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Reversed diastereoselectivity in the Yang photocyclization upon introducing a cyclopropyl group at the alpha position to carbonyls[†]

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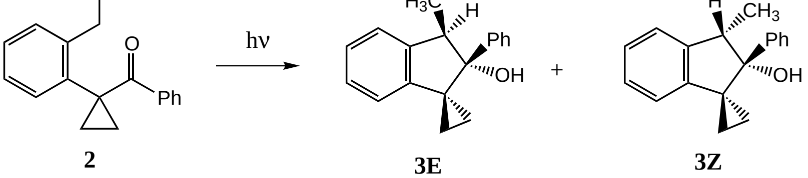
Abstract—1-Benzoy1-1-(*o*-ethylphenyl)cyclopropane favors the *E*-indanol formation in its photochemical reaction and the selectivity is maximized in methanol. These are exactly opposite to the photochemical behavior of α-(*ortho*-ethylphenyl)-acetophenone. Our computational studies suggest that the different stereochemical outcome of the two systems originates from the geometric difference of initially formed biradical intermediates. © 2002 Elsevier Science Ltd. All rights reserved.

For the last decade there has been much interest in asymmetric induction in reactions of electronically excited molecules. Most studies have focused on reactions in rigid environments such as in solid state,[1] but analogous studies in solution phase have also produced many interesting examples in recent years, which cover several different reaction types.[2] Among them photochemical reactions involving triplet 1,4-biradical intermediates have drawn much attention in view of discussing the mechanistic origin of their stereochemical outcome.[3] A few years ago Wagner addressed several important factors to determine stereoselectivities of photochemical reactions involving triplet 1,5-biradicals using the Yang photocyclization of α-(*ortho*-ethylphenyl)acetophenone (**1**) and its derivatives.[4] Several analogues with an extra α-substituent were also tested in their studies, but the data analysis became complicated by competing α-cleavage and by the difficulty in evaluating pre-existing conformational preference and molecular dynamics at the biradical stage at the same time. We have recently found that photolysis of 1-benzoyl-1-(*o*-tolyl)cyclopropane results in an efficient formation of an indanol with no α-cleavage products,[5] which would solve both problems mentioned above. Accordingly 1-benzoy1-1-(*o*-ethylphenyl)cyclopropane (**2**), a structural analogue of **1**, was prepared and diastereoselectivity of its photocyclization was investigated. Interestingly the selectivity was completely reversed where the *E* isomer became the major product, the exact opposite of **1**. Furthermore, **2** showed completely different solvent and temperature effects from **1**. Here we would like to communicate the unique photochemical behavior of **2** and the origin of the reversal (Scheme 1).

The compound **2**[6] was prepared by α-methylenation of **1**, followed by cyclopropanation using the Corey–



Scheme 1.

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[†] This paper is dedicated to Professor Sang Chul Shim of KAIST, on his untimely death.

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Chaykovsky protocol.[7] The ketone **2** in several different solvents (typically 0.01–0.02 M) was irradiated in an immersion well using Pyrex-filtered light of a 450 W Hanovia medium pressure mercury arc lamp until all the starting material had disappeared. After evaporating all the volatiles and chromatographing over silica gel, two isomeric products were isolated, which were assigned to be spiroindanols **3*E*** and **3*Z*** on the basis of their spectroscopic properties.[8] For stereochemical assignment, methyl doublets at higher field were particularly useful because it has been generally accepted that a methyl *cis* to a phenyl is significantly shielded relative to the one *trans* to phenyl.[9] The assignment was confirmed further by two other NMR experiments.[10] No other products were detected and the chemical yield of the sum of two isomers approached 100% within experimental errors. Table 1 summarizes the product ratios in several different reaction media and temperature, which are taken from NMR integration of methyl doublets or methine quartets in NMR scale photolysis in the corresponding deuterated solvents. The E/Z ratios increase with decreasing temperature and there is a linear relationship of $\ln(E/Z)$ versus $1/T$ at the observed temperature range. The Arrhenius plot of the data gives ΔE_a, $E_{a_Z}-E_{a_E}$, of 1.81 kcal/mol and A_E/A_Z of 0.21.[11]

