Photochemistry of Conjugated Polyacetylenes. Photoreaction of 1,4-Diphenylbutadiyne with a Mixture of Olefins

Chang Beom Chung, Geon-Soo Kim, Jang Hyuk Kwon, and Sang Chul Shim*

Department of Chemistry, Korea Advanced Institute of Science and Technology, Taejon 305-701

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Irradiation of 1,4-diphenylbutadiyne (DPB) with a mixture of electron-deficient and electron-rich olefins in deaerated tetrahydrofuran yields a 1:1 primary photoadduct between DPB and electron-deficient olefins. Irradiation of the primary photoadduct of DPB and dimethyl fumarate (DMFu) with various olefins such as DMFu, acrylonitrile (AN), and 2,3-dimethyl-2-butene (DMB) in deaerated tetrahydrofuran yields regiospecific 1:1 photoadducts. The electron-deficient olefins are more reactive than electron-rich olefins in the photoreaction which proceeds through excited triplet state.

Introduction

The \([2+2]\) photocycloaddition reaction of olefins has been extensively studied and the reaction mechanisms have been well understood. On the contrary, the photoreaction of acetylenes with olefins received relative little attention. There are a few reports of photocycloaddition reactions of acetylenes with olefins.\(^1\)\(^-\)\(^8\) In most cases cyclobutenes rings are formed, but cyclopentyl photoadducts as minor products were also observed.\(^5\)\(^-\)\(^8\) When two alkene units are incorporated into a rigid molecule, such as cyclohexa-1,4-diene, the major photoproduct was the bicyclopentyl adduct.\(^2\)\(^-\)\(^4\) From sensitizing and triplet quenching studies on the formation of cyclobutene photoproduct, the photoreaction is suggested to proceed through the lowest triplet excited state of acetylene. The formation of cyclobutyl photoproduct is proposed to be concerted.

We have previously reported interesting photoreactions of 1:1 1,4-diphenylbutadiyne (DPB) with several olefins to yield 1:1 and 1:2 photoadducts.\(^9\)-\(^11\) The photoreaction of DPB with dimethyl fumarate (DMFu) in deaerated THF solution at 300 nm yields one primary 1:1 photoadduct (1) and two secondary 1:2 photoadducts (2 and 3).\(^11\)

![Diagram of photoreaction products]

*To whom correspondence should be addressed

Results and Discussion

Irradiation of 1 with olefins in deaerated tetrahydrofuran at 300 nm yields 1:1 photoadducts and trace amount of 1′ (<1%), a configurational isomer of 1. The structure of these adducts was determined by various physical methods such as UV, IR, NMR, and MS spectroscopy.

Some photoadducts are obtained when 1 is irradiated in deaerated tetrahydrofuran solutions of various olefins such as DMFu, AN, and DMB.

The UV spectra of 7 and 8 are quite different from those of 4, 5, and 6 which are very similar to each other indicating that these adducts have the same chromophore (Figure 1). The absorption maxima were slightly blue shifted in 4, 5, and 6 and considerably in 7 and 8. IR spectra of 4 and 5 show a C≡N stretching band while 6-8 show no acetylenic stretching band. The significant difference of IR spectra of 6 and 7 (or 8) is the C=C stretching band at ~1600 cm\(^{-1}\). Mass spectra of all the photoproducts show molecular ion peaks indicating that all the products are formed by the ad-
Figure 1. UV absorption spectra of photoproducts 4-8 in MeOH.

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\begin{align*}
1 + \text{DMFu} & \xrightarrow{\text{hv} (24 \text{ h})} 2 (12 \%) + 3 (14 \%) \\
1 + \text{CN} & \xrightarrow{\text{hv} (36 \text{ h})} \text{THF/N}_2 \quad 4 (7 \%) + 5 (8 \%) \\
1 + \text{DMB} & \xrightarrow{\text{hv} (36 \text{ h})} \text{THF/N}_2 \quad 6 (14 \%)
\end{align*}
\]

Figure 2. Relative concentration change of 9, 10, and 11.

\[
\begin{align*}
\text{DPB} + \text{DMBu} + \text{DMB} & \xrightarrow{\text{hv} (36 \text{ h})} \text{THF/N}_2 \\
1 (10 \%) + 2 (-1 \%) + 3 (3 \%) + 6 (5 \%) + 7 (2 \%) + 8 (1 \%)
\end{align*}
\]

The reaction of DPB-AN-DMB mixture solution shows less olefin selectivity than that of DPB-DMBu-DMB, and the 1:1 photoadducts 9 and 10 are obtained in almost equal amounts. The concentration of 10 increased linearly but 9 reaches a maximum and decreases on extended irradiation and 11 increases sharply at this point indicating that the major precursor of 11 is 9 (Figure 2). Irradiation of 9 with DMB yields 11 very efficiently (>70% yield in 24 hours) but photoreaction of 10 with AN proceeded very slowly and does not proceed at all when AN/10 concentration ratio is below 10. These reactivity and selectivity differences can be explained applying the frontier orbital theory which states that the energy differences between HOMO and LUMO of the reacting species are decisive in rate determination. The energy difference between reactive radicals and electron-deficient olefins is smaller than that of radicals and electron-rich olefins and consequently electron-deficient olefins are more reactive.

