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Nuclear Magnetic Resonance Spectroscopy. Use of ^{13}C Spectra to Establish Configurations of Oximes[1]

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The use of ^{13}C nmr (cmr) spectra for the determination of configurations of oximes is described. The problems of quantitative analysis of syn–anti mixtures of oximes by cmr, because of differential T_1 and Overhauser effects, are considered. Chemical shifts for the cmr resonances of a number of aldehydes and ketones are reported.

The utility of ^{13}C nmr (cmr) spectra for structural studies is well established.[4] We report here its application to the determination of the configurations and composition of syn and anti isomers of aldoximes and ketoximes. While this investigation was being completed, the results of a similar study were published by Levy and Nelson.[5] We have reached similar conclusions on the basis of a much larger number of examples and have, in addition, considered cases complicated by conformational equilibration. The procedure seems to be of more general application than the elegant solvent-induced shift technique devised by Karabatsos and Taller.[6]

The assignments of the ^{13}C resonances of the oximes investigated in this work are shown in Tables I and II, which also include a substantial collection of new data on the ^{13}C shifts of several ketones and many aldehydes. Because the assignments of the resonances of the carbonyl compounds themselves are relevant to those of the oximes, we shall consider some of the problems involved with the carbonyl compounds.

^{13}C Shifts of Ketones. For many of the ketones in Table I, assignments have already been published.[7] In the case of cyclooctanone, we were not able to resolve the existing ambiguities[7b] of assignment. For methone (44), if one proceeds from menthane[8] with the substituent shifts deduced from various cyclohexane → cyclohexanone comparisons,[7b] one finds that the 3,4 carbons are expected to differ by only 0.5 ppm, whereas the observed difference is 5.7 ppm. Arguing from the respective effects of 4- or 6-methyl substitution on 2- or 3-methylcyclohexanone leads to the expectation that the C4 resonance of menthone should be upfield of the C3 resonance.[7b] However, the opposite conclusion can be derived either from translation of the 4-isopropyl substituent effect on methylcyclohexane to the appropriate carbons of 3-methylcyclohexanone or by consideration of 4-methyl substitution on 2-*tert*-butylcyclohexanone and 6-*tert*-butyl substitution on 3-methylcyclohexanone. That the C4 resonance is indeed the downfield one has been corroborated by the 50% larger lanthanide shift observed for the upfield resonance using $Eu(DPM)_3$.[9]

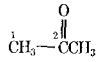
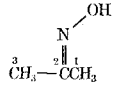
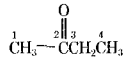
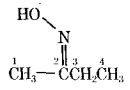
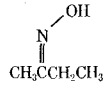
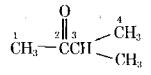
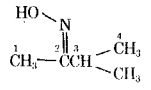
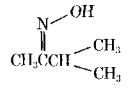
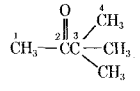
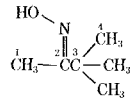
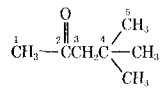
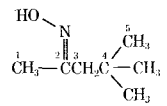
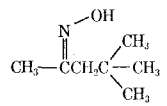
The ring methyl of menthane comes at 22.8 ppm[4] and compares favorably with that in menthone (22.3 ppm). This leaves the two methyl resonances of the isopropyl to be assigned with a shift difference of 2.5 ppm, which is reasonable for an isopropyl methyl adjacent to an asymmetric center.[10]

Isomenthone (47) is more complex. Because of a combination of "3-alkyl- and 2-alkyl-ketone" effects,[11] isomenthone is expected to have a high proportion of that conformation in which the isopropyl group is axial.[12] On the basis of the shifts of menthone, the resonances at 57.2 and 48.2 ppm for isomenthone seem reasonably ascribed to C2 and C6, respectively. The signal at 34.4 ppm was a doublet with single-frequency off-resonance decoupling (SFORD) and assigned to C5, while the signals at 26.8 and 27.0 ppm were too close together to be distinguished as CH_2 or CH by SFORD. Because both C3 and C4 of isomenthone would be expected to be shifted upfield by steric compression with the isopropyl axial (C4) in one conformation and the methyl axial in the other (C3), we have assigned the signals at 27.0 (or 26.8) and 29.6 to C3 and C4, respectively (which means upfield from the corresponding carbons of menthone by 1.5 and 4.5 ppm).

For nortricyclanone (50), the upfield signals at 18.9 and 16.9 ppm were assigned to C4, C5 and C3, respectively (2:1 ratio of intensities), and those at 37.3 and 31.3 ppm were allocated to C1 and C6, C7, respectively (1:2 ratio of intensities and SFORD multiplicities).

^{13}C Shifts of Ketoximes. All of the ketoximes we have investigated (**10, 15, 25,** and **57**) with α quaternary carbons appeared to be single isomers, which are most reasonably believed to have the oxime OH anti to the quaternary carbon. The oximes of symmetrical ketones (**2, 20, 27, 29, 31, 33, 35, 37,** and **59**) also gave just one set of resonances. For the remaining ketoximes, where two isomers might be expected and were observed, the intensity ratios of signals due to the separate isomers are shown in Table

Table I. ^{13}C Chemical Shifts[a] for Ketones and Ketoximes

	No.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
	**1**	30.7	206.2								
	**2**	15.0	155.4	21.7							
	**3**	28.9	208.8	36.4	7.4						
	**4**	13.0	159.1	28.9	10.7						
	**5**	18.9	159.5	21.7	9.6						
	**6**	27.1	212.1	41.3	17.8						
	**7**	10.8	162.2	34.3	19.5						
	**8**	15.1	162.7	25.7	18.7						
	**9**	24.5	213.9	44.3	26.4						
	**10**	10.0	164.1	37.3	27.5						
	**11**	32.3	208.5	55.8	30.9	29.6					
	**12**	16.4	157.0	49.2	31.6	29.9					
	**13**	22.7	157.0	42.0	32.2	30.7					

