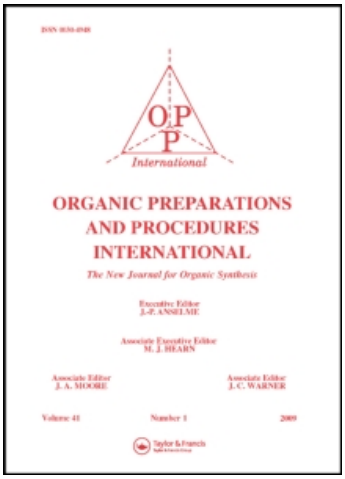

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF 2,6-DIARYLTETRAHYDROPYRAN-4-ONES

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To cite this Article Fakler, Timothy M. and Berlin, K. Darrell(1989) 'SYNTHESIS OF 2,6-DIARYLTETRAHYDROPYRAN-4-ONES', Organic Preparations and Procedures International, 21: 3, 327 — 335
To link to this Article: DOI: 10.1080/00304948909356387
URL: http://dx.doi.org/10.1080/00304948909356387

ORGANIC PREPARATIONS AND PROCEDURES INT. 21(3), 327-335 (1989)

SYNTHESIS OF 2,6-DIARYLTETRAHYDROPYRAN-4-ONES

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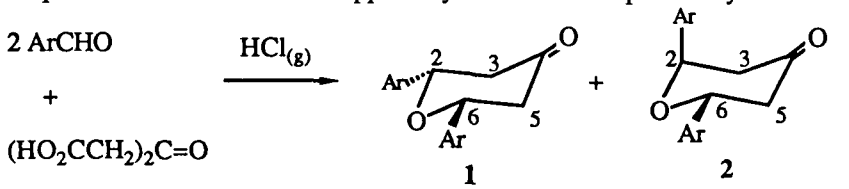
Cycloalkanones are important synthons for polycyclics,[1] and substituted heteracycloalkanones should have similar utility. Although a small number of 1-hetera-2,6-diaryl-4-cyclohexanones containing nitrogen,[2,3] sulfur,[2-4] selenium[5] and phosphorus[6] have been recorded, only the *cis*- and *trans*-2,6-diphenyl derivatives (**1a** and **2a**) of the oxygen analog have been reported.[4] In connection with other studies of heterocyclic medicinal agents, we had occasion to reexamine this chemistry, and we now report the preparation and spectral studies for a number of 2,6-diaryltetrahydropyran-4-ones (**1a-g** and **2a-c**). The synthesis of ketones **1a-g** and isomers **2a-c** was accomplished *via* the condensation of the appropriate aryl aldehyde with 1,3-acetonedicarboxylic acid and without solvent. The purity of the latter acid was a most critical parameter. This factor was apparently not considered previously.[4]



1 **2**

a) Ar = C_6H_5 b) Ar = 2-$H_3COC_6H_4$ c) Ar = 2-ClC_6H_4 d) Ar = 2-$H_3CC_6H_4$
e) Ar = 4-$H_3COC_6H_4$ f) Ar = 4-$H_3CC_6H_4$ g) Ar = 2,5-$(H_3C)_2C_6H_3$

The literature has been confusing for the synthesis of **1a** and **2a**. For example, it was reported that only **1a** formed if the reaction was performed at -10° while **2a** was generated if the reaction proceeded at room temperature.[7] Others[4] had indicated **1a** was favored at -10° but **2a** could be isolated in low yield. All of these results differ from previous work[8] which had suggested that **2a** was the major product at -10°. In our hands, a reaction of purified aldehyde with very pure 1,3-acetonedicarboxylic acid at -10° to -15° gave **1a** consistently in good yields

