superacid[24,25] to promote nucleophilic attack of ethanol on the carbonyl group of the urea to form a tetrahedral intermediate. After a prototropic shift, ammonia is ejected to form the Ni(II) complex of the product. An analogous nucleophilic attack by a water molecule would account for the formation of **3**, since the initially produced carbamate ion would decarboxylate in the acidic assay system.[18]

The activation parameters found here for k'_{EtOH} may be compared with those for k_{cat} of the urease-catalyzed hydrolysis of urea ($\Delta H^{\ddagger} = 6.07 \pm 0.27$ kcal mol^{-1}, $\Delta S^{\ddagger} = -21.8$ cal mol^{-1} K^{-1}).[7] The rate constants k'_{EtOH} and k_{cat} both refer to reactions of a urea which is O-coordinated to a nickel ion. A markedly lower $\Delta H^{\ddagger}$ in the enzymatic system overcomes the less favorable enzymatic $\Delta S^{\ddagger}$ to produce the $\sim 10^{10}$-fold factor by which k_{cat} exceeds k'_{EtOH} at 38 °C. We are continuing to investigate the mechanism of both systems.

Acknowledgment. We thank the Australian Research Grants Committee and the University of Queensland for financial support.

Registry No. 1, 36226-31-0; **2**, 80145-75-1; **3**, 3731-51-9; Ni, 7440-02-0.

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Differentiation between Reaction Pathways in the Photoaddition of Guest *p*-Fluoroacetophenone to Host Deoxycholic Acid via X-ray Analysis of a Complex Undergoing a Single-Crystal-to-Single-Crystal Transformation[1]

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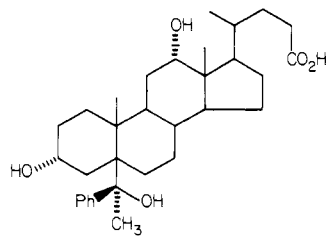
Received August 25, 1981

In a previous communication,[2] we demonstrated that crystalline channel inclusion complexes of DCA may serve as appropriate matrices for elucidation of reaction pathways. Irradiation of the complex DCA-acetophenone yielded a single diastereomeric photoaddition product (**1**) with an absolute configuration *S* at the newly generated chiral carbon, opposite to the configuration ex-



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pected from the host-guest packing at the reaction site.[3] By virtue

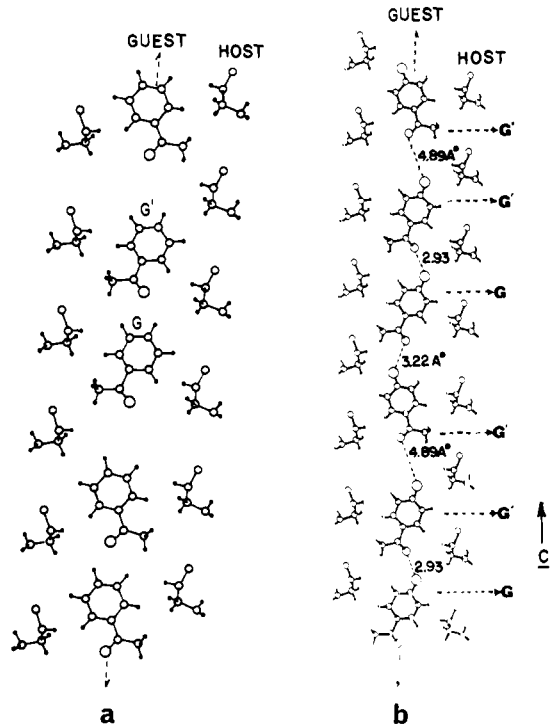

Figure 1. (a) Packing arrangement of acetophenone G and G′ molecules in the channel as viewed perpendicular to the plane of the guest molecule. The two independent guest molecules G and G′ of a close-packed pair are related by pseudotranslation of $C + \Delta C$, where $\Delta C = 0.8$ Å. The sides of the guest molecules are bracketed by the steroid channel wall comprising the side-chain atoms [HO_2C]-CH_2-CH_2-CH-C(methyl). (b) *p*-Fluoroacetophenone packing motif in the channel as viewed perpendicular to the plane of the guest molecule. The guest molecules form chains comprising close-packed triplets G′GG′. . .G′GG′. . .G′, etc., yielding a superstructure with a translation repeat of 4C. The molecules G and G′ expose opposite faces of their acetyl groups to C_5-H_5 of the steroid. G and G′ are related by a pseudotranslation of $C + \Delta C$ where $\Delta C = 1.64$ Å.