Table 1. Product ratios of photocyclization of **2** at various reaction conditions

Conditions	**3*E*/3*Z***
Benzene, 298 K	4/1 (80:20)
Methanol, 298 K	99/1 (99:1)
Acetonitrile, 298 K	32.3/1 (97:3)
THF, 298 K	15.7/1 (94:6)
Toluene, 200 K	19/1 (95:5)
Toluene, 273 K	6.5/1 (86.7:13.3)
Toluene, 298 K	4/1 (80:20)
Toluene, 365 K	2.5/1 (71.8:28.2)

In parentheses are normalized values to 100%.

The above results show that **2** favors the *E*-indanol formation in its photochemical reaction and the selectivity is maximized in methanol. These are exactly opposite to photochemical behavior of **1**. What causes such a difference of **1** and **2**? It is possible to postulate that putting cyclopropyls at α position to carbonyl groups changes preferred conformation, so that geometry of the initially formed biradical intermediate from **2** is quite different from that of the parent system with no cyclopropyls. In fact, it is known that extra α-substituents of α-arylacetophenones perturb their geometry by twisting α-aryl away from the carbonyl.[12] We have tested this idea by searching energy minimized structures of both starting compounds and their biradical intermediates. The ground state geometry were calculated with semiempirical AM1 method and the biradical models were calculated with UHF/AM1.[13] As shown in Fig. 1, the bond between carbonyl carbon and its α-carbon of **1** is rotated such that the carbonyl group becomes almost eclipsed with one cyclopropyl C–C bond in **2**.

Energy minimization of the biradical from **2** gives two low-energy conformers with one of them being a global minimum (Fig. 2). **BR2e** lies 1.46 kcal/mol below **BR2z**. The former is most likely the predominant initial biradical geometry right after hydrogen atom transfer by judging from its geometric resemblance to the global

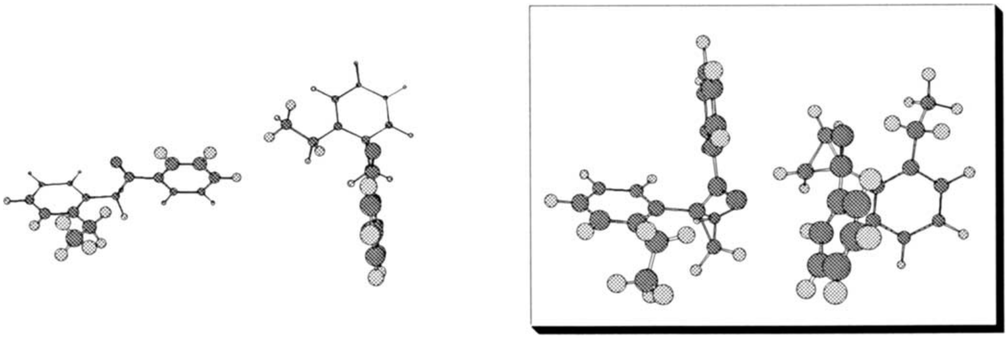

Figure 1. Energy minimized structures of **1** and **2**.

