Intramolecular Photochemistry in β-Turned Dipeptide Bridged Molecules

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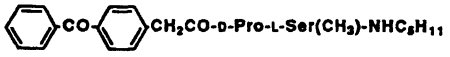
Several benzophenone-β-turned dipeptide-alkyl chain molecules were prepared. In acetonitrile, intramolecular photochemical reaction of the synthetic molecules was investigated. The photoexcited benzophenone moiety abstracted selectively a hydrogen of the alkyl chain in the molecule. Such a site selectivity showed that the β-turned conformation might be rigid enough for the hydrogen abstraction in the excited state.

In the natural system, most reactions occur under a fairly conformationally restricted conditions, e.g., in lipid and protein media. Photochemical reaction in proteins is one of the most important biological processes, for example, selective photoisomerization in rhodopsin (vision) and phytochrome (plant growth).[1] To mimic such a selectivity, the model systems need the structural rigidity. In this paper, we report preparation of benzophenone-β-turned dipeptide-alkyl chain molecules and intramolecular photochemical reaction of the synthetic protected dipeptides. The relative quantum yields for the disappearance of the synthetic molecules appear to demonstrate that the β-turned molecules are rigid enough for a selective intramolecular hydrogen abstraction by the benzophenone moiety to occur in the excited states. The site selectivity was small but first, to our knowledge, achieved in an intramolecular photochemical reaction of the molecules with a linear oligopeptide.

Table 1. Relative Quantum Yield Φ for Disappearance of **1**

1	Φ[a]
	
n=3 : **1a**	0.64
n=4 : **1b**	0.68
n=5 : **1c**	0.90
n=6 : **1d**	1
n=7 : **1e**	1.37
	
1f	1.00
	
1g	0.71

a) Determined by HPLC technique, on 313 nm-light irradition, in CH_3CN (10^{-4} mol dm^{-3}), under deareated conditions (freeze-pump-thaw), at 25 °C, error was within ±0.05. All the Φ were relative values to the Φ in **1d**.

Results and Discussion

To mimic the photochemical reactions in proteins, photo-labile and fairly rigid oligopeptides were synthesized as follows. As a photosensitive group, benzophenone was used whose $^3n\pi^*$ state had a high reactivity in hydrogen abstraction.[2] To avoid the conjugation of benzophenone with the amide in the oligopeptide spacer, a methylene group was inserted. In order to suppress the conformational flexibility, a well-known β-turn structure was adopted; –L-Pro–Gly– (type II β-turn) and heterochiral –D-Pro–L-Ser– sequences (type II′β-turn).[3] The above requirements led the compounds **1** (see Table 1) which were prepared by ordinary stepwise elongation by use of carbodiimide (dicyclohexylcarbodiimide, DCC or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, EDC) as a coupling reagent and 1-hydroxybenzotriazole (HOBt) as a coupling promotion reagent.

UV spectra of **1** in acetonitrile were identical with each other and also their ^{1}H NMR spectra of benzophenone moiety in **1** showed little change (see Table 2). The results indicate that the benzophenone moiety in **1** should have the same conformation in a solution. Temperature and solvent dependency in chemical shifts of amido proton of **1e** (Fig. 1) showed that the NH in C-terminal of **1e** was shielded from solvent than the NH of glycine and that the C-terminal NH should hydrogen-bond to a carbonyl group in the molecule. Since a Pro–Gly sequence in **1** favored a type II β-turn conformation,[3] **1e** might prefer to take a β-turn structure (Fig. 2).

Upon 313 nm-light irradiation of an acetonitrile solution (ca. 10^{-4} mol dm^{-3}) of **1a**—**e** under deareated atmosphere at 25 °C, **1a**—**e** disappeared; unfortunately, the products were too complex to be determined.[4] The relative quantum yields Φ for disappearance of **1c**–**e** were larger than the Φ in **1a** and **1b** (Table 1). Considering the dependency of the Φ on the length of the alkyl chains and the concentration of **1** being low, the desappearance might be due to an intramolecular hydrogen abstraction from the alkyl chain by the photoexcited benzophenone moiety. The above results and estimation of internuclear distances in β-turned **1** by using the space filling models indicated the following; 1) in the β-turn conformers of **1a** and **1b**, the carbonyl oxygen of benzophenone moiety must be apart from the methylene hydrogen of the C-terminal in the molecule and might hardly abstract the hydrogen and 2) in **1c**–**e**, the hydrogen of the C-terminal might be more easily abstracted intramolecularly (Fig. 2). Compounds **1a** and **1b** might disappear by photoinduced hydrogen abstrac-