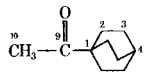
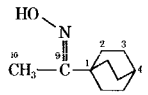
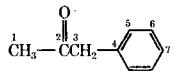
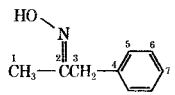
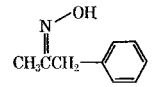
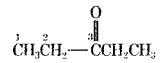
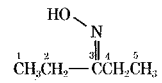
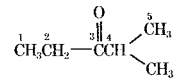
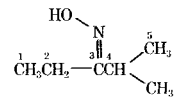
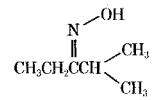
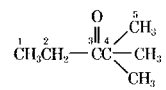
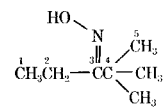
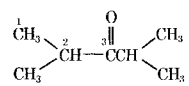
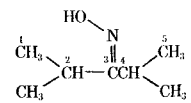
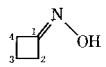
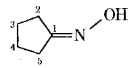
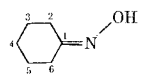
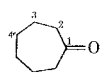
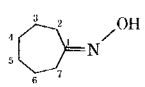
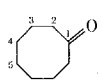
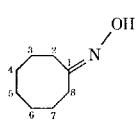
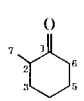
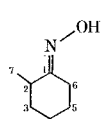
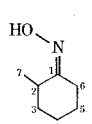
	**14**	44.5	27.5	25.5	24.1				214.2	25.5
	**15**	37.1	28.3	25.7	24.0				163.6	10.1
	**16**	29.0	206.0	50.7	134.3	129.3*	128.6*	126.9		
	**17**	13.4	157.6	42.0	136.9	129.1†	128.6†	126.4		
	**18**	19.5	156.9	34.9	136.7	129.1†	128.6†	126.4		
	**19**	8.0	35.6	212.1						
	**20**	10.1*	21.0	163.5	27.1	10.7*				
	**21**	7.9	33.5	215.2	40.7	18.4				
	**22**	10.7	20.0	166.4	33.6	20.0				
	**23**	10.8	23.3	165.8	26.5	19.0				
	**24**	8.2	29.6	216.3	44.0	26.5				
	**25**	11.1	19.0	168.1	37.6	27.6				
	**26**	18.6	38.9	218.4						
	**27**	18.9	27.7	168.6	30.8	21.3				

Table I (*Continued*)

	No.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
	**28**	208.9	47.8	9.9							
	**29**	159.7	30.7	14.6	31.6						
	**30**	219.6	37.9	22.7							
	**31**	167.1	27.1	25.1*	24.4*	30.6					
	**32**	209.7	41.5	26.6	24.6						
	**33**	160.4	25.7*	25.4*	24.4	26.7	31.9				
	**34**	215.0	43.9	24.4	30.6						
	**35**	164.3	30.49*	27.5‡	30.44*†	28.9†	24.7‡	33.9			
	**36**	218.0	42.0	27.4*	25.8*	24.9					
	**37**	163.7	27.3†	26.9†‡	26.8†‡	24.9‡	25.5‡	24.4‡	33.1		
	**38**	212.9	45.5	36.4	25.3	28.0	42.0	14.8			
	**39**	163.0	37.2	35.7	23.9	24.8	26.1	16.9			
	**40**	163.6	26.8*	26.7*†	20.5‡	28.4†‡	31.7	16.2			

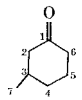
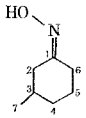
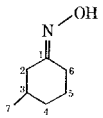
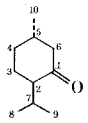
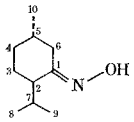
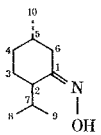
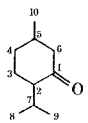
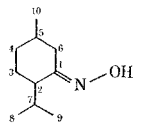
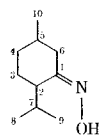
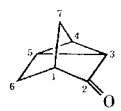
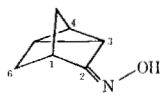
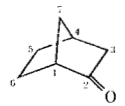
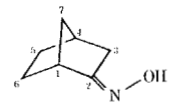
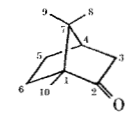
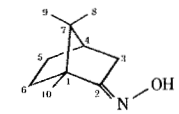
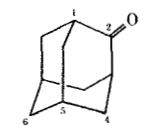
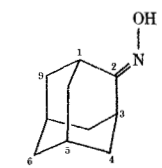
	**41**	211.6	50.0	34.2	33.4	25.3	41.1	22.1		
	**42**	160.4*	34.2†	32.5‡	32.3‖	24.5#	31.7	22.1**		
	**43**	160.5*	40.1	33.4‡	34.3†‖	23.9#	25.8	21.9**		
	**44**	212.0	56.1	28.4	34.1	35.6	51.0	26.0	21.3*	18.8*	22.3
	**45**	161.0	48.8	26.9	32.8†	32.4	31.9†	26.4	21.8‡#	19.1‡	21.4#
	**46**	161.2	40.0	22.0‖	26.7‖**	29.6	35.2	26.6**	20.4$^{****}_{***}$	18.1****	20.8***
	**47**	214.1	57.2	27.0*	29.6	34.4	48.2	26.8*	21.0†‡	19.9†	21.4‡
	**48**	163.0**	47.5	26.7****	28.3	34.5	29.7***	26.7	(21.2	20.6	22.5)#
	**49**	162.6**	39.3	27.3****	37.5	33.2	29.5***	29.7	(20.7	20.4	22.4)#
	**50**	37.3	213.8	16.9	18.9		31.3				

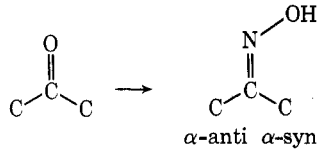
Table I (*Continued*)

