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REACTIVITY DIFFERENCES BETWEEN DIMORPHS IN A CRYSTALLINE PHASE NORRISH TYPE II REACTION

Stephen V. Evans, Nalamasu Omkaram, John R. Scheffer,* and James Trotter*
Department of Chemistry, University of British Columbia, Vancouver, Canada V6T 1Y6

Abstract. The dimorphs of α-adamantyl-p-chloroacetophenone ($P2_1/n$ and C2/c) undergo solid state Norrish type II cyclobutanol formation with different stereoselectivity. Based on the X-ray crystal structure data, it is concluded that conformational factors rather than packing differences control the photoproduct stereochemistry.

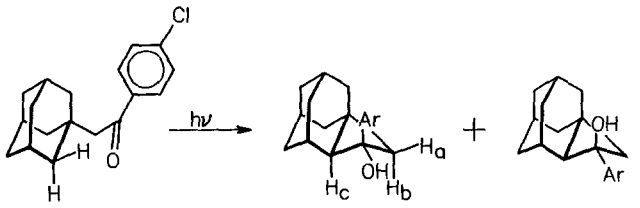
X-ray crystal structure studies of α-adamantyl-p-chloroacetophenone (**1**, Scheme I) have revealed the existence of two polymorphic modifications, crystallization from hexane giving needles, mp 73-74 °C, and from aqueous ethanol, plates, mp 72-73 °C. This observation prompted us to study the solid state photochemical behavior of these materials.

The phenomenon of polymorphism, whereby the molecules that make up an organic crystal pack in different symmetry relationships, suggests that polymorphs should display different bimolecular reactivity in the solid state; an elegant example is found in the variation of the [2+2] photocycloaddition stereochemistry with packing in the trimorphic cinnamic acid system.[1] Similar principles apply in the case of unimolecular processes, but here conformational differences as well as packing differences between polymorphs may be expected to play an important role.[2] In this communication we describe the different unimolecular (Norrish type II) photoreactivity exhibited by the dimorphs of **1**. Based on the crystal and molecular structures of the dimorphs, the reactivity differences are interpreted as being due primarily to conformational rather than packing effects.

Crystals of **1n** (needles) are monoclinic, space group $P2_1/n$, a = 17.352(4), b = 6.5950(8), c = 13.038(3) Å, β = 90.956(13)°, Z = 4. The structure was solved by direct methods, R = 0.039 for 1587 reflections with $I > 3\sigma(I)$ (left stereodiagram, Figure 1). Crystals of **1p** (plates) are monoclinic, space group C2/c, a = 40.603(9), b = 6.5671(8), c = 11.814(3) A, β = 102.053(11)°, Z = 8, R = 0.042 for 1494 reflections with $I > 3\sigma(I)$ (right stereodiagram, Figure 1).

Irradiation (nitrogen laser, 337 nm) of solutions of ketone **1**[3] leads exclusively to the cyclobutanols **2** (cis) and **3** (trans).[4] Cyclobutanol formation is characteristic of the type II photochemistry of α-adamantyl ketones owing to the prohibitive strain energy involved in the formation of the cleavage product, adamantene.[5] The total type II quantum yield for **1** is 0.05 in benzene and 0.25 in acetonitrile containing 2% water. Quenching studies in benzene using 2,5-dimethyl-2,4-hexadiene as the triplet energy quencher give linear Stern-Volmer plots with $k_q\tau = 42.3\ M^{-1}$.

Scheme I.



1 2 3

The photochemistry of ketone **1** was studied as a function of four reaction media: benzene solution, 2% aqueous acetonitrile solution, the needle crystalline modification, and the platelike crystal form. Table I summarizes the **2**:**3** = cis:trans cyclobutanol ratios obtained in each medium. The solid state ratios are the result of extrapolation to 0% conversion; the solution phase conversions were kept below 15%. Lowering the photolysis temperature to -40 °C had no effect on the solid state product ratios, indicating that sample melting with concomitant loss of topochemical control is unimportant.

Table I. Photoproduct Ratios as a Function of Reaction Medium.

Reaction Medium	*cis:trans Cyclobutanol Ratio*
benzene (0.1 M)	27:73
moist acetonitrile (0.1 M)	36:64
dimorph 1n (needles)	26:74 [a]
dimorph 1p (plates)	0:100 [b]

[a]Ratio (% conversion): 26:74 (1.5%); 26:74 (10%).