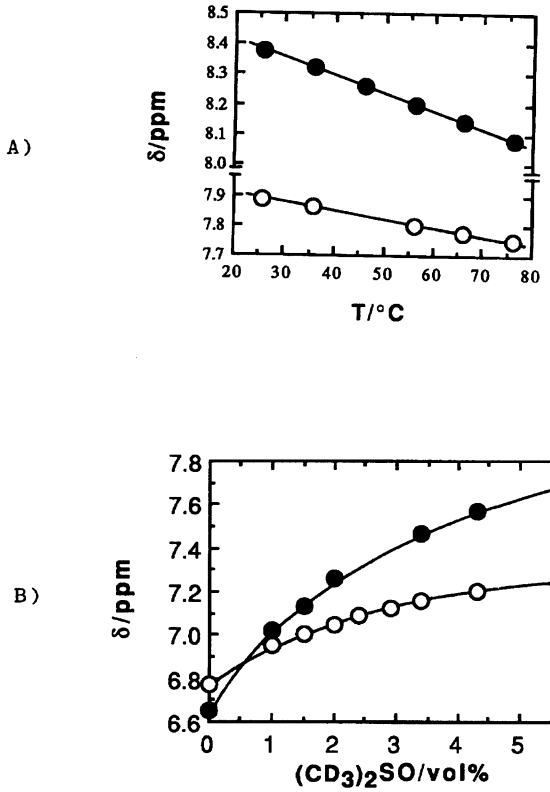


Fig. 1. A) Amido proton chemical shifts δ of ^{1}H NMR spectra of **1e** in $(CD_3)_2SO$ (ca. 10^{-3} mol dm^{-3}) vs. temperature T. B) Amino proton chemical shifts δ of **1e** (ca. 10^{-3} mol dm^{-3}) vs. percentage of $(CD_3)_2SO$ to the $CDCl_3$ solution (vol%) at 25 °C. ●: N**H** in Gly, ○: N**H**C_7H_{15}.

tion in unpreferred random conformations.

When the isomers **1f** and **1g** were irradiated under the above conditions, **1f** disappeared faster than **1g**. The difference might be also ascribed to the distance between the carbonyl and methylene groups (Fig. 2). The carbonyl group of **1f** abstracted easily the methylene hydrogen of C-terminal in the molecule and the C=O of **1g** intramolecularly abstracted the methylene hydrogen of the side-chain of serine with more difficulty. Intramolecular hydrogen bond allowed **1f** and **1g** to form a β-turn structure, which induced such a site selectivity in the intramolecular photoinduced hydrogen abstraction.

In cyclic hydrocarbon and polyether linked molecules, selective intramolecular photochemical reactions have been investigated.[5] We first found the site selectivity in an intramolecular photochemical reaction in β-turned *linear oligopeptide* bridged molecules. Usually, a linear oligopeptide is conformationally flexible but in the oligopeptide to favor a β-turned conformation, the number of possible conformations is reduced. This system shows that β-turned oligopeptides are promising for a biological model system.

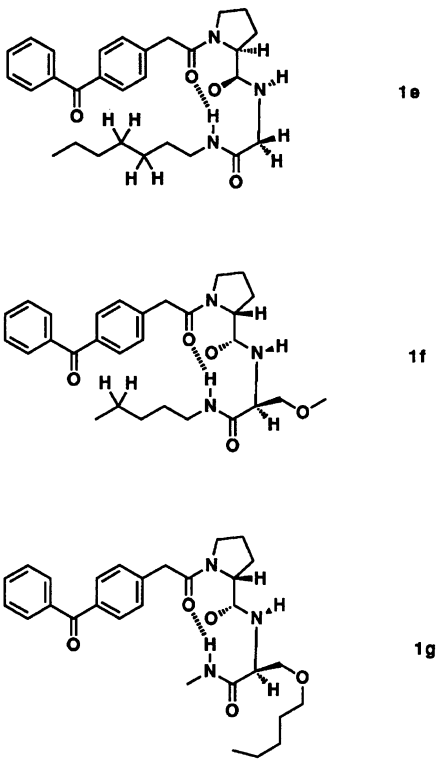
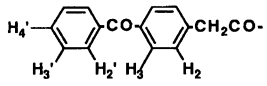


Fig. 2. A schematic β-turn coformation.

Table 2. UV and ^{1}H NMR Data in **1a**—**g**

	λ_{max}/nm[a]		δ_H/ppm[b]				
	ππ*	nπ*	H_2	H_3	H_2'	H_3'	H_4'
1a	256	337	7.35	7.76	7.77	7.47	7.58
1b	257	337	7.36	7.78	7.78	7.48	7.59
1c	257	338	7.37	7.79	7.79	7.48	7.59
1d	256	336	7.37	7.80	7.80	7.48	7.59
1e	257	336	7.37	7.79	7.79	7.48	7.59
1f	256	337	7.34	7.77	7.77	7.47	7.58
1g	256	337	7.35	7.77	7.77	7.47	7.58