A plausible mechanism for the photoreaction of DPB (or 1) with olefins is proposed in Figure 3. The concentration of olefins did not affect the number of products formed but is the most important factor for the product ratio for the reaction. When DPB-mixed olefin system is irradiated, 1:2 adducts including cyclopropane rings between DPB and DMB (or DMB) are obtained in very small amounts indica-
ting that triplet state of 1 or 9 probably reacts fast with AN and DMB before rearranging into carbeneoids. The reactivities of olefins are in the order of DMFU > DMB and AN > DMB.

**Experimental**

**Instruments**

$^1$H-NMR spectra were recorded on a AM-300 spectrometer with chemical shifts being referenced against TMS as an internal standard or the residual proton of the solvent CDCl$_3$. $^{13}$C-NMR spectra were run on an AM-300 spectrometer with CDCl$_3$ as solvent and internal standard. The chemical shifts (δ) are reported in ppm. UV spectra were recorded on a Shimadzu 3100 spectrophotometer. Mass (MS) spectra were determined at 70 eV with a Hewlett-Packard 5985A GC/MS interface by the electron impact (EI) method. FT-IR spectra were recorded on a Bomem MB-100 spectrometer in a NaCl cell or KBr pellet. High-performance liquid chromatography (HPLC) was performed on a Waters Associates Model 244 liquid chromatograph (Milford, MA) equipped with a Model 6000A solvent delivery system, Model 440 UV absorbance detector fixed at 254 nm, Model R401 differential refractometer, and Model U6K universal injector. Lichrosorb Si-60 were used for quantitative and preparative analyses.

**Materials**

1,4-Diphenylbutadiyne (DPB) was purchased from Aldrich Chemical Co. 2,3-Dimethyl-2-butene (DMB) and acrylonitrile (AN) were purchased from Aldrich Chemical Co. and purified by fractional distillation prior to use. Dimethyl fumarate (DMFu) from Aldrich Chemical Co. were used after recrystallization from methanol. Tetrahydrofuran was dried over sodium metal with benzophenone indicator followed by fraction distillation before use. Methylene chloride was dried over phosphorus pentoxide. Chromatographic and spectroscopic grade organic solvents (Merck) were used for normal phase HPLC and absorption spectra, respectively. Doubly distilled and deionized water was also used for reverse phase HPLC.

