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REGIOSELECTIVITY IN A BENZOPHENONE-MEDIATED PHOTO-SUBSTITUTION OF SOME CAGE-SHAPED HYDROCARBONS

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Benzophenone-mediated protolyses of five cage-shaped compounds in benzene solutions result in the formation of phenyl-substituted products with high regioselectivity. The regioselectivity is rationalized based on the relative bond strengths and structural parameters of each molecule.

INTRODUCTION

The cage-shaped hydrocarbon derivatives of heptacyclo-$[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}.0^{10,14}]$tetradecane (**1a**) have attract considerable attentions in recent years owing to their unusual geometry.[1] Selective functionalization of the C—H bond of these cage-shaped compounds is therefore of topical interest. In this study we found that the photolysis of compounds **1a**–**5a** in solutions of benzene in the presence of benzophenone results in the formation of the corresponding phenyl-substituted product with very high regioselectivity.[2] In these reactions the phenyl substituents all appear at β-instead of α-positions. This high regioselectivity prompted us to perform a structural analysis on these interesting molecules.

RESULTS AND DISCUSSION

The reaction apparently proceeded through a hydrogen abstraction by the excited-state benzophenone as the first step, followed by trapping of the resulted radical with benzene. Subsequent aromatisation yielded the corresponding phenyl-substituted product. The structures of **1b**–**5b** were assigned according to their spectroscopic features. For structures **1b**, **3b** and **4b**, the lack of a symmetry plane is evidenced by the presence of 18 absorption peaks in their ^{13}C NMR spectra, whereas the alternative regioisomers (i.e. substituted at the α-position) would exhibit fewer lines.

For radical reactions in general, the regioselectivity is not so apparently predictable as those of nucleophilic or electrophilic reactions.[3,4] In Table 1 the respective bonding enthalpies calculated by the standard MNDO method are given.[5] The estimated values for **1a**, **3a** and **4a** agree well with the observed selectivity (i.e. lower energy for a β-H abstraction), whereas that for **2a** is just the opposite (lower energy for an α-H abstraction). The radical formed at the α-position of **2a** can be stabilized by resonance, but such an effect is not possible in the structure of **3a** since the half-filled p orbital on the radical centre is not aligned properly with those of the C=O moiety. It has been suggested that for radical reactions the degree of stabilization provided by resonance is relatively low compared with common heterolytic reactions.[3] The influences of steric factors sometimes are more pronounced than thermodynamic factors.

Since the skeletons of the cage-shaped molecules are fairly rigid, the conformation at the radical ccentres cannot be readjusted to a sizable scale on losing a hydrogen. Much of the strain that can be released originates from the eclipsed hydrogens. For instance, in the case of **1a**, the total strain of the β-radical [55·6 kcal mol^{-1} (1 kcal = 4·184 kJ)] calculated by MM2[8] is *ca* 1·6 kcal mol^{-1} lower than that of the α-radical (54·0 kcal mol^{-1}), out of which 1·4 kcal mol^{-1} is released in the form of torsional strain. The bonding compressions on the α- and β-carbons can be estimated by measuring their ^{13}C–H coupling constants.[9] The coupling constants listed in Table 1 are related to the percentage of s character of the carbons.[7] A higher s

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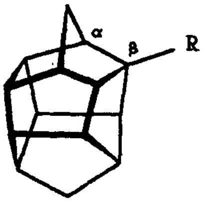

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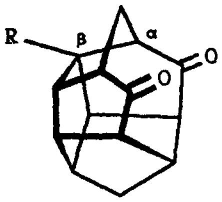

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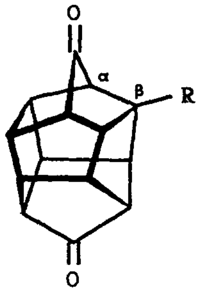

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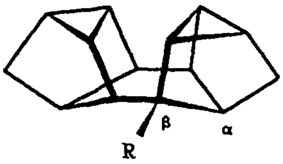

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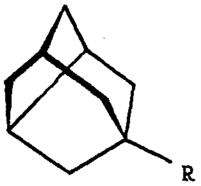

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(a) R = H; (b) R = Ph

character implies a higher strain on that carbon and consequently a higher C—H bonding strength. The observed J_{C-H} values seem to agree reasonably well with the calculated bond energies. For **2a** the difference in the values of J_{C-H} becomes less apparent than that of the estimated bonding strengths.