	No.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
	**51**	33.4	167.1	11.4	17.1		33.6				
	**52**	29.0	167.6	13.8	16.7		33.3				
	**53**	49.3	216.8	44.7	34.8	26.7	23.7	37.1			
	**54**	42.0	167.4	34.9	35.5	27.1	27.8	39.1			
	**55**	38.5*	166.3	37.2	35.6	26.0	27.4	38.3*			
	**56**	57.7	219.1	43.3	43.3	27.2	30.0	46.8	9.3	19.2	19.8
	**57**	51.7	169.5	33.1*	43.8	27.3	32.7*	48.2	11.1	18.5†	19.5†
	**58**	47.1	217.9		39.4	27.6	36.4				
	**59**	29.1	167.4	36.2	37.7*	27.9	36.6			39.0*	

[a] Shifts are in ppm downfield from TMS. Uncertainties of assignments are indicated by *, †, ‡, #, ||, **, ***, and **** according to the following system. For the ketones, the superscripts represent assignments which might reasonably be interchanged in a given horizontal row in the table. For the oximes, when the amounts of each isomer are comparable, then possible interchanges between assignments for a given isomer are shown for the same horizontal row of values and between isomer pairs in different horizontal rows.

III. The method of obtaining these ratios is described in the Experimental Section. The major isomer of the pairs **4-5, 7-8, 12-13, 17-18, 22-23, 39-40, 45-46,** and **54-55** is expected on the basis of steric hindrance to have the OH syn to the least substituted α-carbon. With this assumption, and with the aid of the SFORD spectra, the individual resonances can be assigned to particular carbons of all of these oximes, as has been done in Table I.

As has been noted by Levy and Nelson[5] on the basis of fewer examples, a consistent pattern of α-anti and α-syn carbon shift changes is observed when a ketone is converted to an oxime (eq 1). These changes are listed in Table IV with *upfield* shifts taken to be *negative*. It will be seen that the resonances of the carbonyl carbon and both α-carbons all shift upfield on oxime formation, with the effect for the α-syn carbon being greater than for the α-anti carbon, an effect noted earlier with cis-alkenes.[13] With the aid of this correlation, it is easy to assign the resonances of **2, 20,** and **27** as in Table I. The corresponding substituent effects are shown in Table IV.



α-anti α-syn (1)

The carbon shift changes associated with conversion of a ketone to its oxime and the β-carbons are usually, but not always, small for acyclic ketones (see Table IV). There is a definite trend which speaks for more negative shifts at the syn than the anti β-carbons. This effect was used to assign the β resonances of **27**, which check out well with those of **7** and **8**.

Table I shows selections for α-carbon resonances of the cyclic ketoximes **29, 31, 35,** and **37**. The lowest field CH_2 signal was assigned to the anti α-carbon and the next lowest field CH_2 signal to the syn α-carbon. The latter assignments are hardly unambiguous for **31, 35,** and **37** where two or more carbons come at about the same place. That the syn-anti α-carbon difference is steric in origin fits well with its very small magnitude for cyclobutanone oxime where the constraints on the ring carbons should substantially reduce the hindrance.

The procedures for cyclohexanone oxime and its 2- and 3-methyl derivatives, **33, 39, 40, 42,** and **43,** were somewhat different. Except for the minor isomer of 2-methylcyclohexanone oxime (**40**) (Figure 1), which presented a special problem, a reasonably self-consistent set of assignments (with some uncertainties) was evolved from SFORD data, α syn-anti effects, and the assumption that the methyl substituent effects on the ^{13}C shifts of cyclohexanones[7b] carry over to the ketoximes (Table V). The signals at 24.4 and 26.7 ppm for cyclohexanone oxime were assigned to C4 and C5 on the basis of expected minimal changes at these carbons going from ketone to oxime. Special uncertainties came with **42** and **43** because these isomers were present in nearly equal amounts.

For the minor isomer of 2-methylcyclohexanone oxime (**40**), C2 is clearly at about 26.8 ppm from the SFORD spectrum, and C6 is the lowest field saturated-carbon resonance. None of the remaining oxime ring resonances, especially the one at 20.5 ppm, correlate with the ketone resonances. It seems possible that steric interference between the OH and 2-methyl results in a more or less complete conformational change which brings the methyl axial. If this is so, the 20.5-ppm resonance is likely to be C4, but we have no certain evidence for it.

The assignments for the major isomer of menthone oxime, **45**, were made to be consistent with those of menthone (**44**) and SFORD spectra.[14] For the minor isomer, **46**, C2 and C6 were assigned on the basis of the oxime substituent effects, although the C6 resonance is at a rather unusually high field. As with **40**, there seems to be a possibility that a conformational change takes place on oxime formation when a 2 substituent is syn to the oxime OH, because the ring CH_2 resonances do not correlate well with the ketone CH_2 resonances, especially with the oxime resonance at 22 ppm.

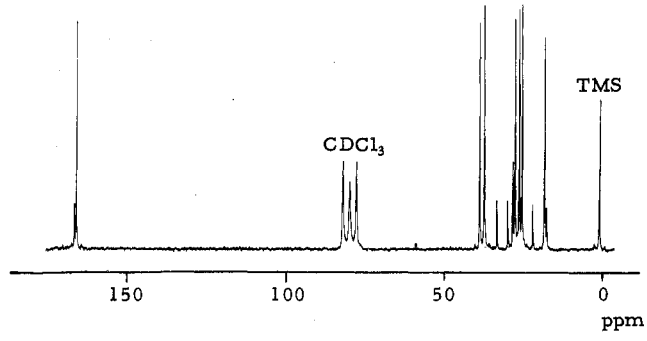


Figure 1. ^{13}C spectrum of 2-methylcyclohexanone oxime + Cr(acac)$_3$.