of the fact that DCA-acetophenone maintained its crystalline integrity[4] on photoconversion, the photoaddition reaction pathway was monitored by determination of the crystal structures before and after reaction. That study showed that on photoexcitation the acetyl group of acetophenone underwent a net rotation of 180° prior to bond formation to the steroid. This unusual molecular reaction pathway made it imperative to design a crystalline DCA-substituted acetophenone complex whose host-guest packing would yield a product analogous to **1** but with absolute configuration *R* at the newly generated chiral carbon. In order to obtain this product it is necessary to modify the observed guest packing (Figure 1a) in the channel so that the acetophenone molecule G would occupy a new position approximately 1.5-2 Å removed along the $-c$ direction.[5] It appeared that such a change might possibly be achieved by para substitution of the guest phenyl ring or by extension of the alkyl side chain of the ketone. We chose *p*-fluoroacetophenone as an appropriate guest. The structure of DCA-*p*-fluoroacetophenone was determined via low-temperature (-170 °C) X-ray diffraction.[6] Two independent guest molecules G and G′ were located in the channel. The molar guest-host ratios

(1) This paper should be considered as "Reactions in Molecular Inclusion Complexes". 5. For part 4, see: Popovitz-Biro, R.; Tang, C. P.; Chang, H. C.; Shochet, N. R.; Lahav M.; Leiserowitz L. *Nouv. J. Chim.*, in press.

(2) Chang, H. C.; Tang, C. P.; Popovitz-Biro, R.; Lahav, M.; Leiserowitz, L. *Nouv. J. Chim.* **1981**, *5*, 475 and references cited therein.

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(4) Nakanishi, N.; Jones, W.; Thomas, J. M.; Burshouse, H. B.; Maltevalli, M. *J. Chem. Soc., Chem. Commun.* **1980**, 611. Ohashi, Y.; Yanagi, K.; Kurihara, T.; Sasada, Y.; Ohgo, Y. *J. Am. Chem. Soc.* **1981**, *103*, 5805.

(5) This point will be elucidated in a full paper (Chang, H. C.; Tang, C. P.; Popovitz-Biro, R.; Lahav, M.; Leiserowitz, L., to be submitted for publication).

(6) The cell constants at -170 °C are $a = 25.270$ (7) Å, $b = 13.579$ (8) Å, $c = 7.198$ (3) Å, space group $P2_12_12_1$. The diffraction data were measured on a CAD-4 diffractometer using Mo Kα radiation filtered with a graphite monochromator; 10280 reflections were measured to a maximum value of $\sin\theta/\lambda = 0.91$ to yield 4916 independent "observed" reflections.