In these reactions, the stereochemistry of the triplet state benzophenone, which acts as the H-acceptor, may have also played an important role in determining the orientation of the transition state. It has been reported that benzophenone may form an exciplex with benzene on UV irradiation.[10] However, its exact structure in these reactions is not clearly realized. It would hence be informative to examine the substitution reaction using a different type of radical H-acceptor. In a subsequent experiment, **1a** was mixed with diacetyl in

Table 1. Calculated C—H bond strengths, measured ^{13}C–H coupling constants and the percentages of s character on the carbon atoms of the cage molecules

Parameter	Position	**1a**	**2a**	**3a**	**4a**	**5a**
Bond strength[a] (kcal mol^{-1})	α	99·47	97·10	101·84	98·42	
	β	97·04	100·78	97·49	91·18	88·49
J_{C-H} (HZ)	α	145·2	136·8	151·6	149·8	
s (%)[b]		29·0	27·4	30·3	30·0	
J_{C-H} (HZ)	β	138·4	137·4	144·2	135·8	132·8
s (%)		27·7	27·5	28·8	27·2	26·6

[a] The bond strength is the enthalpy change of the reaction $R-H \rightarrow R\cdot + H\cdot$, where the heats of formation of RH and R· are calculated by standard MNDO method[5] with full geometry optimization and that of H· is 52·10 kcal mol^{-1}.[6]

[b] $s\ (\%) = 0{\cdot}2(J_{C-H})$.[7]

dichloromethane kept in a thermostat regulated at 2–5 °C, and the solution was irradiated with UV radiation for 10 h. At the end of the reaction a monoacetylated product (**1c**) was isolated in nearly 90% yield (corrected). The structure of the product was confirmed by spectroscopic analyses and it was found that the acetyl substituent is located exclusively at the β-position. The regioselectivity in this reaction is the same as that in the benzophenone-mediated reactions even though the reaction media of the two are different.[11]

CONCLUSION

The results indicate that the H-abstraction process in these cage molecules may be described more suitably by a kinetically controlled mechanism in which the regioselectivity is governed by an early-stage transition state which resembles more closely the structure of the reactant. With **1a**, **3a** and **4a**, both the kinetic and thermodynamic factors operate in the same direction, whereas with **2a** the kinetic factors override stability factors.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were obtained on a Brucker MSL-200 FT spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 297 infrared spectrophotometer. Elemental analyses were obtained on a Perkin-Elmer Model 240 EA instrument. Mass spectra were measured on a VG Analytical Model 70-250 S/SE spectrometer. MM287 and AMPAC programs were obtained from QCPE, Indiana University, and were run on a VAX 8530 or a Micro VAX 3600 computer.

General procedure for the benzophenone-sensitized photolyses. In a typical experiment, equal molar amounts of the cage compound and benzophenone were dissolved in benzene in a quartz vessel. The solution was degassed in an ultrasonic bath by bubbling nitrogen through it for 30 min. It was then irradiated with a 450 W medium-pressure lamp for a period of time. The resulting mixture was then concentrated *in vacuo* and the products were purified by high-performance liquid chromatorgraphy (HPLC) on a silica gel column with column with hexane–ethyl acetate as solvent. In addition to the phenyl-substituted products, other components were isolated including tetraphenylethanediol (pinacol), the condensed adducts of benzophenone and the cage molecule and some highly polar materials. However, among the phenyl-substituted products only the β-isomers were observed. The corrected yields of **1b** and **2b** were 47% and 75%, respectively, as reported previously.[2] The structural features of **5b** (18·5% yield) are identical with those published previously.[12]