The isomenthone oxime isomers presented specially difficult problems because they were present in nearly equal amounts and because of the conformational uncertainties mentioned earlier with regard to menthone itself. Clearly, for the oxime with the OH syn to the isopropyl group (**49**), we expect that this group will be most favorably disposed in the axial position. That there are two upfield ring resonances in the mixture suggests that the isopropyl axial is particularly favored and the highest field resonance is of its C4 atoms. Except when confirmed by SFORD and in accord with the α syn-anti effects, these assignments are speculative.

The major isomer of nortricyclanone oxime has a cyclopropane carbon resonance at 11.4 ppm and two others at 17.1 ppm; the 33.4-ppm signal from its SFORD pattern is a CH resonance and must be C1. The syn and anti α-carbon shifts are thus -5.5 and -3.9 ppm, respectively, from the ketone. This isomer is assigned the configuration with cyclopropane syn to the OH group. The corresponding shifts for the minor isomer are -3.1 and -8.3 ppm which are, as expected for the OH group, syn to C1.

For norcamphor ketoxime, the major isomer should have the OH anti to C1, the more substituted carbon. For this isomer, the methine resonances at 42.0 and 35.5 ppm were assigned to C1 and C4, respectively. The C5, C6, and C7 signals were assigned to be consistent with those of the ketone, which leaves a resonance at 34.9 ppm for C3. These allocations give $\Delta_{\alpha\text{-syn}}$ and $\Delta_{\alpha\text{-anti}}$ of -9.8 and -7.3 ppm, respectively. The signals of the minor isomer were specified in the same way.

Camphor oxime (**57**) shows only one set of ^{13}C resonances which must be from the isomer with OH anti to C1. The assignment procedure here followed that for the major isomer of norcamphor oxime. For adamantanone oxime (**59**) only one isomer is possible. The larger of the methine signals at 27.9 ppm was ascribed to C5 and C7, while the other CH resonances at 29.1 and 36.2 ppm were assigned to C1 and C3, respectively, in accord with the expected syn-anti effect. The weaker CH_2 signal was easily ascribed to C6 but no clear decision between the other two larger signals was possible.

Table IV shows that conversion of $R_2C{=}O$ to $R_2C{=}NOH$ is accompanied by a very consistent mean change in the carbonyl resonance position of -50.0 ppm, with a standard deviation of 1.5 ppm. The only conspicu-

Table II
^{13}C Chemical Shifts[a] for Aldehydes and Aldoximes

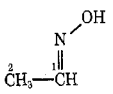
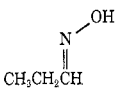
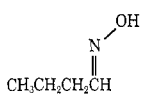
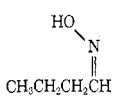
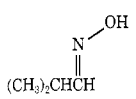
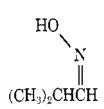
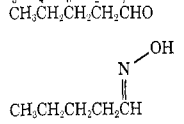
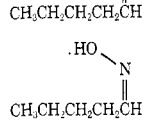
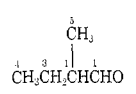
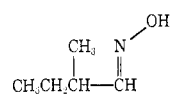
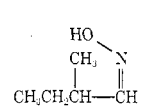
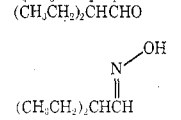
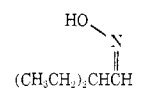
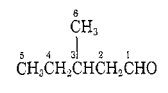
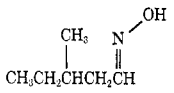
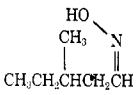
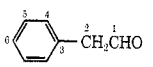
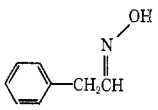
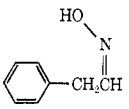
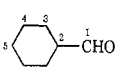
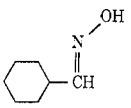
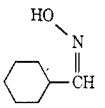
	No.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
$^{2}CH_3{}^{1}CHO$	**60**	199.8	30.9								
	**61**	147.8	11.2								
	**62**	148.2	15.0								
$^{3}CH_3{}^{2}CH_2{}^{1}CHO$	**63**	202.8	37.3	6.0							
	**64**	153.1	23.1	10.9							
	**65**	153.7	18.6	10.4							
$^{4}CH_3{}^{3}CH_2{}^{2}CH_2{}^{1}CHO$	**66**	202.5	45.9	15.8	13.8						
	**67**	152.1	31.5	20.1	13.6*						
	**68**	152.6	27.0	19.5	13.9*						
$(^{3}CH_3)_2{}^{2}CH{}^{1}CHO$	**69**	204.7	41.2	15.5							
	**70**	156.9	29.4	20.0							
	**71**	157.8	24.5	19.7							
$^{5}CH_3{}^{4}CH_2{}^{3}CH_2{}^{2}CH_2{}^{1}CHO$	**72**	202.3	43.7	24.3	22.3	13.8					
	**73**	152.3	29.2	28.8*	22.3	13.7					
	**74**	152.8	24.9	28.4*	22.6	13.7					
	**75**	204.9	47.9	23.2	11.4	12.9					
	**76**	156.4	36.1	27.7	11.4	17.7*					
	**77**	157.0	31.2	27.7	11.4	17.1*					
$(^{4}CH_3{}^{3}CH_2)_2{}^{2}CH{}^{1}CHO$	**78**	205.0	55.0	21.5	11.4						
	**79**	155.6	43.2	25.7	11.5						
	**80**	156.4	38.3	25.4	11.6						
	**81**	202.4	50.9	29.8	29.8	11.4	19.6				

Table II
(*Continued*)

	No.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
	**82**	151.6	36.3	33.2	29.3	11.4	19.2				
	**83**	152.0	31.9	32.8	29.5	11.4	19.6				
	**84**	199.3	50.6	132.0	129.7*	129.1*	127.5				
	**85**	150.9	36.0	136.9	128.9	128.9	126.9				
	**86**	150.9	31.9	136.9	128.9	128.9	126.9				
	**87**	204.7	50.1	26.1	25.2	25.2					
	**88**	155.8	38.5	30.3	25.5*	25.6*					
	**89**	156.3	33.9	29.5	25.6*	25.9*					

[a] See footnote to Table I.