a) In CH_3CN, error was within ±1 nm. b) In $CDCl_3$,



Experimental

Apparatus. All melting points were measured with a Yanagimoto micro melting point apparatus and were uncorrected. Ultraviolet and visible spectra were measured with a Shimadzu UV-3000 spectrometer. Infrared spectra were measured with a Horiba FT-300 spectrometer. ^{1}H NMR spectra were recorded on a JEOL JMN-FX 400 instrument; chemical shift (δ) are expressed in parts per million relative to Me_4Si. FAB mass spectra were measured with a JEOL JMS-DX-300 spectrometer; samples were dissolved in $CHCl_3$ and *m*-nitrobenzyl alcohol was used as the matrix. The elemental analyses were performed at the Microanalysis Center of Kyoto University.

Materials. CH_2Cl_2 was washed with H_2SO_4, dis-

tilled, passed through alumina column, and used. CH_3CN was distilled from P_2O_5 under N_2 and used. 4-Methylbenzophenone[6] and *t*-butoxycarbonylglycine *N*-hydroxysucciniimide ester, Boc–Gly–ONSu[7] were synthesized according to the procedure in the literature. Benzyloxycarbonyl-D-proline, Z–D-Pro–OH (or Z–L-Pro–OH) was given by a stirring of an aqueous $NaHCO_3$ solution of Z–Cl and D-Pro (or L-Pro). Other reagents and solvents were commercially available and used without purification.

Synthesis of 4-Benzolyphenylacetic Acid. 4-Methylbenzophenone (3.92 g; 20 mmol) was dissolved in 30 ml CCl_4 and refluxed with vigorous stirring. To the solution was dropwise added a CCl_4 solution (30 ml) of Br_2 (1.2 ml; 24 mmol) upon irradiation with a W-lamp. After a successive reflux (ca. 6h), the solution was condensed in vacuo and the residue was recrystallized from ethanol to afford 4-bromomethylbenzophenone as white needles (2.67 g; 9.7 mmol, 49%), mp 109—110 °C (lit,[8] 112.5 °C).

According to the procedure by Zderic et al.,[8] cyanation of 4-bromomethylbenzophenone, followed by hydrolysis gave 4-benzoylphenylacetic acid; pale yellow crystals (from CH_2Cl_2 and hexane); mp 110—111 °C (lit,[9] 111 °C).

Synthesis of 4-Benzoylphenylacetyl-L-prolylglycine *N*-Alkylamide 1a—e. An ice-chilled CH_2Cl_2 solution (50 ml) of Boc–Gly–ONSu (1.09 g; 4 mmol) and RNH_2 (4 mmol) was stirred for 4 h with exclusion of moisture. After evaporation, the residue was dissolved in EtOAc, which was washed with aq 10% $NaHCO_3$, aq 5% $KHCO_3$, and brine, dried with Na_2SO_4. The solvent was evaporated and Boc–Gly–NHR was given as colorless oil.

Boc–Gly–NHC$_3$H$_7$: 88%; ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, t, J=7 Hz), 1.46 (9H, s), 1.53 (2H, q, J=7 Hz), 3.24 (2H, dt, J=6 and 7 Hz), 3.76 (2H, d, J=6 Hz), 5.08 (1H, br), and 6.05 (1H, br).

Boc–Gly–NHC$_4$H$_9$: 86%; ^{1}H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7 Hz), 1.34 (2H, m), 1.45 (9H, s), 1.48 (2H, m), 3.26 (2H, dt, J=6 and 7 Hz), 3.76 (2H, d, J=6 Hz), 5.20 (1H, br), and 6.18 (1H, br).

Boc–Gly–NHC$_5$H$_{11}$: 92%; ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7 Hz), 1.32 (4H, m), 1.45 (9H, s), 1.50 (2H, m), 3.26 (2H, dt, J=6 and 7 Hz), 3.76 (2H, d, J=6 Hz), 5.11 (1H, br), and 6.07 (1H, br).

Boc–Gly–NHC$_6$H$_{13}$: 87%; ^{1}H NMR ($CDCl_3$) δ=0.87 (3H, t, J=7 Hz), 1.27 (6H, m), 1.44 (9H, s), 1.45 (2H, m), 3.24 (2H, dt, J=6 and 7 Hz), 3.75 (2H, d, J=6 Hz), 5.24 (1H, br), and 6.24 (1H, br).

Boc–Gly–NHC$_7$H$_{15}$: 85%; ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=7 Hz), 1.30 (8H, m), 1.46 (9H, s), 1.50 (2H, m), 3.26 (2H, dt, J=6 and 7 Hz), 3.76 (2H, d, J=6 Hz), 5.08 (1H, br), and 6.02 (1H, br).