**Irradiation of 1,4-Diphenylbutadiyne (DPB) with Dimethyl Fumarate (DMFu).** 1,4-Diphenylbutadiyne (DPB, 4 mM) solution in tetrahydrofuran (500 ml) with dimethyl fumarate (DMFu, 100 mM) was deaerated by nitrogen purging. Deaerated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 36 hours, the reaction mixture was evaporated in vacuo. Unreacted DMFu and DPB was crystallized out in methanol. The photoproducts 1, 1-cis, 2, and 3 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylene chloride; 3/1/1 to 6/1/1 (v/v/v), in 13, 4, 12, and 14% yields, respectively. Compound 1-cis: $^1$H-NMR (300 MHz, CDCl$_3$) δ 7.74-7.35 (m, 10H), 4.24/4.08 (d/d, $J_{ac}$=5.55 Hz, 1H, 1H), 3.77 (s, 3H), and 3.71 (s, 3H) ppm; $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 170.70, 170.08, 147.08, 132.50, 131.78, 129.32, 128.91, 128.49, 128.40, 126.04, 122.58, 118.38, 97.28, 83.71, 52.23, 52.18, 47.59, and 46.66 ppm; MS (70 eV) m/e 346 (M$^+$, 28.9), 331 (M$^+$- CH$_3$, 1.6), 314 (64.6), 299 (6.8), 286 (76.3), 271 (21.4), 226 (51.5), 215 (Cr$_2$H$_4$, 100.0), and 202 (DPB+$^*$, 22.3%); UV (MeOH) $\lambda_{max}$ 343, 322, 310, and 243 nm; IR (NaCl) 3060-3025, 2952, 2195 (m), 1735, 1572, 1439, 1218, 1027, 759, and 691 cm$^{-1}$. **Irradiation of 1 with DMFu.** 1 (4 mM) solution in tetrahydrofuran (200 ml) with DMFu (100 mM) was deaerated by nitrogen purging. Deaerated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 24 hours, the reaction mixture was evaporated in vacuo. Unreacted DMFu was crystallized out in methanol. Unreacted reactant 1 and the photoproducts 1-cis, 2, and 3 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylene chloride; 3/1/1 to 6/1/1 (v/v/v), in ~1, 12, and 14% yields, respectively. **Irradiation of 1 with Acrylonitrile (AN).** 1 (4 mM) solution in tetrahydrofuran (200 ml) with acrylonitrile (AN, 100 mM) was deaerated by nitrogen purging. Deaerated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor for 36 hours. After removal of unreacted AN and solvent under reduced pressure, the reaction mixture was subjected to column chromatography using n-hexane/ethyl acetate/methylene chloride; 3/1/1 (v/v/v) as an eluent. The photoproducts 4 and 5 were purified by HPLC using n-hexane/ethyl acetate/methylene chloride; 4/1/1 (v/v/v) as an eluting solvents in 7 and 8%, respectively. Compound 4: $^1$H-NMR (300 MHz, CDCl$_3$) δ 7.27-7.16 (m, 10H), 4.22 (d, $J_{ac}$=18.8 Hz, 1H), 4.19 (d, $J_{ac}$=1.88 Hz, 1H), 3.95 (t, $J_{ac}$=3.64 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), and 3.22 (d, $J_{ac}$=3.64 Hz, 2H) ppm; $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 171.19, 171.17, 144.64, 142.83, 133.15, 132.50, 130.48, 129.26, 129.04, 128.09, 127.20, 127.10, 126.65, 119.40, 77.20, 52.40, 52.33, 48.58, 46.15, 32.45, and 26.53 ppm; MS (70 eV) m/e 399 (M$^+$, 7.0), 367 (21.0), 339 (11.1), 308 (24.3), 280 (M$^+$-C$_2$H$_2$O$_2$, 100.0), 279 (39.1), 253 (42.6), 252 (46.5), 239 (26.4), 202 (DPB+$^*$, 21.7), 139 (32.2), 105 (24.4), and 77 (46.8%); UV (MeOH) $\lambda_{max}$ 322, 257, and 249 nm; IR (NaCl) 3111-3004, 2953, 2931, 2236 (w), 1737, 1722, 1438, 1200, 1174, and 699 cm$^{-1}$. Compound 5: $^1$H-NMR (300 MHz, CDCl$_3$) δ 7.27-7.16 (m, 10H), 4.18 (d, $J_{ac}$=1.88 Hz, 1H), 4.03 (d, $J_{ac}$=1.88 Hz, 1H), 3.89 (q, $J_{ac}$=4.97 Hz, $J_{ac}$=2.37 Hz, 1H), 3.79 (s, 3H), 3.79 (s, 3H), 3.22 (d, $J_{ac}$=4.54 Hz, $J_{ac}$=13.92 Hz, 1H), and 3.15 (dd, $J_{ac}$=2.68 Hz, $J_{ac}$=13.92 Hz, 1H) ppm; $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 171.76, 171.13, 145.02, 143.04, 133.11, 132.48, 130.79, 129.32, 129.06, 128.16, 128.13, 127.00, 126.93, 126.80, 119.62, 77.19, 52.54, 52.44, 47.02, 46.44, 32.47, and 27.03 ppm; MS (70 eV) m/e
Irradiation of DMB. DMB (4 mM) solution in tetrahydrofuran (200 ml) with a mixture of AN-DMB (100 mM-100 mM) was deasated by nitrogen purging. Deasated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 36 hours, the reaction mixture was evaporated in vacuo. Unreacted DMF was crystallized out in methanol. The photoproducts 1-cis, 2, 3, 6, 7, and 8 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylenylene chloride: 3/1 to 6/1 (v/v/v), in ~1, 1, 3, 12, 2 and 1% yields, respectively.

Irradiation of 1 with a Mixture of AN and DMB. DMB (4 mM) solution in tetrahydrofuran (200 ml) with a mixture of AN-DMB (100 mM-100 mM) was deasated by nitrogen purging. Deasated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 36 hours, the reaction mixture was evaporated in vacuo. Unreacted DMF was crystallized out in methanol. The photoproducts 4, 5, 6, 7, and 8 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylenylene chloride: 4/1 to 20/1 (v/v/v), in 7, 8, 13, 2, and 1% yields, respectively.

Irradiation of DPB with Mixture of DMF and DMB. DPB (4 mM) solution in tetrahydrofuran (200 ml) with a mixture of DMF-DMB (100 mM-100 mM) was deasated by nitrogen purging. Deasated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 36 hours, the reaction mixture was evaporated in vacuo. Unreacted DMF was crystallized out in methanol. The photoproducts 1, 2-cis, 2, 3, 6, 7, and 8 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylenylene chloride: 3/1 to 6/1 (v/v/v), in 10.1, ~1, 3, 5, 2, and 1% yields, respectively.