Table III
Ketoxime Isomer Distributions Determined from the ^{13}C Spectra

Ketoximes[b]	Carbons[c]	% of major isomer[a] With Cr(acac)$_3$[d]		Pulse delay[e]		Lit.[f]	$-\Delta G°$[g]
4, 5	C3	78	78	73	75		0.77
	C4	77		76		74	
	C1	71		68		72	
7, 8	C3	86	86	88	86	91	1.11
	C1	86		84		86	
12, 13	C3	83	82	81	82		0.93
	C1	80		82			
22, 23	C3	78	78	78	78		0.78
	C4	78		78			
17, 18	C3	74	72	71	71	74	0.58
	C1	70		70			
39, 40	C1	84	84	83	83		1.01
	C3 (**39**), C5 (**40**)	84		82			
42, 43		~50		~50			~0.00
45, 46	C2	82		74			0.93
48, 49		~50		~50			~0.00
51, 52	C2	79	79	79	80		0.81
	C3	79		80			
54, 55	C2	85	85	87			1.06
	C1 (**54**), C3 (**55**)	84					

[a] The uncertainties of the values determined from the ^{13}C spectra are probably of the order ±5%. [b] Presumed major isomer listed first. [c] The ^{13}C signals used for peak height measurements. [d] From ^{13}C spectra obtained with added Cr(acac)$_3$ to reduce differential NOE effect. [e] From ^{13}C spectra without Cr(acac)$_3$, but with a 12-sec pulse delay. [f] Literature values from ref 6, and K. D. Berlin and S. Rengaraju, *J. Org. Chem.*, **36**, 2912 (1971). [g] Free energies (kcal mol^{-1}) at 35°; these were determined from mean values.

ous deviations are of **37**, **51**, and **52** which are about 4 ppm from the mean.

There is only one exception (**49**, which, as discussed, may involve a major conformational change) to the generalization that $\Delta_{\alpha\text{-syn}} - \Delta_{\alpha\text{-anti}}$ is positive.

Values of Δ_β are also listed in Table IV. These are seen to be consistently positive for aliphatic ketones and of variable sign for alicyclic ketones.

^{13}C Shifts of Aldehydes. The spectral assignments in Table II for a number of aldehydes have been confirmed by SFORD spectra where possible and seem sufficiently unambiguous to preclude detailed discussion.

^{13}C Spectra of Aldoximes. The substituent shifts for the change $C_\beta C_\alpha CH{=}O \rightarrow C_\beta C_\alpha CH{=}NOH$ for aldehydes are sufficiently regular to be quite helpful in making assignments. Where both syn and anti isomers were present, these could often be identified by comparing the ^{13}C resonance intensities with the isomer ratios determined by Karabatsos and Taller from proton spectra.[6] Thus, the more intense methyl signal of acetaldoxime is at higher field, consistent with a larger upfield shift for the oxime OH syn than OH anti to the methyl group, and the finding that the syn isomer is the major one.[6] For the other aldoxime isomer mixtures, carbon shifts of the major components were consistent with the alkyl group being anti to the OH (see Table VI).

Brief comments seem desirable for a few specific substances. Thus, with valeraldoxime (**73**, and **74**), the closeness of the chemical shifts and the nearly equal isomer proportions allowed only the signal at 24.9 ppm to be surely assigned to the minor isomer. The other resonances were assigned by comparison with the shifts of propionaldoxime (**64** and **65**) and butyraldoxime (**67** and **68**). For

Table IV
^{13}C Substituent Shift Parameters for Conversion of Ketones to Ketoximes[a]

Oxime	$\Delta_{C=X}$[b]	$\Delta_{\alpha\text{-syn}}$[b]	$\Delta_{\alpha\text{-anti}}$[b]	$\Delta_{\alpha\text{-syn}} - \Delta_{\alpha\text{-anti}}$	Δ_{β}[b]
4	−49.7	−15.9	−7.5	−8.4	+3.3
5	−49.3	−14.7	−10.0	−4.7	+2.2
7	−49.9	−16.3	−7.0	−9.3	+1.7
8	−49.4	−15.6	−12.0	−3.6	+0.9
10	−49.8	−14.5	−7.0	−7.5	+1.1
12	−51.5	−15.9	−6.6	−9.3	+0.7
13	−51.5	−13.8	−9.6	−4.2	+1.3
15	−50.6	−14.4	−7.4	−7.0	+0.8
17	−48.4	−15.6	−8.7	−6.9	+2.6
18	−49.1	−15.8	−9.5	−6.3	+2.4
22	−48.8	−13.5	−7.1	−6.4	+1.8, +1.6
23	−49.4	−14.2	−10.2	−4.0	+1.9, +0.6
25	−48.2	−10.6	−6.4	−4.2	+2.9, +1.1
2	−50.8	−15.8	−9.0	−6.8	
20	−48.6	−14.6	−8.5	−6.1	+2.1, +2.7
27	−49.8	−11.2	−8.1	−3.1	+0.3, +2.7
29	−49.2	−17.1	−16.2	−0.9	+3.7
31	−52.5	−10.8	−7.3	−3.5	+2.4, +1.7
33	−49.3	−15.8 (−16.1)	−9.6	−6.2 (5)	−1.2, +0.1
35	−50.7	−13.4 (5)	−10.0	−3.4 (5)	+3.1, +0.3
37	−54.3	(−14.7)	−8.9	(−5.8)	?
39	−49.9	−15.9	−8.3	−7.6	−0.7, −3.2
40	−49.3	−18.7 (8)	−10.3	−8.4 (5)	−9.7, ? (−8.0)
42	−51.2 (1)	−15.8 (7)	−9.4	−6.4 (3)	−1.7, −0.8 (−0.8) (−1.4)
43	−51.1 (2)	−15.3	−9.9	−5.4	−0.8, −1.4 (−1.7) (−0.8)
45	−51.0	−19.1 (−18.2)	−7.3	−11.8 (−10.9)	−1.5, −3.2
46	−50.8	−16.1	−15.8	−0.3	−6.4, −6.0 (−1.7)
48	−51.1 (5)	−18.5 (7)	−9.7	−8.8 (−9.0)	−0.3 (1), +0.1 +0.3 (5)
49	−51.5 (1)	−17.9	−19.0 (−18.7)	+1.1 (+0.8)	+0.3 (1), −1.2 −0.3 (5)
51	−46.7	−5.5	−3.9	−1.6	−1.8, +2.3
52	−46.2	−8.3	−3.1	−5.2	−2.2, +3.0
54	−49.2	−9.8	−7.3	−2.5	+0.8, +3.9, +2.0
55	−50.5	−10.8 (−11.0)	−7.5	−3.3 (5)	+0.8, +3.7, +1.2 (4)
57	−49.6	−10.2 (6)	−6.0	−4.2 (6)	+0.5, +2.7, +1.4 (+3.1)
59	−50.5	−18.0	−10.9	−7.1	−1.7, −0.4