An ice-chilled 4 mol cm^{-3} HCl–EtOAc (20 ml) solution of Boc–Gly–NHR (2 mmol) was stirred for 2 h with exclusion of moisture. After evaporation in vacuo, the residue was rinsed with Et_2O and H–Gly–NHR·HCl was given as white deliquescent solids.

To an ice-chilled CH_2Cl_2 solution (20 ml) of the salt and Et_3N (298 μl; 2 mmol) was added Z–L-Pro–OH (548 mg; 2.2 mmol), HOBt·H_2O (368 mg; 2.4 mmol), DCC (454 mg; 2.2 mmol) and the solution was stirred for 4 h with exclusion of moisture. After evaporation, the residue was triturated with EtOAc and dicyclohexylurea (DCU) was removed by filtration. The filtrate was washed with aq 10% $NaHCO_3$, aq 2% HCl, and brine, dried with Na_2SO_4. Flash column chromatography on silica gel with $CHCl_3$ and MeOH as eluents gave Z–L-Pro–Gly–NHR as white solids.

Z–L-Pro–Gly–NHC$_3$H$_7$: 53%; ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, t, J=7 Hz), 1.53 (2H, m), 1.92 (1H, m), 2.02 (1H, m), 2.17 (2H, m), 3.20 (2H, m), 3.57 (2H, m), 3.90 (1H, br-dd), 3.97 (1H, br-dd), 4.26 (1H, m), 5.12 (1H, d, J=12.5 Hz), 5.18 (1H, d, J=12.5 Hz), 6.68 (2H, br), and 7.35 (5H, m).

Z–L-Pro–Gly–NHC$_4$H$_9$: 100%; ^{1}H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7 Hz), 1.3 (2H, m), 1.5 (2H, m), 1.9 (1H, m), 2.0 (1H, m), 2.2 (2H, m), 3.2 (2H, m), 3.6 (2H, m), 3.90 (1H, br-dd), 3.98 (1H, br-dd), 4.25 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.20 (1H, d, J=12.5 Hz), 6.67—6.73 (2H, m), and 7.36 (5H, m).

Z–L-Pro–Gly–NHC$_5$H$_{11}$: 87%; ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=7 Hz), 1.32 (4H, m), 1.50 (2H, m), 1.91 (1H, m), 2.05 (1H, m), 2.18 (2H, m), 3.21 (2H, m), 3.58 (2H, m), 3.90 (1H, br-dd), 3.97 (1H, br-dd), 4.25 (1H, m), 5.10 (1H, d, J=12 Hz), 5.18 (1H, d, J=12 Hz), 6.69 (2H, br), and 7.35 (5H, m).

Z–L-Pro–Gly–NHC$_6$H$_{13}$: 100%; ^{1}H NMR ($CDCl_3$) δ=0.86 (3H, t, J=6.5 Hz), 1.26 (6H, m), 1.50 (2H, m), 1.88 (1H, m), 2.04 (1H, m), 2.16 (2H, m), 3.20 (2H, m), 3.57 (2H, m), 3.87 (1H, dd, J=17.5 and 5.5 Hz), 3.97 (1H, dd, J=17 and 6 Hz), 4.24 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.18 (1H, d, J=12.5 Hz), 6.84 (2H, br), and 7.35 (5H, m).

Z–L-Pro–Gly–NHC$_7$H$_{15}$: 90%; ^{1}H NMR ($CDCl_3$) δ=0.86 (3H, t, J=7 Hz), 1.27 (8H, m), 1.5 (2H, m), 1.9 (1H, m), 2.0 (1H, m), 2.2 (2H, m), 3.2 (2H, m), 3.6 (2H, m), 3.90 (1H, br-dd), 3.97 (1H, br-dd), 4.25 (1H, m), 5.11 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 6.66 (2H, br), and 7.35 (5H, m).

A MeOH suspension (10 ml) of Z–L-Pro–Gly–NHR (1 mmol) and 10% Pd–charcoal (30 mg) was stirred under H_2 atmosphere. After disappearance of the starting material, the catalyst was removed by filtration and the solvent was evaporated to give quantitatively H–L-Pro–Gly–NHR as white solids.

H–L-Pro–Gly–NHC$_3$H$_7$: ^{1}H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7 Hz), 1.52 (2H, heptet, J=7 Hz), 1.72 (2H, m), 1.92 (1H, m), 2.17 (1H, m), 2.92 (1H, dt, J=10 and 6 Hz), 3.03 (1H, dt, J=10 and 7 Hz), 3.22 (2H, m), 3.78 (1H, dd, J=9 and 5 Hz), 3.88 (2H, d, J=6 Hz), 6.18 (1H, br), and 8.21 (1H, br).