[b]Ratio (% conversion): 0:100 (0.4%); 0:100 (4.0%); 9:91 (10%).

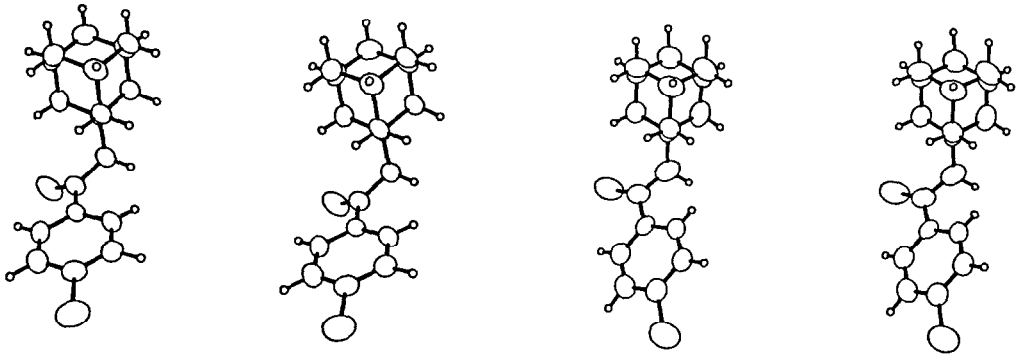
The data in Table I indicate that the photochemical behavior of **1** in the needle crystal modification is identical to its reactivity in the non-polar solvent benzene. The reduced stereoselectivity of cyclobutanol formation observed in the polar solvent medium is typical of most type II systems and has been discussed.[6] What is striking in the present results is the total stereoselectivity of cyclobutanol formation in the case of the platelike crystal form.

The stereodiagrams reveal that **1p** and **1n** have significantly different solid state conformations.[7] While the hydrogen abstraction geometry is chairlike for both, in dimorph **1n** (photoproduct ratio 26% cis, 74% trans), the aromatic ring exposes its face to the adamantyl moiety, resulting in a much closer, more cis-like relationship between the two. Formation of the cis photoproduct is thus relatively favorable in comparison to **1p**, even though the less hindered trans isomer is still the major product. In the case of **1p** (100% trans photoproduct), the aromatic ring has undergone a 40° rotation about the (carbonyl carbon)-to-(aromatic carbon) bond resulting

in an edge-on relationship with the adamantane ring system. This forces the ring away from the adamantyl group leading to an increased bias to trans photoproduct formation.[8] The ortho hydrogen facing inwards is wedged between an adamantyl methylene hydrogen (2.48 Å) and one of the methylene hydrogen atoms adjacent to the carbonyl group (2.21 Å). Rotation of the aromatic ring is thus restricted, and attempted formation of the cis cyclobutanol photoproduct from this conformation would drive the ortho hydrogen into the adamantane moiety, an impossible steric situation.

It is interesting to compare the photochemistry and crystallography of the p-chloro derivative **1** with that of its p-methoxy analogue. α-Adamantyl-p-methoxyacetophenone crystallizes in a conformation intermediate between that of **1n** and **1p**. Its solid state photochemistry, however, is quite different, with cis cyclobutanol actually predominating (cis:trans = 2:1).[5d] This was attributed to a packing arrangement involving strongly overlapping, parallel, face-to-face aromatic rings which sterically impede the rotation necessary for trans cyclobutanol formation. This feature is absent in dimorphs **1n** and **1p**. The prediction can thus be made that dichloro substitution, which is known to lead to face-to-face stacking of aromatic rings,[9] will bring about predominant cis cyclobutanol formation. We are engaged currently in testing this prediction.

Figure 1. Stereodiagrams of the Molecular Conformations of Dimorphs **1n** and **1p**.