1-Phenylheptacylco $[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5,9}.0^{10,14}]$ *tetradecane-7,12-dione* (**3b**). Compound **3a** (530 mg, 2·5 mmol) and benzophenone (455 mg, 2·5 mmol) were dissolved in 70 ml benzene and subjected to UV irradiation for 20 h. Compound **3b** (72 mg, 0·25 mmol, 10% yield) was isolated by HPLC, m.p. 149–150 °C. ^1H NMR ($CDCl_3$), 2·55 (s, 1H), 2·63 (t, 1H, $J = 4{\cdot}2$ Hz), 2·80–2·90 (m, 3H), 2·90–3·00 (m, 6H); ^{13}C NMR ($CDCl_3$), 48·23 (d), 48·47 (d), 48·89 (d), 49·36 (d), 49·43 (d), 50·21 (d), 50·63 (d), 50·71 (d), 54·22 (d), 55·05 (d), 59·95 (d), 64·80 (s), 125·26 (d), 126·62 (d), 128·87 (d), 144·48 (s), 213·58 (s), 213·80 (s); MS (15 meV), *m/z* (relative intensity) 288 (M^+, 100%), 260 (25), 232 (15), 182 (14).

2-Phenylheptacyclo $[8.4.0.0^{2,12}.0^{3,8}.0^{4,6}.0^{5,9}.0^{11,13}]$ *tetradecane* (**4b**). Binor-S (200 mg, 1·09 mmol) and benzophenone (198 mg, 1·09 mmol) were dissolved in 10·0 ml of benzene. After UV irradiation for 28 h, **4b** was collected (50 mg, 0·192 mmol, 28% corrected yield) together with 75 mg of recollected Binor-S. IR (KBr), 3057, 3020, 2931, 2865, 1212 cm^{-1}; ^1H NMR ($CDCl_3$), 1·03–1·50 (m, 10H), 1·76 (s, 1H), 1·92 (s, 2H), 2·06–2·11 (AB pattern, 2H), 7·11–7·19 (m, 1H), 7·24–7·36 (m, 4H); ^{13}C NMR ($CDCl_3$) 15·23 (d), 15·90 (d), 17·13 (d), 17·24 (d), 18·52 (d), 20·22 (d), 31·53 (t), 32·57 (d), 33·41 (t), 38·22 (d), 39·99 (d), 41·38 (d), 50·39 (d), 52·89 (s), 125·30 (d), 126·80 (d), 127·83 (d), 149·33 (s); MS (10 eV), *m/z* (relative intensity) 260 (M^+, 20%), 194 (70), 179 (30), 167 (15), 154 (15), 142 (100).

1-Acetylheptacyclo $[6.6.0.0^{2,6}.0^{3,13}.0^{4,11}.0^{5.9}.0^{10,14}]$ *tetradecane* (**1c**). In a Pyrex photochemical immersion well reactor, jacketed with a cooling water circulator, were placed freshly distilled diacetyl (16·5 ml, 0·19 mol), **1a** (3·00 g, 16·3 mmol), and dichloromethane (70 ml). The solution was degassed in an ultrasonic bath by purging with nitrogen, then kept at *ca* 2–5 °C and irradiated with a 450 W medium-pressure mercury lamp for 10 h. The mixture was quenched by adding 5% $NaHCO_3$ and extracted several times with dichloromethane. The products were purified by silica gel column chromatography with benzene as eluent. The acetyl adduct **1c** [454 mg, 2·00 mmol, 88% yield (corrected)] was collected together with 2·58 g of recollected starting material. ^1H NMR ($CDCl_3$), 1·78 (m, 2H), 1·82 (s, 2H), 2·15 (s, 3H), 2·40–2·70 (m, 9H), 2·80 (m, 2H) ; ^{13}C NMR ($CDCl_3$) 26·73 (q), 42·04 (t), 42·49 (t), 50·84 (d), 51·09 (d), 51·20 (d), 52·51 (d), 53·00 (d), 53·15 (d), 53·26 (d), 53·53 (d), 53·83 (d), 56·79 (d), 57·78 (d), 76·53 (d), 211·15 (s); MS (1·4 eV), *m/z* (relative intensity) 266 (M^+, 15%), 211 (M^+-CO, 100), 183 (81); anlysis, calculated for $C_{16}H_{18}O$, C 84·91, H 8·02; found, C 84·69, H 8.31%.

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