H–L-Pro–Gly–NHC$_4$H$_9$: ^{1}H NMR ($CDCl_3$) δ=0.91 (3H, t, J=7 Hz), 1.33 (2H, heptet, J=7 Hz), 1.47 (2H, quintet, J=7 Hz), 1.72 (2H, quintet, J=7 Hz), 1.91 (1H, m), 2.15 (1H, m), 2.92 (1H, dt, J=10 and 6 Hz), 3.02 (1H, dt, J=10 and 7 Hz), 3.24 (2H, m), 3.78 (1H, dd, J=9 and 4 Hz), 3.87 (2H, d, J=6 Hz), 6.23 (1H, br), and 8.21 (1H, br).

H–L-Pro–Gly–NHC$_5$H$_{11}$: ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7 Hz), 1.30 (4H, m), 1.49 (2H, quintet, J=7 Hz), 1.72 (2H, m), 1.92 (1H, m), 2.15 (1H, m), 2.93 (1H, dt, J=10 and 6 Hz), 3.03 (1H, dt, J=10 and 7 Hz), 3.23 (2H, m), 3.79 (1H, dd, J=5 and 4 Hz), 3.87 (2H, d, J=6 Hz), 6.18 (1H, br), and 8.20 (1H, br).

H–L-Pro–Gly–NHC$_6$H$_{13}$: ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=7 Hz), 1.28 (6H, m), 1.48 (2H, quintet, J=7 Hz), 1.71 (2H, quintet, J=7 Hz), 1.91 (1H, heptet, J=6 Hz), 2.15 (1H, ddt, J=13, 9, and 8 Hz), 2.92 (1H, dt, J=10 and 6

Hz), 3.02 (1H, dt, J=10 and 7 Hz), 3.23 (2H, nonatet, J=6 Hz), 3.77 (1H, dd, J=9 and 5 Hz), 3.87 (2H, d, J=6 Hz), 6.22 (1H, br), and 8.21 (1H, br).

H–L-Pro–Gly–NHC$_7$H$_{15}$: ^{1}H NMR ($CDCl_3$) δ=0.87 (3H, t, J=7 Hz), 1.28 (8H, m), 1.48 (2H, m), 1.71 (2H, quintet, J=7 Hz), 1.91 (1H, m), 2.15 (1H, ddt, J=13, 9, and 7.5 Hz), 2.92 (1H, dt, J=10 and 6 Hz), 3.02 (1H, dt, J=10 and 7 Hz), 3.23 (2H, m), 3.77 (1H, dd, J=9.5 and 5 Hz), 3.87 (2H, d, J=6 Hz), 6.22 (1H, br), and 8.21 (1H, br).

An ice-chilled CH_2Cl_2 solution (10ml) of H–L-Pro–Gly–NHR (1 mmol), 4-benzoylphenylacetic acid (240 mg; 1 mmol), HOBt·H_2O (184 mg; 1.2 mmol), and DCC (227 mg; 1.1 mmol) was stirred in the dark under N_2 overnight. After removal of precipitated DCU, the solution was washed with aq 10% $NaHCO_3$, aq 2% HCl, and brine, dried with Na_2SO_4. 4-Benzoylphenylacetyl-L-prolylglycine *N*-alkylamide was isolated by using flash column chromatography on silica gel with $CHCl_3$ and MeOH as eluents. Recrystallization from EtOAc and hexane gave an analytically pure sample.

4-Benzoylphenylacetyl-L-prolylglycine *N*-Propylamide (1a) : 50%; UV (CH_3CN) 256 and 332 nm; IR (KBr) 3350, 3290 (NH), 1658, and 1637 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.79 (3H, t, J=7 Hz), 1.38 (2H, heptet, J=7 Hz), 1.97 (1H, m), 2.15 (3H, m), 3.09 (2H, dt, J=6 and 8 Hz), 3.57 (1H, dt, J=10 and 7 Hz), 3.68 (1H, dd, J=17 and 5 Hz), 3.68 (1H, m), 3.77 (2H, s), 4.09 (1H, dd, J=17 and 7 Hz), 4.31 (1H, dd, J=7 and 5 Hz), 7.00 (2H, br), 7.35 (2H, d, J=8.5 Hz), 7.47 (2H, t, J=8 Hz), 7.58 (1H, tt, J=7 and 1.5 Hz), 7.76 (2H, d, J=8 Hz), and 7.77 (2H, d, J=8 Hz); MS m/z 436 (MH$^+$). Found: C, 68.85; H, 6.68; N, 9.52%. Calcd for $C_{25}H_{29}N_3O_4$: C, 68.95; H, 6.71; N, 9.65%.