Dimorph **1n** (needles)

Dimorph **1p** (plates)

Acknowledgement. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

1. G.M.J. Schmidt, Pure Appl. Chem., 27, 647 (1971).
2. The only previous report of which we are aware that describes different unimolecular photochemistry for polymorphs is that of M.D. Cohen, G.M.J. Schmidt, and S. Flavian, J. Chem. Soc., 2041 (1964). These authors found that certain anils of salicylaldehyde crystallize in dimorphic modifications that exhibit different photochromic and thermochromic behavior.
3. Prepared by Friedel-Crafts acylation of chlorobenzene with α-adamantylacetyl chloride, IR (KBr) 1665 (needles) and 1660 (plates) (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, 2H, J = 8.5 Hz, aromatics), 7.42 (d, 2H, J = 8.5 Hz, aromatics), 2.68 (s, 2H, $-CH_2-C=O$), 1.85 (m, 3H, adamantyl methines), 1.74-1.59 (m, 12H, adamantyl methylenes); mass spectrum m/e (relative intensity) 288 (M^+, 5), 253 (100), 154 (5), 141 (23), 139 (63), 135 (36), 111 (14); Anal. calcd. for $C_{18}H_{21}OCl$: C, 74.86; H, 7.33; O, 5.54. Found: C, 74.85; H, 7.28; O, 5.50.
4. Cis-cyclobutanol **2**: elutes last on silica gel column chromatography and first on gas chromatography (DB-1); mp 101-102 °C; IR (KBr) 3330 (OH) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ7.33 (m, 4H, aromatics), 3.00 (br s, 1H), 2.71 (d, 1H, J = 11 Hz, H_b), 2.90-2.35 (m, 13 H), 2.38 (br s, 1H, H_c), 2.07 (d, 1H, J = 11 Hz, H_a); mass spectrum m/e (relative intensity) 288 (M^+, 3), 270 (66), 253 (100), 235 (87), 227 (31), 193 (19), 179 (25), 139 (83), 91 (36), 79 (30); Anal. calcd. for $C_{18}H_{21}OCl$: C, 74.86; H, 7.33; O, 5.54. Found: C, 74.58; H, 7.31; O, 5.46. Trans-cyclobutanol **3**: elutes first on silica gel column chromatography and last on gas chromatography (DB-1); mp 91-93 °C; IR (KBr) 3550 (OH) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ7.29 (m, 4H, aromatics), 2.89 (br d, 1H, J = 12 Hz, H_c), 2.39-1.98 (m, 5H), 2.23 (d, 1H, J = 11 Hz, H_b), 2.11 (d, 1H, J = 11 Hz, H_a), 1.86-1.65 (m, 9H); mass spectrum m/e (relative intensity) 288 (M^+, 4), 270 (6), 253 (100), 235 (12), 149 (54), 141 (24), 139 (64), 93 (27), 79 (21); Anal. calcd. for $C_{18}H_{21}OCl$: C, 74.86; H, 7.33; O, 5.54. Found: C, 74.86; H, 7.25; O, 5.50. The doublet at δ= 2.9 is characteristic of trans cyclobutanols in this series, and is found not only in **3** (Ar = p-chlorophenyl), but in the phenyl[5c] and p-methoxyphenyl[5d] derivatives as well. The stereochemistry of p-methoxy-**3** was established by X-ray crystallography (S.V. Evans and J. Trotter, unpublished results).
5. (a) R.R. Sauers, M. Gorodetsky, J.A. Whittle, and C.K. Hu, J. Am. Chem. Soc., **93**, 5520 (1971); (b) R.B. Gagosian, J.C. Dalton, and N.J. Turro, J. Am. Chem. Soc., **97**, 5189 (1975); (c) F.D. Lewis, R.W. Johnson, and D.R. Kory, J. Am. Chem. Soc., **96**, 6100 (1974); (d) S. Evans, N. Omkaram, J.R. Scheffer, and J. Trotter, Tetrahedron Lett., **26**, 5903 (1985).
6. P.J. Wagner, Acc. Chem. Res., **4**, 168 (1971).
7. This situation has been termed conformational polymorphism, J. Bernstein and A.T. Hagler, J. Am. Chem. Soc., **100**, 673 (1978).
8. This outward displacement of the aromatic ring of **1p** is accompanied by an inward translation of the carbonyl group that results in a shorter O···H abstraction distance for **1p** (2.53 Å) than for **1n** (2.78 Å).
9. (a) G.M.J. Schmidt, Pure Appl. Chem., **27**, 647 (1971); (b) K. Gnanaguru, N. Ramasubbu, K. Venkatesan and V. Ramamurthy, J. Org. Chem., **50**, 2337 (1985).

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