

The Role of Nonaromatic Isomers in the Photochemistry of 3,5-Dimethoxybenzyl Acetate

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More than 20 years ago, Jaeger reported^{1,2} that photolysis of 3,5-dimethoxybenzyl acetate (DMBA), **1**, in hexane, gave a 17% yield of the isomer **2** along with radical-derived coupling products, the in-cage one, **3** (47%), being the major one (Scheme 1). We were intrigued by the possibility that **2** might also be a primary photoproduct in polar, nucleophilic solvents, like methanol, where photolysis of DMBA gives, as the major product, the ether **4** (56%),³ clearly derived from an intermediate arylmethyl cation. If **2** is formed in methanol, it might be expected to undergo rapid ground-state solvolysis to **4** complicating mechanistic arguments^{4,5} centered on the yield of ion-derived products in this "photosolvolysis" reaction, i.e., is **4** formed entirely in the primary photochemistry of DMBA or, at least in part, in a secondary ground-state process from **2**? This is an important question because DMBA, and other multiple methoxy substituted benzyl acetates, has been shown³ to give a higher yield of ion-derived products than expected on the basis of a mechanism that emphasizes formation of ion pairs from radical pairs by electron transfer. Moreover, on the basis of the pioneering study by Zimmerman⁶ on the influence of *meta* methoxy substituents on benzene excited state reactivity, the 3,5-dimethoxybenzyl chromophore in benzoin derivatives has recently been advocated in the design of practical examples of photo labile protecting groups.^{7,8}

We therefore decided to isolate and examine the reactivity of **2** and now report that (1) the compound previously reported as **2** is, in fact, the bicyclic isomer **5**; (2) **2** can be prepared from **5** by pyrolysis in hexane; (3) **2** does undergo rapid ground-state solvolysis in methanol; and (4) **2** is formed as a primary photoproduct of DMBA in methanol.

Photolysis⁹ in hexanes results, as previously reported,¹ in the rapid¹⁰ disappearance of DMBA. By integration

of the ¹H NMR spectrum of the crude reaction mixture, using the signals previously reported and assigned to **2**, the yield of the photoisomer was 9%. This compound was then partially purified by preparative chromatography.¹¹ The original assignment of **2** was made only on the basis of 100 MHz ¹H NMR spectra, and two of the reported features were puzzling. First, the signal for H_a was at δ 3.58, a very low value for a doubly allylic methine hydrogen at an ester carbon (an approximate value of δ 6.6 can be predicted using the corresponding CH₂ in *o*-isotoluene (C₇H₈) at δ 3.17 (C₆H₆)¹² and δ 3.32 (CCl₄)¹³ and the expected substituent effect of an ester oxygen of δ 3.4¹⁴) and, second, the two methoxy groups, although in very similar chemical environments, gave quite different chemical shifts (δ 3.24 and δ 3.62). When ¹H–¹³C-correlated spectra¹⁵ demonstrated that both H_a and H_c were on sp³-hybridized carbons at δ 76.6 and δ 52.6, respectively, assignment of the structure **2** to this compound became untenable. In contrast, the NMR spectra are consistent with structure **5**, particularly when the ¹H and ¹³C chemical shifts, after correcting for substituent effects, are compared with those of the previously reported¹³ unsubstituted compound, C₇H₈, another isomer of toluene. Moreover, the structure of **5** makes chemical sense, because an obvious mechanism for its formation is the allowed disrotatory butadiene to cyclobutene ring closure by secondary photochemistry of **2**.¹⁶

As expected, freshly isolated samples of **5** were transparent at 320 nm; however, **5** slowly isomerized to **2**, and this first-order conversion could be monitored by either ¹H NMR or the increasing absorbance at 320 nm (*t*_{1/2} approximately 10 h at room temperature).¹⁷ The conversion of **5** to **2** was clearly first order in hexanes at 50 °C (*t*_{1/2} = 89 min)¹⁸ and **2** could then be isolated, spectra¹⁹ taken, and its reactivity studied. NMR samples of **2** in CDCl₃ were relatively unstable as **2** rearranged to the toluene derivative **6**; this process was quantitative after 2 h at 50 °C.²⁰ In acetonitrile, **2** rearranges back to

(11) Silica gel dry-flash chromatography using 5% ethyl acetate in hexanes as eluant gave fractions with purity as high as 90% but always contaminated with DMBA.