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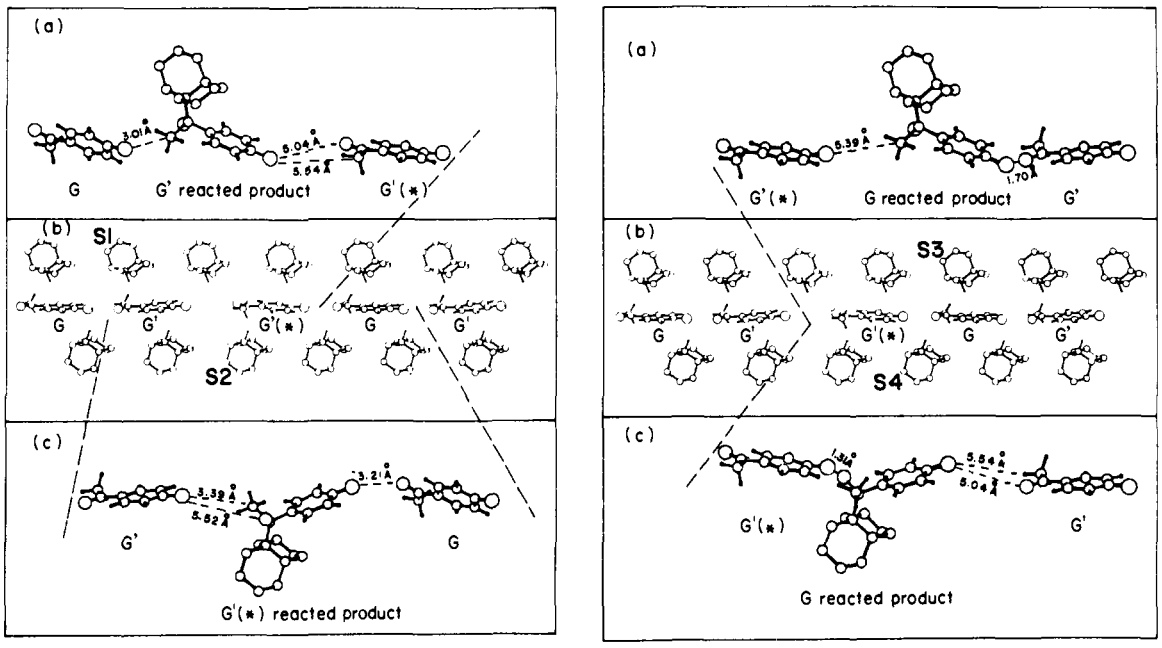


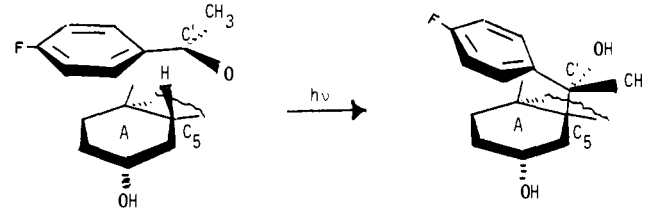
Figure 2. Left: (a) Contacts between reacted G′ molecule and its neighboring G and G′(*) molecules. (b) Unreacted host–guest structure. (c) Contacts between reacted G′(*) molecule and its neighboring G′ and G molecules. The host molecules participating in the reaction are labeled S1, S2. Right: (a) Contacts between addition product of G to the steroid above S3 (were it to react) and its neighboring G′(*) and G′. (b) Unreacted host–guest structure. (c) Contacts between addition product of G to the steroid below S4 (were it to react) and its neighboring G′(*) and G molecules.

of G′ and G were, at first, refined freely by least squares to values 0.258 (5) and 0.113 (6), respectively, yielding a total value of 0.37 (1). This is very close to a total molar guest–host ratio of 3:8 = 0.375, comprising an occupancy of 2:8 = 0.25 for G′ and 1:8 = 0.125 for G, to yield the close-packed guest structure shown in Figure 1b. Any other reasonable arrangement, given the crystallographic locations of G and G′ and a G′/G ratio near 2:1, would yield a total occupancy less than 0.375 and thus a less dense structure.[7] Hence the occupancies of G′ and G were fixed at 0.25 and 0.125, respectively, during the later refinement. The oxygen and methyl carbon atoms of the guest acetyl group were clearly distinguishable via structure-factor least-squares calculations. A final R value of 0.06 was obtained for 4916 reflections by employing 426 parameters.

The guest molecules (Figure 1b) form close-packed triplets G′GG′. . .G′G G′ along the channel. Molecules G′ and G expose opposite faces of their acetyl groups to the potentially reactive C5–H5 bond of the steroid. Therefore purely on the basis of host–guest packing, photoirradiation should yield two diastereomeric products, one from G′ and the other from G.