with a small amount of **2a** as a contaminant. Isomer **1a** could be obtained free of **2a** by recrystallization from hot ethanol. If the original reaction was run at room temperature, both **1a** and **2a** were formed, a situation found in other examples investigated. The procedure reported herein gave the most consistent results when care was taken to use very pure aldehyde and *freshly* purified 1,3-acetonedicarboxylic acid (from EtOAc-slow crystal formation) with a melting range of not less than 135-136°.[9] Although no mechanism has been reported for the formation of both the *cis*- and *trans*-2,6-diaryltetrahydropyran-4-ones (**1** and **2**), it was anticipated that both isomers could be formed from an aromatic aldehyde under essentially the same conditions, a result confirmed by ^{1}H NMR analyses of reaction mixtures. However, it has not been possible to isolate pure *trans* isomers **2d-g**. It is conceivable that allylic-type enols expected to form during this ring closure might experience steric difficulties in the final step which could govern the nature of the major isomer formed. Information concerning the stereochemistry of ketones **1a-g** and **2a-c** can be gleaned from the ^{1}H NMR spectral data (see Table 1). The signals for axial H(2) and H(6) in the cis ketones **1a-g** occur either as a doublet of doublets (dd) or as a dd merged into a triplet (t) at $\delta \equiv 5$. The corresponding signals for H(2,6) in the *trans* isomers **2a-c** are significantly downfield and in the range of δ 5.1-5.6 Comparison of the signals for H(2,6) in the *cis* ketones **1a-c** with the corresponding signals for H(2,6) in *trans* ketones **2a-c** reveals a downfield shift of 0.3 ppm (see Table 1) for the latter ketones which are presumably mobile with average signals for H(2,6) due to a ring reversal process (chair-chair interconversion). The ^{13}C NMR spectral data are recorded in Table 2. The presence of the axial aryl groups in the *trans* isomers causes upfield shifts [1,3-axial or γ-shielding][10] of 5.42, 4.51, and 5.14 ppm for C(2,6) in the *cis* isomers **1a**, **1b** and **1c**. There is also a small shielding effect (3.27, 2.61 and 2.16 ppm) for C(3,5) when an axial aryl group is present at C(2) [or C(6)]. The presence of an ortho substituent on the aromatic ring (**1b**,**c**,**d** and **g**) resulted in additional shielding of C(2,6). This enhanced shielding is presumably caused by long range electronic interactions induced by and arising from the orientation of the aromatic rings. This agrees with the findings of Hasan and co-workers for 2,6-diarylpiperidin-4-ones[3] and supported by an evaluation of space-filling models