4-Benzoylphenylacetyl-L-prolylglycine *N*-Butylamide (1b) : 46%; UV (CH_3CN) 256.5 and 337 nm; IR (KBr) 3338, 3315 (NH), 1655, and 1639 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, J=7 Hz), 1.24 (2H, heptet, J=7 Hz), 1.38 (2H, quintet, J=7 Hz), 1.98 (1H, m), 2.09 (1H, m), 2.19 (2H, m), 3.15 (2H, m), 3.61 (1H, m), 3.67 (1H, m), 3.70 (1H, dd, J=17 and 5 Hz), 3.79 (2H, s), 4.12 (1H, dd, J=17 and 7 Hz), 4.33 (1H, dd, J=8 and 4 Hz), 6.74 (1H, br), 6.86 (1H, br), 7.36 (2H, d, J=8 Hz), 7.48 (2H, t, J=8 Hz), 7.59 (1H, t, J=7 Hz), and 7.78 (2H+2H, d, J=8 Hz); MS m/z 450 (MH$^+$). Found: C, 69.37; H, 6.98; N, 9.30%. Calcd for $C_{26}H_{31}N_3O_4$: C, 69.45: H, 6.96; N, 9.35%.

4-Benzoylphenylacetyl-L-prolylglycine *N*-Pentylamide (1c) : 33%; UV (CH_3CN) 256.5 and 337.5 nm; IR (KBr) 3327 (NH), 1655, and 1637 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, J=7 Hz), 1.24 (4H, m), 1.43 (2H, quintet, J=7 Hz), 2.01 (1H, m), 2.14 (1H, m), 2.21 (2H, m), 3.15 (2H, m), 3.59 (1H, m), 3.68 (1H, m), 3.72 (1H, dd, J=17 and 5 Hz), 3.79 (2H, s), 4.12 (1H, dd, J=17 and 7 Hz), 4.36 (1H, dd, J=8 and 4 Hz), 6.70 (1H, br), 6.82 (1H, br), 7.37 (2H, d, J=8 Hz), 7.48 (2H, t, J=8 Hz), 7.59 (1H, t, J=8 Hz), and 7.79 (2H+2H, d, J=8 Hz); MS m/z 464 (MH$^+$). Found: C, 69.66; H, 7.11; N, 9.02%. Calcd for $C_{27}H_{33}N_3O_4$: C, 69.94; H, 7.19; N, 9.07%.

4-Benzoylphenylacetyl-L-prolylglycine *N*-Hexylamide (1d) : 75%; UV (CH_3CN) 256 and 334 nm; IR (KBr) 3334, 3290 (NH), 1662, and 1637 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, J=7 Hz), 1.22 (6H, m), 1.41 (2H, quintet, J=7 Hz), 1.98 (1H, m), 2.10 (1H, m), 2.22 (2H, m), 3.15 (2H, m), 3.58 (1H, m), 3.69 (1H, m), 3.79 (2H, s), 3.72 (1H, dd, J=17 and 5 Hz), 4.11 (1H, dd, J=17 and 7 Hz), 4.35 (1H, dd, J=8 and 4 Hz), 6.70 (1H, br), 6.82 (1H, br), 7.37 (2H, d, J=8 Hz), 7.48 (2H, t, J=7.5 Hz), 7.59 (1H, t, J=7.5 Hz), and 7.80 (2H+2H, d, J=8 Hz); MS m/z 478 (MH$^+$). Found: C, 70.39; H, 7.43; N, 8.77%. Calcd for $C_{28}H_{35}N_3O_4$: C, 70.42; H, 7.39; N, 8.80%.

4-Benzoylphenylacetyl-L-prolylglycine *N*-Heptylamide (1e) : 62%; UV (CH_3CN) 257 and 336 nm; IR (KBr) 3354, 3294 (NH), 1655, and 1635 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, J=7 Hz), 1.98 (8H, m), 1.41 (2H, m), 2.0 (1H, m), 2.1 (1H, m), 2.2 (2H, m), 3.14 (2H, m), 3.59 (1H, m), 3.69 (1H, m), 3.72 (1H, dd, J=17 and 5.5 Hz), 3.79 (2H, s), 4.11 (1H, dd, J=17 and 7 Hz), 4.36 (1H, dd, J=8 and 4 Hz), 6.71 (1H, br), 6.81 (1H, br), 7.37 (2H, d, J=8 Hz), 7.48 (2H, t, J=8 Hz), 7.59 (1H, t, J=8 Hz), and 7.79 (2H+2H, d, J=8 Hz); MS m/z 492 (MH$^+$). Found: C, 70.74; H, 7.62; N, 8.52%. Calcd for $C_{29}H_{37}N_3O_4$: C, 70.84; H, 7.60; N, 8.55%.

Synthesis of 4-Benzoylphenylacetyl-D-prolyl-*O*-methyl-L-serine *N*-Pentylamide (1f) : The coupling of Boc-L-Ser–OH and pentylamine by EDC–HOBt in CH_2Cl_2 gave Boc-L-Ser–NHC$_5$H$_{11}$ as white solids (84%): mp 70—72 °C; ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7 Hz), 1.28—1.32 (4H, m), 1.46 (9H, s), 1.50 (2H, quintet, J=7 Hz), 3.07 (1H, br), 3.19—3.30 (2H, m), 3.63 (1H, br-t), 4.09 (1H, q, J=7 Hz), 4.14 (1H, br), 5.55 (1H, br), and 6.63 (1H, br).