[a] In ppm, figures in parentheses represent uncertainties in assignment (see Table I). [b] These are ^{13}C shifts for ketoxime − ^{13}C shifts of ketone, and negative values indicate that the ketoxime signal is at higher field.

Table V
Methyl ^{13}C Chemical Shift Parameters[a] for Cyclohexanone and Cyclohexanone Oxime

Compound	C2	C3	C4	C5	C6
38	+5.0	+9.8	+0.7	+1.4	+0.5
39	+5.3	+9.0	−0.5	−0.6	+0.4
41	+8.5	+7.6	+8.8	−1.3	−0.4
42	+8.5	+7.1	+7.9	−2.2	−0.2
43	+8.2	+6.7	+9.9	−1.5	+0.1

[a] Shift differences between the methyl-substituted cyclohexanones (**38** and **41**) and cyclohexanone (**32**), and the methyl-substituted cyclohexanone oximes (**39**, **42**, and **43**) and cyclohexanone oxime (**33**). Negative values indicate the signals for the methyl-substituted compounds and are at higher field.

phenylacetaldoxime (**85** and **86**), the ortho and meta carbons give a single unresolved signal. With cyclohexanecarboxaldoxime (**88** and **89**), the C2 and C6 resonances of the ring were assigned on the basis of a quite uniform downfield Δ_{β} effect for aldoximes (*cf.* Table VI). The remaining ring resonances were very close together.

The α-carbon substituent shifts for aldoximes, as mea-

Table VI
Aldoxime ^{13}C Substituent Parameters[a]

Aldoxime	$\Delta_{C=X}$[b]	$\Delta_{\alpha\text{-syn}}$[b]	$\Delta_{\alpha\text{-anti}}$[b]	$\Delta_{\alpha\text{-syn}} - \Delta_{\alpha\text{-anti}}$	Δ_{β}[b]
61	−52.0	−19.7		−3.8	
62	−51.6		−15.9		
64	−49.7		−14.2	−4.5	+4.9
65	−49.1	−18.7			+4.4
67	−50.4		−14.4	−4.5	+4.3
68	−49.9	−18.9			+3.7
70	−47.8		−11.8	−4.9	+4.5
71	−46.9	−16.7			+4.2
73	−50.0		−14.5	−4.3	+4.5 (1)
74	−49.5	−18.8			+4.1 (5)
76	−48.5		−11.8	−4.9	+4.5, +4.8
77	−47.9	−16.7			+4.5, +4.2
79	−49.4		−11.8	−4.9	+4.2
80	−48.6	−16.7			+3.9
82	−50.8		−14.6	−4.4	+3.4
83	−50.4	−19.0			+3.0
85	−48.4		−14.6	−4.1	+4.9
86	−48.4	−18.7			+4.9
88	−48.9		−11.6	−4.2	+4.2
89	−48.4	−16.2			+3.4

[a,b] See footnotes to Table IV.

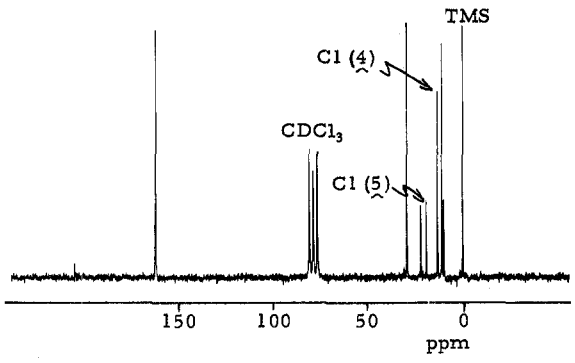


Figure 2. ^{13}C spectrum of butanone oxime + $Cr(acac)_3$.

sured by $\Delta_{\alpha\text{-syn}}$ and $\Delta_{\alpha\text{-anti}}$ (Table VI) fall into two ranges. If there is one substituent on the α-carbon, then $\Delta_{\alpha\text{-syn}}$ = −18.8 ppm (std dev = 0.13) and $\Delta_{\alpha\text{-anti}}$ = −14.4 ppm (std dev = 0.17), while with two substituents on the α-carbon $\Delta_{\alpha\text{-syn}}$ = −16.6 ppm (standard deviation = 0.25) and $\Delta_{\alpha\text{-anti}}$ = −11.8 ppm (std dev = 0.10). These differences seem regular enough to have diagnostic value.

Experimental Section

Oximes of cyclohexananone, camphor, and acetaldehyde were available commercially. The others were prepared from the carbonyl compound with a 20% excess of hydroxylamine hydrochloride in 15% aqueous sodium hydroxide solution at 60–70°. The oximes were distilled under reduced pressure or recrystallized before the spectra were taken. With menthone, this procedure gave four oxime isomers because of base-catalyzed interconversion of menthone and isomenthone. The oximes of these ketones were therefore synthesized using sodium acetate in methanol[15] in place of aqueous sodium hydroxide solution.