TABLE 1. ^{1}H NMR Data For Tetrahydropyran-4-ones

Compound	Chemical Shift[a] H (2,6)	H (3,5)	Other
1a	4.86 (dd, 2 H, J = 9.9, 4.2 Hz)	2.68-2.77 (m, 4 H)	7.3-7.5 (m, 10 H, Ar-H)
1b	5.22 (dd, 2 H, J = 11.6, 1.9 Hz)	2.48 [dd, 2 H, H_a(3,5), J = 14.5, 11.6 Hz] 2.85 [dd, 2 H, H_e(3,5), J = 14.7, 1.9 Hz]	3.82 [s, 6 H, H(OC<u>H</u>$_3$)] 6.91 [d, 2 H, H(6')] 7.09 [t, 2 H, H(4')] 7.32 [t, 2 H, H(5')] 7.77 [d, 2 H, H(3')]
1c	5.27 (dd, 2 H, J = 11.4, 2.1 Hz)	2.51 [dd, 2 H, H_a(3,5), J = 14.9, 11.4 Hz] 2.94 [dd, 2 H, H_e(3,5), J = 14.7, 1.5 Hz]	7.34 [d, 2 H, H(6')] 7.40-7.60 [m, 4 H, H(4',5')] 7.84 [d, 2 H, H(3')]
1d	5.03 (t, 2 H, J = 8 Hz)	2.70 (d, 4 H, J = 8 Hz)	2.36 [s, 6 H, H(C<u>H</u>$_3$)] 7.15-7.65 (m, 8 H, Ar-<u>H</u>)
1e	4.77 (dd merged into t, 2 H)	2.67-2.70 (m, 4 H)	3.81 [s, 6 H, H(OC<u>H</u>$_3$)] 6.90 [d, 4 H, H(3',5')] 7.36 [d, 4 H, H(4',6')
1f	4.78 (dd merged into t, 2 H)	2.66-2.70 (m, 4 H)	2.36 [s, 6 H, H(C<u>H</u>$_3$)] 7.18 (d, 4 H, Ar-<u>H</u>) 7.32 (d, 4 H, Ar-<u>H</u>)
1g	4.99 (dd, 2 H, J = 9, 5 Hz)	2.66-2.72 (m, 4 H)	2.33 [s, 6 H, H(C<u>H</u>$_3$)] 2.38 [s, 6 H, H(C<u>H</u>$_3$)] 7.08 (bs, 4 H, Ar-<u>H</u>) 7.45 (bs, 2 H, Ar-<u>H</u>)
2a	5.16 (dd merged into t, 2 H)	2.85 [dd, 2 H_a(3,5), J = 15.0, 5.1 Hz] 2.95 [dd, 2 H, H_e(3,5), J = 14.9, 6.5 Hz]	7.3-7.4 (m, 10 H, Ar-<u>H</u>)
2b	5.52 (dd, 2 H, J = 7.4, 4.9 Hz)	2.71 [dd, 2 H, H_a(3,5), J = 16.1, 7.9 Hz] 2.94 [dd, 2 H, H_e(3,5), J = 16.1, 4.9 Hz]	3.76 [s, 6 H, H(OC<u>H</u>$_3$)] 6.88 [d, 2 H, H(6')] 6.99 [t, 2 H, H(4')] 7.29 [t, 2 H, H(5')] 7.48 [d, 2 H, H(3')]
2c	5.56 (dd, 2 H, J = 8.2, 4.7 Hz)	2.77 [dd, 2 H, H_a(3,5), J = 16.1, 8.2 Hz] 3.01 [dd, 2 H, H_e(3,5), J = 15.8, 4.7 Hz]	7.24-7.37 [m, 6 H, H(4',5',6')] 7.55 [dd, 2 H, H(3')]

[a]NMR values are in δ units downfield from TMS.

of **1**. It is noteworthy that the ^{13}C signals for C(4) in **1a** and **2a** are very similar to that (206.2 ppm) of tetrahydropyran-4-one.[11]

The R-value method proposed by Lambert has been used to assess conformations via an

estimate of the dihedral angle in certain heterocyclics.[12] The *trans* ketones **2a-c** are three such molecules. Each contains a CH_2CHR moiety with two rapidly equilibrating, equivalent conformers. The ^3J, R and calculated ϕ values are listed in Table 3.

TABLE 2. ^{13}C NMR Chemical Shift Data For Tetrahydropyran-4-ones

	Chemical Shifts[a]			
Compound	C (2,6)	C (3,5)	C (4)	Other
1a	78.95	49.71	206.08	Ar-C: 140.70, 128.63, 128.08, 125.63
1b	73.45	48.41	207.03	OCH_3, 55.18; Ar-C: 155.15, 129.70, 128.39, 125.80, 120.72, 110.10
1c	75.67	47.65	204.85	Ar-C: 138.38, 131.27, 129.54, 129.06,127.40, 126.86
1d	76.37	48.53	206.46	CH_3, 19.05; Ar-C: 138.84, 134.22, 130.49, 127.86, 126.54, 125.41
1e	78.66	49.64	206.45	OCH_3, 55.28; Ar-C, 159.37, 132.95, 127.06, 113.95
1f	78.88	49.73	206.45	CH_3, 21.15; Ar-C, 137.87, 137.80, 129.25, 125.66
1g	76.48	48.51	206.73	2-CH_3, 18.62; 5-CH_3, 21.19; Ar-C: 138.46, 135.96, 131.24, 130.45, 128.59, 126.07
2a	73.53	46.44	206.47	Ar-C: 139.79, 128.62, 128.06, 126.69
2b	68.94	45.80	208.54	OCH_3, 55.19; Ar-C: 156.53, 129.24, 128.95, 127.56, 120.62, 110.63
2c	70.53	45.49	206.84	Ar-C: 137.56, 132.92, 129.91, 129.37, 128.78, 127.06

[a]Chemical shift values are in ppm downfield from TMS.