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(15) NMR spectra for **5**: ¹H NMR (CDCl₃ at 250 MHz) δ 5.66 (H_a), 5.24 (H_c or H_d), 5.16 (H_e or H_f), 4.74 (H_b), 3.71 (3H, s), 3.66 (H_g), 3.33 (3H, s) and 2.09 (3H, s); the observed multiplets could be simulated using the program NMRSIM (Dr. T. P. Forrest, Chemistry Department, Dalhousie) to give the following coupling constants, *J* (Hz): eb (1.22), ec (0.91), ed (1.83), ca (2.44), and da (2.14); ¹³C NMR (CDCl₃ at 250 MHz) δ 170.5 (C=O), 158.3 (=COCH₃), 144.6 (C=CH₂), 112.3 (C=CH₂), 95.7 (CH_b), 81.0 (COCH₃), 76.6 (CH_a), 56.9 (CH₃O), 52.6 (CH_g), 52.3 (CH₃O), and 21.1 (CH₃). Assignments were made on the basis of ¹H–¹H and ¹³C–¹H correlated spectra.

(16) Although we have no evidence to support the assignment, the acetate functional group is assumed to be in the more stable *exo* position.

(17) This observation clarified several experimental observations. First, the initial report¹ on the isolation of **5** (thought to be **2**) included a UV absorption band at 315 nm with ε = 400 M⁻¹ cm⁻¹; the wavelength agrees with expectations for **2** but the ε value is too low for a conjugated triene. Our estimate of ε = 5500 M⁻¹ cm⁻¹ at 320 nm is more reasonable, particularly when compared to the value of 4400 reported¹² for the unsubstituted compound, *o*-isotoluene (C₇H₈). Second, in our attempts to isolate the photoisomer, we monitored chromatography fractions by HPLC with UV detection at 320 nm. Those fractions that contained **5**, when first obtained, were transparent but, after standing overnight at room temperature, were strongly absorbant. Both of these observations result from increasing amounts of **2** contaminating **5** with time.

(18) For the unsubstituted compound, a value of *t*_{1/2} = 210 min in THF can be calculated from the Arrhenius values reported.¹³

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(1) Jaeger, D. A. *J. Am. Chem. Soc.* **1974**, *96*, 6216–6217.

(2) We thank Professor Jaeger for sending us his original laboratory notebooks, including spectra. This material was of invaluable help. Although we are reinterpreting his observations, the quality of his experiments and the clarity of the notebooks would serve as models for anyone. Without the visual incentive of his spectra, we would have had even more difficulty completing these experiments.

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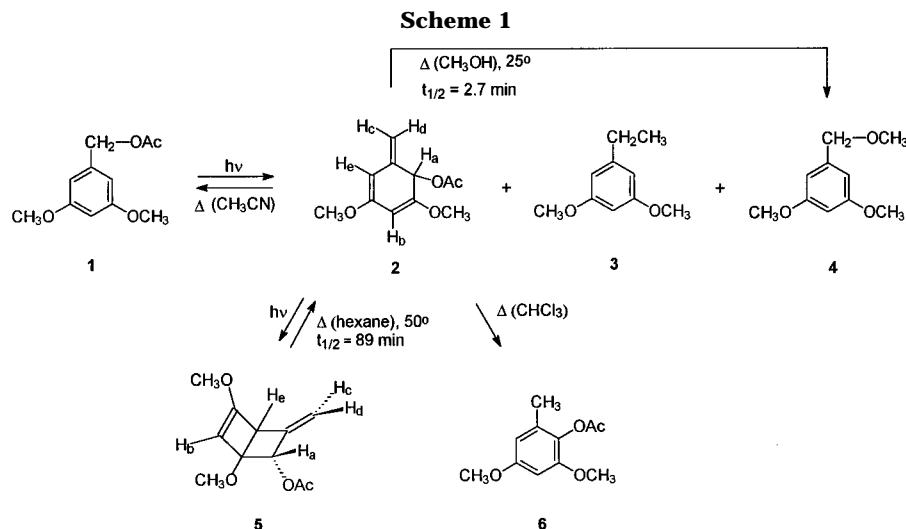
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(7) Pirrung, M. C.; Bradley, J.-C. *J. Org. Chem.* **1995**, *60*, 1116–1117.

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(9) Vycor-filtered, 450 W, medium-pressure Hanovia mercury lamp.

(10) Greater than 90% conversion of 400 mg of **1** in 280 mL of hexanes after 30 min as determined by HPLC on silica gel with 5% ethyl acetate in hexanes as eluant.



DMBA, presumably because this more polar solvent induces contact ion pair formation. Of particular relevance to the photochemistry of DMBA in polar, nucleophilic solvents, the half-life for first-order solvolysis of **2** in methanol at room temperature is only 2.7 min at 25 °C! The products result from partitioning of the ion pair between nucleophilic capture by methanol to give the methyl ether, **4** (60%) and internal return to DMBA (40%).