The methylation of Boc-L-Ser–NHC$_5$H$_{11}$ by CH_2N_2–SiO_2 in Et_2O[9] and purification by silica-gel chromatography (CH_2Cl_2 as an eluent) gave Boc-L-Ser(Me)–NHC$_5$H$_{11}$ as colorless oil (56%); ^{1}H NMR ($CDCl_3$) δ=0.83 (3H, t, J=7 Hz), 1.21—1.29 (4H, m), 1.39 (9H, s), 1.44 (2H, quintet, J=7 Hz), 3.16 (1H, dq, J=13 and 7 Hz), 3.23 (1H, dq, J=13 and 7 Hz), 3.31 (3H, s), 3.41 (1H, dd, J=9 and 6 Hz), 3.71 (1H, dd, J=9 and 4 Hz), 4.14 (1H, br), 5.42 (1H, br), and 6.48 (1H, br-t).

The EDC–HOBt coupling of Z-D-Pro–OH and H-L-Ser(Me)–NHC$_5$H$_{11}$ (deprotection of Boc-L-Ser(Me)–NHC$_5$H$_{11}$ by 4 mol dm^{-3} HCl-1,4-dioxane and successive neutralization by Et_3N) in CH_2Cl_2 gave Z-D-Pro-L-Ser(Me)–NHC$_5$H$_{11}$ as white needles (75%; CH_2Cl_2 and hexane); mp 119—122 °C; ^{1}H NMR ($CDCl_3$) δ=0.87 (3H, br-t, J=7 Hz), 1.25—1.30 (4H, m), 1.52 (2H, br-quintet, J=7 Hz), 1.58 (9H, s), 1.89 (1H, br-q, J=6 Hz), 2.14 (3H, m), 3.19 (1H, dq, J=13 and 7 Hz), 3.23 (1H, dq, J=13 and 7 Hz), 3.36 (3H, s), 3.48 (1H, dd, J=9.5 and 4 Hz), 3.51—3.56 (1H, m), 3.58—3.63 (1H, m), 4.03 (1H, dd, J=10 and 2 Hz), and 4.13 (1H, t, J=5 Hz), 4.49 (1H, br-t, J=4 Hz), 5.06 (1H, d, J=12 Hz), 5.19 (1H, d, J=12 Hz), 6.77 (1H, d, J=8.5 Hz), 7.24 (1H, br), and 7.34 (5H, m).

The EDC–HOBt coupling of 4-benzoylphenylacetic acid and H-D-Pro-L-Ser(Me)–NHC$_5$H$_{11}$ (hydrogenation of Z-D-Pro-L-Ser(Me)–NHC$_5$H$_{11}$) in CH_2Cl_2 gave 4-benzoylphenylacetyl-D-prolyl-*O*-methyl-L-serine *N*-pentylamide. By SiO_2-chromatography (CH_2Cl_2–MeOH) and recrystallization (AcOEt–hexane) was given an analytically pure sample (69%); white needles; mp 131—133 °C; UV (CH_3CN) 256 and 337 nm; IR (KBr) 3303, 3271 (NH), 1655, and 1641 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.80 (3H, t, J=7 Hz), 1.12—1.25 (4H, m), 1.37 (2H, quintet, J=7 Hz), 1.96 (1H, d-quintet, J=12 and 7 Hz), 2.13 (1H, dt, J=2 and 7 Hz), 2.15 (1H, t, J=7 Hz), 2.26 (1H, d-hextet, J=5 and 7 Hz), 3.06 (1H, ddt, J=13, 6, and 7 Hz), 3.16 (1H, ddt, J=13,

6, and 7 Hz), 3.33 (3H, s), 3.48 (1H, dd, J=9 and 4 Hz), 3.59 (1H, dt, J=9 and 7 Hz), 3.69 (1H, dt, J=9 and 7 Hz), 3.76 (2H, s), 4.02 (1H, dd, J=9 and 3 Hz), 4.25 (1H, t, J=7 Hz), 4.44 (1H, dt, J=8 and 4 Hz), 6.76 (1H, d, J=9 Hz), 7.34 (2H, d, J=8 Hz), 7.37 (1H, t, J=6 Hz), 7.47 (2H, t, J=7.5 Hz), 7.58 (1H, tt, J=7.5 and 1.5 Hz), 7.77 (2H, d, J=8 Hz), and 7.77 (2H, dd, J=1.5 and 7.5 Hz); MS m/z 508 (MH^+). Found: C, 68.52; H, 7.41; N, 8.25%. Calcd for $C_{29}H_{37}N_3O_5$: C, 68.62; H, 7.35; N, 8.28%.