Irradiation of DPB with Mixture of AN and DMB. DPB (4 mM) solution in tetrahydrofuran (200 ml) with a mixture of AN-DMB (100 mM-100 mM) was deasated by nitrogen purging. Deasated solution was irradiated with 300 nm UV light in a Rayonet Photochemical Reactor equipped with RUL 3000 Å lamps. After the irradiation for 36 hours, the reaction mixture was evaporated in vacuo. Unreacted DMB was crystallized out in methanol. The photoproducts 9, 10, 11, 12, and 13 were separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylenylene chloride: 3/1 to 6/1 (v/v/v), in 2, 3, 18, 5, and 7% yields, respectively. Compound 11: H-NMR (300 MHz, CDCl3) δ 7.26-7.21 (m, 2H), 7.14-7.05 (m, 8H), 3.76 (dd, J1H=4.93 Hz, J2H=2.49 Hz, 1H), 3.22 (J2H=4.93 Hz, J3H=13.8 Hz, 1H), 3.14 (dd, J1H=4.93 Hz, J2H=13.8 Hz, 1H), 1.42 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), and 1.25 (s, 3H) ppm; 13C-NMR (75 MHz, CDCl3) δ 149.60, 142.38, 139.49, 134.53, 133.73, 128.69, 128.51, 127.93, 128.74, 128.51, 127.51, 126.65, 120.41, 48.23, 46.67, 32.52, 27.40, 23.66, 23.27, 22.98, and 22.92 ppm; MS (70 eV) m/e 346 (M+), 289, 331 (M+1, 1.6), 314 (64.6), 299 (6.8), 286 (76.3), 271 (2.4), 226 (51.5), 215 (C8H18), 100.0, and 202 (DBP+, 22.3%); UV (MeOH) λmax 324, 260, and 251 nm; IR (NaCl) 3096-3004, 2990-2860, 2238, 1492, 1458, 1369, 757, and 692 cm⁻¹.
The photoprodut 11 was separated by column chromatography followed by HPLC using n-hexane/ethyl acetate/methylene chloride: 8/1/1 (v/v/v) as an eluent to give 11 in 80% yield.

Irradiation of 10 with AN. 10 (4 mM) solution in tetrahydrofuran (50 ml) with a mixture of AN (100 mM) was deaerated by nitrogen purging. Deaerated solution was irradiated with 300 nm UV light in a Rayonet Photocatalytic Reactor equipped with RUL 3000 Å lamps. After the irradiation for 24 hours, the reaction mixture was evaporated in vacuo. The photoprodut 11 was separated by column chromatography followed by HPLC using n-hexane/ethanol acetate/methylene chloride: 8/1/1 (v/v/v) as an eluent to give 11 in 80% yield.

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References


A Study of the Retention Behavior of Proteins in High-Performance Liquid Chromatography(I):
The Effect of Solvent and Temperature on Retention Behavior of Proteins in Reversed-Phase Chromatography

Dai Woon Lee* and Byung Yun Cho

Department of Chemistry, Yonsei University, Seoul 120-749
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The retention behavior of proteins was investigated by using reversed-phase chromatography (RPC), comparing to the retention behavior of small molecules in RPC. The evaluation was carried out on a SynChropak RP-PC(18) column with 0.1% aq. TFA-organic solvent modifier such as acetonitrile, isopropanol, and ethanol. The Z value (the number of solvent molecules required to displace the solute from the surface) was a general index for the characterization of protein retention as a function of organic concentration over a range of temperature between 5 and 70°C. Vant'Hoff plots provided the basis for evaluating the enthalpic and entropic changes associated with the interaction between protein and the stationary phase. Z values did not change significantly at the range of temperature showing the consistent ΔH° and ΔS° values. From these investigation, it was concluded that the retention behavior of proteins in RPC was able to be predicted by the retention parameters applied to small molecules. Furthermore, myoglobin and hemoglobin in RPC as stated above showed a similar retention behavior regardless of their molecular weights.

Introduction

In the 1970s, high-performance liquid chromatography (HPLC) has become a powerful technique widely used for the separation of large biological substances and for their purification. In particular, RPC has been the prime method of peptide analysis and purification, and has also become a widely used chromatographic tool for protein analysis. According to Snyder et al., linear solvent strength (LSS) gradient elution theory developed for small molecules can also be used to characterized the retention behavior of proteins even though there exist some differences between the RPC behavior of proteins and low-molecular-weight molecules. It was suggested by Regnier et al. that the analysis of protein mixtures by RPC is complicated due to the nature of the solutions usually employed to effect high-resolution separations. These conditions include low pH and the use of high concentrations of organic solvents as eluents, and both conditions are known to alter protein structure substantially. Karger et al. studied the changes in peak shape as a function