The ^{13}C spectra were obtained by the pulse-Fourier transform technique at 15.09 MHz, using the spectrometer described elsewhere.[16] The time for a 90° pulse was 10 μsec and the noise-modulated proton decoupling[17] covered a band width of 600 Hz. The single-frequency off-resonance decoupling (SFORD) technique has been described earlier.[17] The samples were run as approximately 1.5 *M* solution in $CDCl_3$ containing tetramethylsilane (TMS) as internal reference. The sample temperatures were about 35°.

For quantitative measurements, the following procedures were employed. First, from the full spectrum (5000 Hz, ~330 ppm) at least two completely resolved lines (one for each isomer) were singled out, usually in the saturated carbon region. Then, 55–60 mg of $Cr(acac)_3$ was dissolved in 2 ml of a 1.8–2.0 *M* solution of the oxime mixture and the spectrum repeated with a 3000-Hz spectral width, using the full 8K of available data storage of the computer to accumulate the free-induction decays. The flip angle was approximately 60° (7 μsec pulses) and the delay between pulses was 5–10 sec. The frequency-domain spectra then showed full peak widths at half-peak height of 3.5–4 Hz, compared to 1 Hz or less in the absence of $Cr(acac)_3$. There was 0.8 Hz/point in the resulting digitized spectra, which gave reasonably consistent peak height measurements. Further increase in the $Cr(acac)_3$ concentration resulted in loss of resolution without substantial improvement in the analyses. The chemical shifts were not substantially affected—there being less than 0.5 ppm change of the C=NOH resonance and 0.1 ppm of the other carbon signals.

Check determinations were made without $Cr(acac)_3$, using a 12-sec delay between 60° pulses. The way in which these were run did not eliminate the possibility of differential Overhauser effects from the proton decoupling. That this is important can be seen from results with acetone oxime where the ratios of the peak heights for the methyl carbons were 63:37 without $Cr(acac)_3$ and 52:48 with $Cr(acac)_3$. In some cases, as with methyl ethyl ketoxime (**4** and **5**), even with $Cr(acac)_3$, the peak intensities were still not in the expected ratios. With this substance, the syn α-methyl carbon of the dominant isomer shows a distinctly low intensity (Figure 2) compared to the other resonances.

With the aldoximes, a new problem arose in that, with added $Cr(acac)_3$, there often appears to be substantial differential line broadening and changes in intensity of the minor isomer relative to the major isomer. This appears to be the result of differential complexing between isomers with the doping agent, and, for this reason, the isomer ratios reported in Table VII are only the result of determinations with 12-sec pulse delays. Hopefully, the use of ratios between analogously situated carbons in each isomer has diminished the contribution of differential Overhauser effects to these ratios. Where comparisons are possible, agreement with isomer ratios obtained by proton spectra[6] are reasonably satisfactory.

Table VII
Aldoxime Isomer Distribution Obtained from ^{13}C Spectra

Aldoximes[a]	Percentage of major isomer— Pulse delays[b]	Lit.[c]
61, 62	64	61
64, 65	67	56
67, 68	56	54
73, 74	56	
70, 71	77	73
76, 77	68	70
79, 80	72	67
82, 83	51	
85, 86	49[d]	54
88, 89	71	70

[a] Presumed major isomer listed first. The uncertainties of the values obtained by the ^{13}C spectra are probably ±5%. [b] From ^{13}C spectra with 12-sec pulse delay. [c] Literature values from ref 1. [d] As reported in ref 1, the ratio changed with time: 17% after 1 hr, 34% after 3 hr, 44% after 10 hr, and 49% after 18 hr of the time the solution was prepared.

Registry No.—**1**, 67-64-1; **2**, 127-06-0; **3**, 78-93-3; **4**, 10341-63-6; **5**, 10341-59-0; **6**, 563-80-4; **7**, 10341-62-5; **8**, 10341-60-3; **9**, 75-97-8; **10**, 10341-64-7; **11**, 590-50-1; **12**, 49805-39-2; **13**, 49805-40-5; **14**, 24623-10-7; **15**, 49805-41-6; **16**, 103-79-7; **17**, 10048-64-3; **18**, 10048-65-4; **19**, 96-22-0; **20**, 188-11-0; **21**, 565-69-5; **22**, 49805-38-1; **23**, 49805-42-7; **24**, 564-04-5; **25**, 49775-30-6; **26**, 565-80-0; **27**, 1113-74-2; **28**, 1191-95-3; **29**, 2972-05-6; **30**, 120-92-3; **31**, 1192-28-5; **32**, 108-94-1; **33**, 100-64-1; **34**, 502-42-1; **35**, 2158-31-8; **36**, 502-49-8; **37**, 1074-51-7; **38**, 583-60-8; **39**, 32179-89-8; **40**, 49805-43-8; **41**, 591-24-2; **42**, 31661-10-6; **43**, 31661-09-3; **44**, 89-80-5; **45**, 49805-45-0; **46**, 49805-46-1; **47**, 491-07-6; **48**, 49775-31-7; **49**, 49805-47-2; **50**, 695-05-6; **51**, 49805-48-3; **52**, 49805-49-4; **53**, 497-38-1; **54**, 49805-50-7; **55**, 49805-51-8; **56**, 76-22-2; **57**, 37939-80-3; **58**, 700-58-3; **59**, 4500-12-3; **60**, 75-07-0; **61**, 5775-72-4; **62**, 5780-37-0; **63**, 123-38-6; **64**, 5775-80-4; **65**, 5780-46-1; **66**, 123-72-8; **67**, 5775-75-7; **68**, 5780-41-6; **69**, 78-84-2; **70**, 5775-73-5; **71**, 5780-39-2; **72**, 110-62-3; **73**, 5775-76-8; **74**, 5780-42-7; **75**, 96-17-3; **76**, 49805-55-2; **77**, 49805-56-3; **78**, 97-96-1; **79**, 49805-57-4; **80**, 49805-58-5; **81**, 15877-57-3; **82**, 49805-59-6; **83**, 49805-60-9; **84**, 122-78-1; **85**, 20268-21-7; **86**, 20259-49-8; **87**, 2043-61-0; **88**, 30950-35-7; **89**, 30950-34-6.