The calculated dihedral angles for **2a** (49°), **2b** (53.4°) and **2c** (54.7°) support the hypothesis that these compounds exist in flattened chair forms in solution. Although the R-value method cannot be used with the *cis* ketones **1a-g**,[12] the Karplus relationship can be used to *estimate* the angle between two vicinal protons (Table 4). Thus the Karplus equation[13] and the modified equations of Gandour[14] and Altona[15] were included in Table 4 to predict the torsional angles between protons [H(2)-C(2)-C(3)-H(3) or H(6)-C(6)-C(5)-H(5)] in **1a-c,g**. The Huggins,[16] Cavanaugh,[17] and Allred-Rochow[18] electronegativity scales were used in the Altona equation. It is clear that the latter gave the most consistent results when the Cavanaugh electronegativity scale was used and compared with the Karplus and Gandour equations. This

TABLE 3. Dihedral Angles (°) Calculated From ^3J Values For *trans* Ketones **2a-c**

Compound	J_{trans}	J_{cis}	R	Φ[a]
2a	6.5	5.2	1.25	49
2b	7.9	4.9	1.61	53
2c	8.2	4.7	1.74	54

[a]Dihedral angle of O(1)-C(2)-C(3)-C(4) or O(1)-C(6)-C(5)-C(4).

supports our supposition that the rings are slightly flattened with little internal angular deformation and C=O groups still exposed and vulnerable to attack by large nucleophiles.

TABLE 4. Torsional Angles[a] (°) Calculated From ^3J (Hz) Values

				Altona[b]		
Compound	^3J	Karplus[13]	Gandour[14]	Huggins	Cavanaugh	Allred-Rockow
1a	4.2	48	49	43	48	46
1b	1.9	70	74	60	68	63
1c	2.1	69	71	58	66	61
1g	3.6	53	54	47	52	50

[a]The angle between $H_a(2)$-$H_e(3)$ and $H_a(6)$-$H_e(5)$.
[b]Three separate electronegativity scales were used with the equation proposed by Altona.[15]

EXPERIMENTAL SECTION

The ^1H and ^{13}C NMR spectral data were obtained on a Varian XL-300 NMR spectrometer operating at 299.944 MHz for ^1H NMR and at 75.429 MHz for ^{13}C NMR. All NMR data were recorded in δ or ppm values downfield from TMS with $DCCl_3$ as the solvent. IR spectral data were obtained as KBr pellets on a Perkin-Elmer 681 IR spectrophotometer. Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and were uncorrected. Chromatography was accomplished using a Chromatotron Model 7924T (Harrison Research Inc., 840 Moana Court, Palo Alto, California 94306) as described in the Instruction Manual with silica gel as the adsorbent. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. The procedure and yields of **1a** and **2a** reported below are markedly altered and improved from that recorded.[4]

cis-2,6-Diphenyltetrahydropyran-4-one (**1a**).-A mixture of 1.461 g (10.0 mmol) of 1,3-acetonedicarboxylic acid and 4.245 g (40.0 mmol) of benzaldehyde was placed in a 2-necked, round-bottomed flask (25 mL) equipped with an HCl(g) inlet. This reaction mixture was then cooled with an ice/NaCl bath to -15°. After a thorough mixing of the ingredients (10 min), $HCl_{(g)}$ was bubbled (~2 bubbles/sec) into the slurry. The resulting orange slurry was extracted with H_2O (20 mL) and made basic (Na_2CO_3, satd solution) to pH 9-10. This mixture was extracted with ethyl ether (3 x 25 mL), and the ethereal extract was discarded. The resulting aqueous layer, upon standing for 48 hours, deposited a white, granular solid. The solid was

collected and dried over P_2O_5 under vacuum (24 hrs RT, 0.01 mm Hg), to give 1.69 g (67%), of an isomeric mixture (*cis*:*trans* estimated at 9:1) of ketones, mp. 68-70°. Recrystallization (hot ethanol) gave a pure sample (1.42 g, 56%) of ketone **1a**, mp. 69-70° (lit.[4] mp. 69-70°); IR 1720 cm^{-1} (C=O).