However, UV irradiation of the DCA–*p*-fluoroacetophenone complex resulted in the formation of a single diastereomeric product PFDCA (Scheme I) as characterized by ^{13}C NMR spectroscopy[8] and X-ray structure analysis.[9,10] The absolute

Scheme I



configuration S at the new chiral center is the same as that of the acetophenone addition product **1**.[2] In order to explain the stereospecificity of this photoreaction the crystal structure of the complex after 30 days of UV irradiation was determined via low-temperature X-ray diffraction.[11] The occupancy factors of the unreacted and reacted steroids, DCA and PFDCA, respectively, were refined by least squares to values of 0.87 (1) and 0.13 (1) under the constraint that their sum be unity. The occupancies of G′ and G were refined freely to values of 0.118 (5) and 0.107 (4), respectively. We conclude that the guest molecule G′ reacted but not G, its occupancy factor remaining unchanged. The occupancy of G′ was reduced by 0.13 (i.e., from 0.25 to 0.12), which fits perfectly the refined occupancy of 0.13 of the reacted steroid. The photoaddition yield for total guest population was 35%, i.e., 0.13/0.375. The final R factor was 0.099 for 2327 reflections, employing 233 parameters. The observation that G remains unaffected may be understood on steric grounds according to

(7) (a) For details of the structure refinement of DCA–*p*-fluoroacetophenone, see: H. C. Chang Ph.D. thesis, Feinberg Graduate School, Rehovot, Israel, 1981. (b) The translation repeat of the guest molecular chain structure G′GG′. . 4*c*, . .G′ is 4*c*, i.e., 28.2 Å. There is lack of order between the different guest chains in the crystal. Moreover, the X-ray diffraction photographs show no evidence of one-dimensional order along the *c* direction which would be a manifestation of the superstructure (see Figure 1b). We therefore assume occasional faults in the repeating pattern within each chain. All such faults would reduce the overall guest occupancy from a maximum of 0.375.

(8) Samples of 1-g powdered complex were irradiated for 1 week in Pyrex dishes ($\lambda > 290$ nm). The product was separated by chromatography on silica gel 1:100 and eluted with CH_2Cl_2/MeOH/AcOH in ratio of 94.5:5.0:0.5 and by preparative TLC using CH_2Cl_2/MeOH/AcOH in ratio of 90.5:9.0:0.5 using phosphormolybdic acid as coloring spray. The product has $R_f = 0.65$ (for DCA, $R_f = 0.6$) mp = 215–220 °C. ^1H NMR δ 0.71 (3 H, s, 18-H), 0.98 (3 H, d, 21-H), 1.24 (3 H, s, 19-H), 1.72 (3 H, s, CH_3–C(OH)–Ar); ^{13}C NMR δ (Me_4S_i, CD_3COOD) 32.4 (C_1), 30.9 (C_2), 69.4 (C_3), 38.0 (C_4), 49.15 (C_5), 29.7 (C_6), 28.5 (C_7), 37.5 (C_8), 36.4 (C_9), 41.7 (C_{10}), 30.6 (C_{11}), 75.2 (C_{12}), 46.7 (C_{13}), 49.1 (C_{14}), 24.7 (C_{15}), 28.4 (C_{16}), 47.8 (C_{17}), 13.0 (C_{18}), 20.6 (C_{19}), 36.4 (C_{20}), 17.6 (C_{21}), 31.6 (C_{22} and C_{23}), 85.0 (Ar-C(OH)CH_3); UV (MeOH) 257 nm (ϵ 2800).

(9) The space group constants of PFDCA are a = 12.20 Å, b = 15.19 Å, c = 7.47 Å, β = 94.5°, space group $P2_1$, Z = 2. The crystal structure was solved with 2051 observed reflections yielding an R value of 0.06 for 242 parameters. This crystal structure is essentially isomorphous with that of product **1**.

(10) Frolow, F, to be published.

(11) The structure of the irradiated crystal (containing DCA, guest and product PFDCA) was determined via constrained least squares on X-ray diffraction data measured at −170 °C. The cell constants at −170 °C are a = 25.155 (7) Å, b = 13.679 (6) Å, c = 7.135 (2) Å, space group $P2_12_12_1$. 2327 independent observed reflections were measured to a sin θ/λ value of 1.0. In the least-squares refinement the rigid moieties of the unreacted and reacted steroid molecules (i.e., the four fused rings) as well as the unreacted guest molecules G′ and G were each refined as rigid bodies. For the flexible groups bonded to atom C5 of the reacted steroid [i.e., CH_3–C(OH)C_6H_4F] constraints were imposed on interatomic distances. The occupancy factors of the unreacted and reacted steroids were refined with the sum of their occupancies constrained to unity.

Figure 2; the G molecule, which is sandwiched between the two G′ molecules, would make impossibly short contacts with the neighboring G′ molecules were it to react.