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and W. C. Jankowski, ref 4a, Wiley, New York, N. Y., 1972. (b) Rather different conclusions have been reached about the nature and/or configurations of menthone, isomenthone, and camphor oximes on the basis of their proton spectra than those given here on the assis of ^{13}C spectra; see Z. W. Wolkowski, J. Cassan, L. Elegant, and M. Azzaro, *C. R. Acad. Sci., Ser. C*, **275**, 1244 (1971). The ^{13}C spectra clearly give more information and seem much more definitive.

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Photochemical, Thermal, and Acid-Catalyzed Rearrangements of α,β-Epoxy Ketones. Synthesis of Spiro β-Diketones[1]

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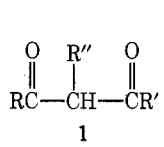
2-Cyclopentylidenecyclopentan-1-one oxide (**6**) and 2-cyclohexylidenecyclohexan-1-one oxide (**8**) have been isomerized thermally and photochemically *via* a 1,2-alkyl shift to spiro[4.5]decane-1,6-dione (**7**) and spiro-[5.6]dodecane-1,7-dione (**12**), respectively. Acid-catalyzed isomerization of **6** proceeds *via* a 1,2-acyl shift to yield spiro[4.5]decane-6,10-dione (**26**). Thermolysis of **8** also formed 1,2,3,4,6,7,8,9-octahydrodibenzofuran (**17**) in low yield. The mechanisms of these reactions are discussed. Photolysis and thermolysis of the epoxy ketones **6** and **8** in the presence of tri-*n*-butylstannane yielded the enones, 2-cyclopentylidenecyclopentan-1-one (**21**) and 2-cyclohexylidenecyclohexan-1-one (**22**), respectively.

Recent work has indicated that isomerization of appropriately substituted α,β-epoxy ketones can serve as a useful preparative method for the synthesis of mono- (**1**) and disubstituted (**2**) β-dicarbonyl compounds.[2,3] This isomerization has been effected thermally,[4] photochemically,[5-14] and by using acidic catalysts.[2,3,15,16]

Owing to the number of isomerization products possible, it was of interest to learn the regiospecificity of the rearrangement for each of the various reaction conditions involved, and which was the preferred method to use synthetically.



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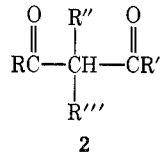
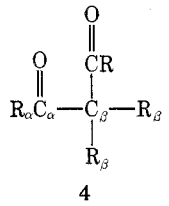
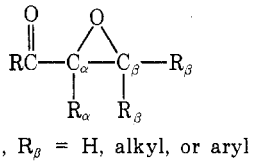


2

The isomerization of the α,β-epoxy ketones **3** can proceed *via* two major pathways. Isomerization *via* a 1,2-acyl migration yields the β-diketone **4**, whereas a 1,2-alkyl migration of R_β affords the different β-diketone **5**. A 1,2-alkyl migration of R_α affords an α-diketone. In this paper we report the results of the photochemical, thermal, and acid-catalyzed isomerizations of a series of spiro α,β-epoxy ketones *via* 1,2-acyl and 1,2-alkyl shifts to yield spiro β-diketones.



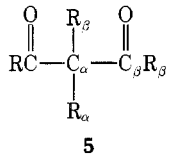
4



R, R_α, R_β = H, alkyl, or aryl

3

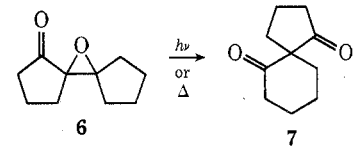
1,2-acyl migration
1,2-alkyl migration



5

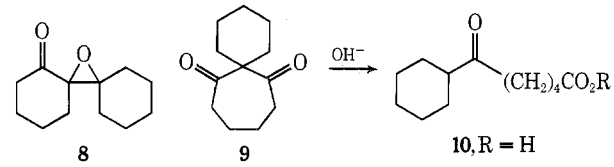
Results and Discussion

Recent studies[17-19] on the photolysis of the α,β-epoxy ketone **6** led to the convenient preparation of the spiro β-diketone **7**. However, the yield of **7** *via* this path was low (30%).[17,19] To improve the yield of this reaction, **6** was heated for 15 min at 225° and **7** was obtained as the only product in 89% yield.



6 **7**

This result is in sharp contrast to the results of House and Wasson,[2] who reported that thermolysis of the six membered ring homolog of **6**, *i.e.*, **8**, afforded the spiro β-diketone **9**.



8 **9** **10**, R = H; **11**, R = CH_3

Reexamination of their structure proof for **9** showed that their structure was wrong. Alkaline hydrolysis of the proposed spiro β-diketone **9** afforded a keto acid to which the structure **10** was assigned.[2] The keto acid was characterized as its semicarbazone, mp 270–271°.[2] However, the literature melting point of the semicarbazone of **10** was 175°,[20] thereby indicating that **10** was not the correct structure for the hydrolysis product. Furthermore, authentic keto acid **10** was prepared according to the method of Reese[20] and shown to be different from the keto acid obtained as a hydrolysis product.

Since the keto acids had melting points near room temperature and were difficult to recrystallize, their methyl esters were prepared. Again the authentic methyl ester **11** showed different spectral properties from those of the ester obtained from the hydrolysis product. Therefore, what is the structure of the hydrolysis product and that of the β-diketone from which it is derived?