trans-2,6-Diphenyltetrahydropyran-4-one (**2a**)-The same procedure used for **1a**, but at *room temperature*, gave 0.863 g (34.2%) of an isomeric mixture of ketones (*cis*:*trans* isomers estimated at 4:1).from 1.461 g (10.0 mmol) of 1,3-acetonedicarboxylic acid and 4.245 g (40.0 mmol) of benzaldehyde after workup and washing with water (2 x 25 mL) and drying over P_2O_5 under vacuum (24 h, RT, 0.01 mm Hg). Recrystallization (hot ethanol) gave a pure sample of ketone **2a**, mp. 131-133° (lit[4] mp. 131°); IR 1715 cm^{-1} (C=O).

2,6-bis(2-Methoxyphenyl)tetrahydropyran-4-ones (**1b** & **2b**).-Following the procedure for **1a** at room temperature gave 2.94 g (63%) of an isomeric mixture ketones (estimated ratio of *cis*:*trans* was 3:2) from 2.192 g (15.0 mmol) of 1,3-acetonedicarboxylic acid, 5.5 mL (6.2 g, 45 mmol) of 2-anisaldehyde and 10 mL of dry THF. A resulting white precipitate was filtered, washed with water (50 mL) and dried over P_2O_5 under vacuum (24 h, RT, 0.01 mm Hg). A 1.00 g sample of the isomeric mixture was separated on a silica gel plate (4 mm) using a Chromatotron. The separation was accomplished by using a gradient elution series with hexanes as the nonpolar solvent and a mixture of ethyl acetate and chloroform (1:1) as the polar solvent system. The first band (0.60 g) was found to be *cis*-2,6-bis(2-methoxyphenyl)tetrahydropyran-4-one (**1b**). Recrystallization (hot hexanes) gave a pure sample (0.59 g, 59%) of ketone **1b**, mp. 170.0-171.0°; IR 1710 cm^{-1} (C=O).

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.69; H, 6.37

The second band eluted was recrystallized (hot ethanol) to yield 0.21 g (21%) of *trans*-2,6-bis(2-methoxyphenyl)tetrahydropyran-4-one (**2b**), mp. 168.0-169.0°; IR 1715 cm^{-1} (C=O)

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.89; H, 6.52

2,6-bis(2-Chlorophenyl)tetrahydropyran-4-ones (**1c** & **2c**).-Following the procedure for **1a** at room temperature gave 0.321 g (27%) of a mixture of isomeric ketones (estimated ratio of *cis*:*trans* isomers was 4:1), using 0.548 g (3.75 mmol) of 1,3-acetonedicarboxylic acid and

1.406 g (10.0 mmol) of 2-chlorobenzaldehyde. The resulting white precipitate was filtered, washed with water (50 mL) and dried under vacuum (24 h, RT, 0.01 mm Hg) over P_2O_5 to yield 0.321 g (27%) of a mixture of ketones (*cis*:*trans* = 2:1). The mixture was dissolved in acetone (10 mL) and allowed to stand (about 24 hrs) until crystals formed. Two types of crystals were evident, namely square blocks and oval-shaped crystals, which were mechanically separated. The square blocks were found to be *cis*-2,6-bis(2-chlorophenyl)tetrahydropyran-4-one (**1c**), mp. 146-147°; IR 1715 cm^{-1} (C=O).

Anal. Calcd. for $C_{17}H_{14}O_2Cl_2$: C, 63.57; H, 4.39; Cl, 22.08
Found: C, 63.79; H, 4.37; Cl, 22.18

The oval crystals were gathered, analyzed, and determined to be only *trans*-2,6-bis(2-chlorophenyl)tetrahydropyran-4-one (**2c**), mp 101.5-102.5°; IR 1720 cm^{-1} (C=O).