The crystallographic result has provided us with the means of differentiating between possible reaction pathways. Moreover, the stereochemical correlation of the absolute configuration of the product PFDCA with the relative orientation of G′ to the reactive center C5–H5 of the steroid indicates a net rotation of 180° of the photoexcited acetyl group prior to bond formation. This is the same behavior found previously in DCA–acetophenone, supporting once again the previously suggested mechanism of hydrogen abstraction by the Py orbital solely and not by the π^* orbital.[2]

This work suggests that in order to obtain the lacking diastereomer it is necessary to design a looser packing arrangement where G′ is still further separated from G. Such an arrangement appears to be fulfilled by propiophenone, on which work is in progress.

Acknowledgment. We thank the U.S./Israel Binational Science Foundation, Jerusalem, for financial support. We are indebted to Dr. Felix Frolow for assistance in structure determination.

Experimental Analysis of γ-Hydrogen Hyperfine Splittings in Acyclic Aliphatic Radicals. Confirmation of Theoretical Predictions[1]

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Received July 13, 1981

Ellinger et al.[4,5] have reported the results of an ab initio investigation of the methyl (i.e., γ-H) proton hyperfine splittings (hfs's) for the *n*-propyl radical (**1**). It was predicted[4,5] that the γ-H hfs's would be dependent on θ_{Me}, the dihedral angle between the $C_\beta(H_\gamma)_3$ group[6] and the semioccupied Ċ $2p_z$ orbital (see **1a**), *and* θ_γ, the dihedral angle between the $C_\beta H_\gamma$ bond and the $\dot{C}C_\alpha C_\beta$ plane[6] (see **1b**). Values of a^{H_γ} (together with other H and ^{13}C hfs's) were computed for various *n*-propyl conformations. In agreement with experiment,[7-12] the minimum energy geometry for a "freely rotating"[13] CH_3 group was found to have $\theta_{Me} = 90°$ [14] and $a^{H_\gamma}(3H) = -0.21$ G[15] which was compared with a measured

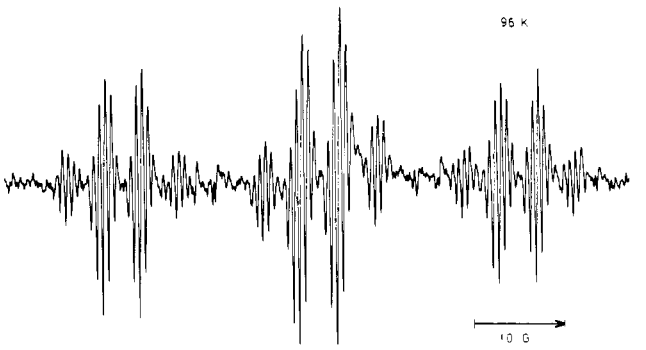


Figure 1. EPR spectrum of neopentyl radical at 96 K in *n*-propane. Several lines from the isopropyl radical can also be observed.

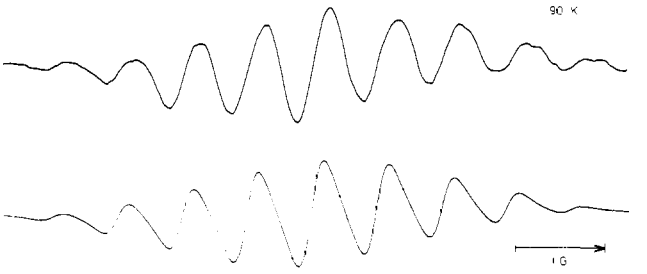
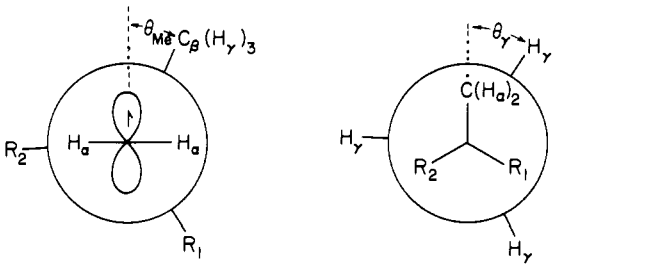


Figure 2. Fine structure of the central line in the low field triplet of isobutyl radical. Top: experiment at 90 K; bottom: simulation with $a(2H) = 1.45$ G, $a(4H) = 0.72$ G.