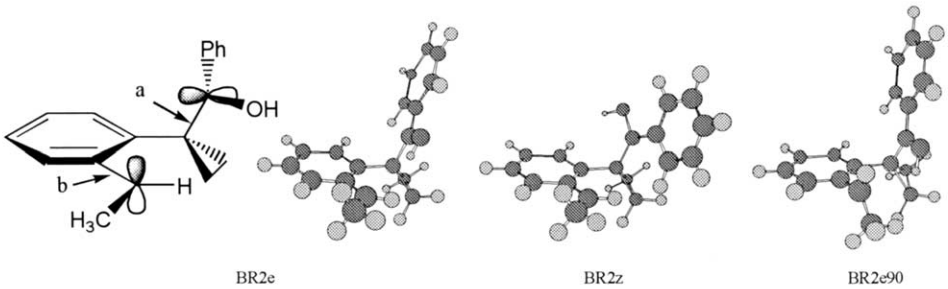

Figure 2. Energy minimized structures of biradical intermediates in the photocyclization of **2**.

minimum of the starting ketone. **BR2e** and **BR2z** can form the *E*- and *Z*-indanol, respectively, with minimal bond rotations. However, our calculation suggests that the barrier for bond rotation from **BR2e** to **BR2z** is enormous, so the formation of **BR2z** under the reaction condition is unlikely. With only one methyl at the alpha position to the carbonyl group, the barrier is reported to be ca. 5 kcal/mol,[4a] which becomes an important factor deciding diastereoselectivity of photoproducts from α-(*o*-ethylphenyl)propiophenone. Having extra alkyl group as in **2**, it becomes almost impossible to rotate bond a in **BR2e** to form precursors of *Z*-indanol because steric hindrance caused by the cyclopropyl ring does not allow the phenyl group nearby.

Therefore, the remaining rotation to determine the diastereoselectivity is around bond b of **BR2e**. In **BR2e**, two singly occupied p orbitals are almost orthogonal and can become pointed at each other with slight rotation of bond b clockwise to produce efficient $T_1 \rightarrow S_0$ intersystem crossing before bond formation.[14] It is, however, necessary to twist the bond b counterclockwise about 90° in order to give *Z*-isomer. Our calculation suggests that this motion from **BR2e** to **BR2e90** is ca. 7 kcal/mol uphill energetically. The rotation would be more hindered if the hydroxy group is solvated by hydrogen bonding acceptors such as methanol, acetonitrile or THF. The fact that lowering reaction temperature and using H-bonding acceptor solvents increase the *E*/*Z* ratio support the above mechanistic scheme.

In summary, **2** shows the opposite diastereoselectivity to **1** in its Yang photocyclization, whose different behavior originated from the geometric change of initially formed biradical intermediates. At low temperature or in methanol the selectivity is maximized where the *E*-indanol becomes almost a sole product. Currently we are investigating stereoselectivities in the Yang reaction of other α-substituted ketones in order to see how general the reversal in diastereoselectivities is upon introducing extra α-substituents to carbonyl groups.