Anal. Calcd. for $C_{17}H_{14}O_2Cl_2$: C, 63.57; H, 4.39; Cl, 22.08
Found: C, 63.51; H, 4.40; Cl, 22.51

cis-2,6-bis(2-Methylphenyl)tetrahydropyran-4-one (**1d**).-Following the procedure for **1a** in an ice/NaCl bath (-10°) gave 0.582 g (14%) of an isomeric mixture (only a trace of the *trans* isomer present) of ketones (melting range 96.5-98.5°) from 5.0 mL (5.2 g, 43 mmol) of 2-tolualdehyde and 2.192 g (15 mmol) of 1,3-acetonedicarboxylic acid. Recrystallization (hot hexanes) gave fine needles which were filtered cold and dried (vacuum, 24 hrs) over fresh wax chips to yield pure *cis*-2,6-bis(2-methylphenyl)tetrahydropyran-4-one (**1d**), mp. 99.0-100.0°; IR 1715 cm^{-1} (C=O).

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.62; H, 7.42

cis-2,6-bis(4-Methoxyphenyl)tetrahydropyran-4-one (**1e**).-Following the procedure for **1a** at room temperature gave 0.158 g (13.5%) of ketone **1e** (mp 126.0-127.0°; evacuated sealed tube) from 2.3 g (17 mmol) of 4-anisaldehyde and 0.548 g (3.75 mmol) of 1,3-acetonedicarboxylic acid (only a trace of the *trans* isomer was detected); IR 1720 cm^{-1} (C=O).

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.10; H, 6.62

cis-2,6-bis(4-Methylphenyl)tetrahydropyran-4-one (**1f**).-Following the procedure for **1a** at room temperature gave 2.663 g (48%) of ketone **1f** as a white/cream colored precipitate (estimate of *cis*:*trans* was 4:1) from 2.92 g (20.0 mmol) 1,3-acetonedicarboxylic acid and 5.0

mL (5.1 g, 43 mmol) of 4-tolualdehyde. Recrystallizations (hot hexanes) afforded a pure sample of **1f**, mp 92.0-92.5°; IR 1765 cm^{-1} (C=O).

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.38; H, 7.34

cis-2,6-bis(2,5-Dimethylphenyl)tetrahydropyran-4-one (**1g**).-Following the procedure for **1a** at room temperature gave 0.723 g, (7.8%) of *cis*-2,6-bis(2,5-dimethylphenyl)tetrahydropyran-4-one (**1g**) from 4.384 g (30.0 mmol) of 1,3-acetonedicarboxylic acid and 13.0 mL (12.4 g, 92 mmol) of 2,5-dimethylbenzaldehyde. The white precipitate (no *trans* isomer was detected by NMR analysis) which formed was filtered out and crystallized (hot hexanes) to yield 0.427 g (4.6%) of pure **1g**, mp. 107.0-108.0°; IR 1715 cm^{-1} (C=O).

Anal. Calcd. for $C_{21}H_{24}O_2$: C, 81.79; H, 7.84. Found: C, 81.81; H, 8.08

Attempted Isolation of *trans*-**2d-2f**.-Although the reaction mixtures could be concentrated, after removal of the majority of the *cis* isomer, all efforts to obtain pure *trans*-**2d-2f** proved unfruitful. Recrystallization attempts from many solvents (C_2H_5OH, H_3COH, hexanes, hexanes:CH_2Cl_2) failed. Column chromatography or use of the Chromatotron with various combinations and ratios of solvents (hexanes:ether; hexanes:$HCCl_3$; hexanes:C_2H_5OH; hexanes:EtOAc; hexane:ether:EtOAc; hexanes:$HCCl_3$:EtOAc) using silica gel and alumina did not effect a separation of the *trans* isomer from traces of the *cis* ketone, in the above examples.

Acknowledgment.-We gratefully acknowledge the support of the College of Arts and Sciences in the form of salary. We thank the National Science Foundation (CHE81-06157) for partial funding to purchase the XL-300 NMR spectrometer.