Finally, to demonstrate that **2** is formed in methanol, laser flash photolysis²¹ of DMBA at 266 nm gave an absorbance spectrum with a maximum at 320 nm that remained constant on the millisecond time scale. Moreover, samples subjected to multiple 266 nm laser pulses could be transferred to a diode array spectrometer and the decay of the photogenerated transient monitored. The lifetime obtained was identical to that obtained from the preparative-scale NMR samples, conclusively demonstrating that **2** is a primary photoproduct in methanol.²²

These observations have important implications in the ongoing debate concerning the mechanism for formation of ion-derived products in the photochemistry of benzyl acetates.^{4,5} There are three possible mechanisms for the formation of **2** from DMBA in methanol: (1) concerted sigmatropic rearrangement; (2) recombination of an initially formed radical pair; and (3) recombination of an initially formed ion pair. If either mechanism (1) or (2) is important in nucleophilic solvents such as methanol,

then the yield of ion-derived product, the methyl ether **4**, will be increased by a ground-state pathway for its formation that is independent of the photochemical pathway. By analogy with the photo-Fries reaction where solvent caged radical pairs generated from the singlet excited state are proven intermediates,²³ mechanism 2 would seem to be preferred.

Moreover, preliminary results for DMBP (the *tert*-butyl, or pivalate, ester derivative of **1**) also support mechanism 2. Both DMBA and DMBP produce an absorbance at 320 nm after multiple 266 nm laser pulses. For DMBA, after the decay of **2** is complete, the residual absorbance remaining is still 15% of the starting absorbance value. This residual absorbance is assigned to the more stable alkyl-substituted triene product that would result by combination of the radical pair after the decarboxylation of the acyloxy radical.²⁴ In contrast, for DMBP, the residual absorbance is 77% of the original value. For the radical pair in this case, decarboxylation of the acyloxy radical is faster²⁵ so that formation of the solvolytically reactive trienyl ester²⁶ is less efficient relative to the formation of hydrocarbon products.

Future experiments will be directed toward establishing the photochemical yield and reactivity of isomers analogous to **2** as a function of substrate (substituents and leaving group) and reaction conditions (solvent, wavelength of irradiation, etc.).

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(19) Samples of **2** were still contaminated with the DMBA that had been in **5**. The ¹H NMR spectrum of **2** in CDCl₃ could not be analyzed because the signals for H_b, H_c, H_d, and H_e were almost coincident at 250 mHz, giving an unresolved multiplet. In contrast, these signals were well dispersed in acetonitrile: ¹H NMR (CD₃CN at 250 mHz with δ values reported relative to a value of δ 5.04 for the methylene hydrogens of DMBA, their chemical shift in CDCl₃) δ 6.10 (H_b), 5.33 (H_b), 5.24 (H_c), 5.19 (H_c or H_d), 5.08 (H_c or H_d), 3.67 (3H, s), 3.65 (3H, s), 2.04 (3H, s); ¹³C NMR (CD₃CN) δ 158.4 (C), 142.8 (C), 115.9 (CH₂=), 97.5 (CH₂), 92.0 (CH₂), 69.3 (CH₂), 56.3 (CH₃O), 55.7 (CH₃O), 21.4 (CH₃). Assignments were made on the basis of ¹H-¹³C correlated spectra.

(20) Jaeger¹ reported the same process in benzene at 50 °C, and this observation was used as support for the assignment of the structure **2** to the photoisomer isolated. In fact, the process observed was thermal conversion of **5** to **2** to **6**.

(21) Continuum NY-61 Nd:YAG laser at 266 nm, ≤ 15 mJ/pulse, ≤ 8 ns/pulse.

(22) Similar laser experiments as a function of temperature in methanol gave $\Delta H^\ddagger = 16$ kcal/mol and $\Delta S^\ddagger = -14$ eu and in other solvents (ethanol, 2-propanol) at 25 °C gave a linear *mY* correlation with *Y* = 0.57.

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(24) We have not been able to isolate this compound because it is contained in chromatography fractions that are mixtures of hydrocarbons dominated by the aromatic isomer, 3,5-dimethoxyethylbenzene.

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(26) The rate of solvolysis of the trienyl ester from DMBP is a factor of 2 slower than for **2**. This is in agreement with the fact that acetic acid (*pK_a* = 4.75) is a slightly stronger acid than pivalic acid (*pK_a* = 5.03), and therefore, acetate is the better leaving group.