. **78**, 3166 (1956).

11) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley-Interscience, New York (1965).

12) N. L. Allinger, J. Amer. Chem. Soc. **81**, 5727 (1959).