$|a^{H_\gamma}(3H)| = 0.27$ G at 163 K.[9] There was no experimental data to support their conclusion that a^{H_γ} depended on θ_{Me}. While there was evidence to support a dependence of a^{H_γ} on θ_γ, it was not explicitly employed in support of the calculations. The evidence in question consisted of the EPR observation[7] that the three H_γ of *n*-propyl are equivalent[13] at 128 K, $|a^{H_\gamma}(3H)| = 0.38$ G, but at 93 K the spectrum represents a single orientation of the CH_3 in which coupling to only two of the three protons can be seen, $|a^{H_\gamma}(2H)|$ 0.69 G, the hfs due to the third H_γ bein≤0.1 G. It was pointed out[7] that the H_γ hfs's must be strongly orientation dependent.



1a	$R_1 = R_2 = H$	1b	$R_1 = R_2 = H$
2a	$R_1 = H$, $R_2 = CH_3$	2b	$R_1 = H$, $R_2 = CH_3$
3a	$R_1 = R_2 = CH_3$	3b	$R_1 = R_2 = CH_3$

It occurred to us that Ellinger et al.'s[4,5] ab initio calculations should be subject to qualitative and even quantitative experimental verification since at low temperatures the propyl[7] (**1**), isobutyl (**2**), and neopentyl (**3**) radicals should provide probes of the a^{H_γ} dependence on θ_{Me} and, incidentally, on θ_γ. That is, the conformational preferences of these radicals are $\theta_{Me} = 90°$ for *n*-propyl,[7-12] $\theta_{Me} = 60°$ for isobutyl,[7-12,16] and $\theta_{Me} = 45°$ for neopentyl.[17] For the latter two radicals the barrier to CH_3 rotation

(1) Issued as N.R.C.C. No. 19923.
(2) N.R.C.C.
(3) St. Andrews.
(4) Ellinger, Y.; Rassat, A.; Subra, R.; Berthier, G. *J. Am. Chem. Soc.* **1973**, *95*, 2372–2373.
(5) Ellinger, Y.; Subra, R.; Levy, B.; Millie, P.; Berthier, G. *J. Chem. Phys.* **1975**, *62*, 10–29.
(6) Following Ellinger et al.'s nomenclature[5] the atoms in all radicals considered herein are identified as follows: $H_\alpha\dot{C}C_\alpha H_\beta C_\beta H_\gamma$.
(7) Fessenden, R. W.; Schuler, *J. Chem. Phys.* **1963**, *39*, 2147–2195.
(8) Fessenden, R. W. *J. Chim. Phys. Physicochim. Biol.* **1964**, *61*, 1570–1575.
(9) Krusic, P. J.; Kochi, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 846–860.
(10) Krusic, P. J.; Meakin, P.; Jesson, J. P. *J. Phys. Chem.* **1971**, *75*, 3438–3453.
(11) Fischer, H. in "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. II., Chapter 19.
(12) Kochi, J. K. *Adv. Free Radical Chem.* **1975**, *5*, 189–317.
(13) That is, rapid jumping between the three orientations allowed by the threefold barrier to rotation about the C_α–C_β bond.[7]
(14) The possibility that this is a double minimum potential well, i.e., $\theta_{Me} = (90 + \delta)°$ and $(90 - \delta)°$, rather than a single minimum is discussed.[5]
(15) Following Ellinger et al.[5] only the results obtained with quasi-localized MO's will be discussed. The canonical MO's led to similar conclusions.[5]
(16) That is, the tertiary H is eclipsed by the Ċ $2p_z$ orbital, probably for steric reasons: Ingold, K. U.; Kemball, M.; Walton, J. C., manuscript in preparation.
(17) Rotation about the Ċ–C_α bond is expected to be rapid[13] because two groups of C_{2v} and C_{3v} symmetries attached to the same single bond lead to a very small (≤0.5 kcal/mol[7-10,18,19]) sixfold rotation barrier; θ_{Me} therefore has an average value of 45°.

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