Acknowledgements

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References

1. Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755–12769 and references cited therein.
2. Inoue, Y. *Chem. Rev.* **1992**, *92*, 741–770.
3. (a) Griesbeck, A. G.; Henz, A.; Kramer, W.; Wamser, P.; Peters, K.; Peters, E.-M. *Tetrahedron Lett.* **1998**, *39*, 1549–1552; (b) Griesbeck, A. G.; Mauder, H.; Sradtmuller, S. *Acc. Chem. Res.* **1994**, *27*, 70–75; (c) Hu, S.; Neckers, D. C. *J. Org. Chem.* **1997**, *62*, 564–567.
4. (a) Zand, A.; Park, B. S.; Wagner, P. J. *J. Org. Chem.* **1997**, *62*, 2326–2327; (b) Wagner, P. J.; Zand, A.; Park, B. S. *J. Am. Chem. Soc.* **1996**, *118*, 12856–12857.
5. (a) Chang, D. J.; Koh, E.; Kim, T. Y.; Park, B. S.; Kim, T. G.; Kim, H.; Jang, D.-J. *Tetrahedron Lett.* **1999**, *40*, 903–906; (b) Kim, H.; Kim, T. G.; Hahn, J.; Jang, D.-J.; Chang, D. J.; Park, B. S. *J. Phys. Chem. A* **2001**, *105*, 3555–3563.
6. Spectroscopic data of **2**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.60 (d, 2H, $J=7.0$ Hz), 7.47 (d, 1H, $J=6.9$ Hz), 7.36–7.05 (m, 6H), 2.53 (q, 2H, $J=7.5$ Hz), 1.84 (m, 2H, AA′XX′), 1.33 (m, 2H, AA′XX′), 1.04 (t, 3H, $J=7.5$ Hz). ^{13}C NMR ($CDCl_3$, 56 MHz) δ 202.5, 145.3, 139.3, 138.7, 131.9, 129.9, 129.3, 128.7, 128.1, 128.0, 126.3, 35.5, 25.4, 18.5, 14.4. IR (KBr): 3064, 2967, 1665. EIMS 77, 105, 225, 250 (M^+).
7. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364.
8. Spectroscopic data of ***3E***: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.30–7.10 (m, 7H), 7.06 (m, 1H), 6.80 (m, 1H), 3.52 (q, 1H, $J=7.2$ Hz), 1.69 (s, 1H, -OH), 1.53–1.45 (m, 1H), 1.33–1.23 (m, 1H), 1.06 (d, 3H, $J=7.2$ Hz), 0.78–0.58 (m, 2H). ^{13}C NMR ($CDCl_3$, 56 MHz) δ 147.2, 144.6, 143.7, 127.9, 127.8, 127.3, 127.0, 126.8, 123.3, 118.1, 86.5, 52.6, 37.3, 16.8, 14.0, 12.3. IR (KBr): 3562, 3064, 2965, 1056. EIMS 77, 105, 222, 250 (M+); Spectroscopic data of ***3Z***: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.52 (d, 2H, $J=7.8$ Hz), 7.41–7.21 (m, 6H), 6.77 (m, 1H), 3.82 (q, 1H, $J=6.8$ Hz), 1.95 (s, 1H, -OH), 1.31 (d, 3H, $J=6.8$ Hz), 1.10–0.60 (m, 4H). ^{13}C NMR ($CDCl_3$, 56 MHz) δ 145.5, 145.3, 142.0, 128.2, 127.8, 127.4, 127.1, 127.0, 123.8, 119.4, 86.4, 50.4, 38.7, 18.9, 11.7, 9.4. IR (KBr): 3553, 3461, 3058, 2965, 1069. EIMS 77, 105, 222, 250 (M+).
9. (a) Wagner, P. J.; Meador, M. A.; Zhou, B.; Park, B. S. *J. Am. Chem. Soc.* **1991**, *113*, 9630–9639; (b) Pappas, S. P.; Blackwell, J. E., Jr. *Tetrahedron Lett.* **1966**, 1175–1178.
10. In an NMR experiment using $Eu(dpm)_3$ as a shift reagent, the methyl protons *cis* to the OH in **3*Z*** showed larger shift than the methine proton did while the opposite effect was shown in **3*E***. When doublets at 7.52 ppm (**3*Z***) and 7.30 ppm (**3*E***) that correspond to the two *ortho* protons were irradiated in an NOE experiment, both methyl and methine resonances were enhanced in both isomers presumably due to the unique ring puckering of five membered ring systems. However, the intensity ratio of methyl to methine NOE was larger for **3*E*** than for **3*Z***.
11. The plot of $\ln(E/Z)$ versus $1/T$ (K) gives the slope of 906±4 and the intercept of −1.56±0.058.
12. Wagner, P. J.; Zhou, B.; Hasegawa, T.; Ward, D. L. *J. Am. Chem. Soc.* **1991**, *113*, 9640–9654.
13. Gaussian 98, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.;

Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A., Gaussian, Inc., Pittsburgh, PA, 1998.

14. For discussion of $T_1 \rightarrow S_0$ intersystem crossing of biradicals in relation to molecular geometry, see: Michl, J. *J. Am. Chem. Soc.* **1996**, *118*, 3568.