REFERENCES

1. A. J. Fuhrhop and G. Penzlin, *Organic Synthesis*, Verlag Chemie, Weinheim, 1983; *Organic Synthesis Today and Tomorrow*; B. M. Trost and C. R. Hutchinson, Eds.; Pergamon: Oxford, 1981. Several cycloalkanones are used in synthesis of polycyclic systems.

2. K. Ramalingam, K. D. Berlin, N. Satyamurthy and R. Sivakumar, *J. Org. Chem.*, **44**, 471 (1979); S. Sivasubramanian, M. Sundharavadivelu and N. Arumugam, *Ind. J. Chem.*, **20B**, 878 (1981).

3. M. U. Hasan, M. Arab, K. P. Rajan, R. Sekar and D. Marko, *Magn. Reson. Chem.*, **23**, 292 (1985).

4. C. A. R. Baxter and D. A. Whiting, *J. Chem. Soc.* (C), 1174 (1968).

5. P. Nanjappan, K. Ramalingam, M. D. Herd, P. Arjunan and K. D. Berlin, *J. Org. Chem.*, **45**, 4622 (1980); W. Ziriakus, W. Hansel and R. Haller, *Arch. Pharm. (Weinheim)*, **304**, 681(1971); P. Nanjappan, K. Ramalingam and V. Baliah, *Ind. J. Chem.*, **22B**, 403 (1983).

6. J. B. Rampal, N. Satyamurthy, J. M. Bowen, N. Purdie and K. D. Berlin, *J. Am. Chem. Soc.*, **103**, 7602 (1981); J. B. Rampal, G. D. Macdonell, J. P. Edasery, K. D. Berlin, A. Rahman, D. van der Helm and K. M. Pietrusiewicz, *J. Org. Chem.*, **46**, 1156 (1981).

7. V. Baliah and G. Mangalam, *Ind. J. Chem*, **16B**, 213 (1978).

8. F. Arndt, P. Nachtwey and J. Pusch, *Ber.*, **58B**, 1633 (1925); R. Cornubert, R. Delmas, S. Monteil and J. Viriot, *Bull. Soc. Chem. Fr.*, 40 (1950); R. Cornubert and P. Robinet, *Bull. Soc. Chem. Fr.*, 90 (1934); P. Petrenko-Kritschenko and D. Plotnikoff, *Ber.* **30**, 2801 (1897).

9 Our evaluation of the situation is that is that 1,3-acetonedicarboxylic acid is very unstable and produces by-products which likely affect the yields of **1** and **2**. It was noted that this acid decomposed rapidly even when stored cold and in the dark for one day.

10. E. L. Eliel and K. M. Pietrusiewicz in *Topics in Carbon-13 Spectroscopy*; G. C. Levy, Ed.; Wiley-Interscience: New York, 1979; Vol 3, Chapter 3.

11. J. A. Hirsch and E. Havinga, *J. Org. Chem.*, **41**, 455 (1976).

12. J. B. Lambert, *Acc. Chem. Res.*, **4**, 87 (1971); J. B. Lambert, *J. Am. Chem. Soc.*, **89**, 1836 (1967); J. B. Lambert and R. G. Keske, *Tetrahedron Lett.*, 4755 (1967).

13. M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); M. Karplus, *J. Am. Chem. Soc.*, 85, 2870 (1963).

14. W. J. Colucci, S. J. Jungk and R. D. Gandour, *Mag. Reson. Chem.*, **23**, 335 (1985).

15. C. A. G. Haasnoot, F. A. A. M. deLeeuw and C. Altona, *Tetrahedron*, **36**, 2783 (1980); C. A. G. Haasnoot, F. A. A. M. deLeeuw, H. P. M. deLeeuw and C. Altona, *Org. Magn. Reson.*, **15**, 43 (1981).

16. M. L. Huggins, *J. Am. Chem. Soc.*, *75*, 4123 (1953).

17. J. R. Cavanaugh and B. P. Daily, *J. Chem. Phys.*, **34**, 1099 (1961).

18 A. L. Allred, *J. Inorg. Nucl. Chem.*, **17**, 215 (1961).

(Received September 12, 1988; in revised form April 3, 1989)