Synthesis of 4-Benzoylphenylacetyl-D-prolyl-*O*-pentyl-L-serine *N*-Methylamide (1g) : The coupling of Boc–L-Ser–OH and pentyl iodide by NaH in *N*,*N*-dimethylformamide[10] gave Boc-L-Ser(C_5H_{13})–OH as colorless oil. Addition of an equimolar amount of cyclohexylamine to an ether solution of Boc–L-Ser(C_5H_{13})–OH and successive addition of hexane gave a pure salt, Boc–L-Ser(C_5H_{13})–OH·$C_6H_{11}NH_2$ as white needles (49%); mp 115—118 °C; ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7 Hz), 1.14—1.36 (4H+5H, m), 1.44 (9H, s), 1.53 (2H, quintet, J=7 Hz), 1.63 (1H, br-d, J=13 Hz), 1.77 (2H, br-d, J=10 Hz), 1.98 (2H, br-d, J=10 Hz), 2.92 (1H, tt, J=10.5 and 4 Hz), 3.42 (2H, t, J=7 Hz), 3.68 (2H, br-dd, J=9.5 and 3 Hz), 3.81 (2H, dd, J=9.5 and 4 Hz), 4.07 (1H, dt, J=7 and 3.5 Hz), and 5.46 (1H, d, J=6 Hz).

The EDC coupling of Boc–L-Ser(C_5H_{13})–OH (CH_2Cl_2 extraction from aq 5% $KHSO_4$ solution of Boc–L-Ser(C_5H_{13})–OH·$C_6H_{11}NH_2$) and $MeNH_2$ ($MeNH_2$·HCl–Et_3N) in CH_2Cl_2, and purification by SiO_2-chromatography (CH_2Cl_2) gave Boc–L-Ser(C_5H_{13})–$NHCH_3$ as colorless oil (17%); ^{1}H NMR ($CDCl_3$) δ=0.88 (3H, t, J=7 Hz), 1.24—1.36 (4H, m), 1.45 (9H, s), 1.55 (2H, quintet, J=7 Hz), 2.83 (3H, d, J=5 Hz), 3.40—3.50 (3H, m), 3.81 (1H, dd, J=4 and 9 Hz), 4.19 (1H, br), 5.38 (1H, br), and 6.47 (1H, br).

The EDC–HOBt coupling of Z–D-Pro–OH and H–L-Ser(C_5H_{13})–$NHCH_3$ (derived from Boc–L-Ser(C_5H_{13})–$NHCH_3$) in CH_2Cl_2 gave Z–D-Pro–L-Ser(C_5H_{13})–$NHCH_3$ as white solids (83%); mp 80—82 °C; (CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7 Hz), 1.23—1.37 (4H, m), 1.55 (2H, quintet, J=7 Hz), 1.85—1.93 (1H, m), 2.14 (3H, m), 2.74 (2H, d, J=5.5 Hz), 3.43 (1H, d, J=6 Hz), 3.46 (1H, d, J=6 Hz), 3.50—3.56 (2H, m), 3.59—3.64 (1H, m), 4.04 (1H, dd, J=9 and 2 Hz), 4.13 (1H, t, J=6 Hz), 4.48 (1H, br-t, J=5 Hz), 5.09 (1H, d, J=12.5 Hz), 5.18 (1H, d, J=12.5 Hz), 6.77 (1H, d, J=8.5 Hz), and 7.35 (5H, m).

The EDC–HOBt coupling of 4-benzoylphenylacetic acid and H–D-Pro–L-Ser(C_5H_{13})–$NHCH_3$ (derived from Z–D-Pro–L-Ser(C_5H_{13})–$NHCH_3$) in CH_2Cl_2, purification by SiO_2-chromatography (CH_2Cl_2–MeOH), and recrystallization (EtOAc–hexane) afforded an analytically pure 4-benzoylphenylacetyl-D-prolyl-*O*-pentyl-L-serine *N*-methylamide as white needles (66%): mp 112—114 °C; UV (CH_3CN) 256 and 337 nm; IR (KBr) 3327, 3288—3294 (NH), 1622, and 1633 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=0.87 (3H, t, J=7 Hz), 1.21—1.34 (4H, m), 1.52 (2H, quintet, J=7 Hz), 1.97 (1H, d-quintet, J=12 and 7 Hz), 2.11 (1H, dd, J=13 and 7 Hz), 2.18 (1H, dd, J=13 and 7 Hz), 2.28 (1H, septet, J=6.5 Hz), 2.65 (3H, d, J=5 Hz), 3.40 (1H, dt, J=9.5 and 7 Hz), 3.43 (1H, dt, J=9.5 and 7 Hz), 3.52 (1H, dd, J=9.5 and 4 Hz), 3.61 (1H, dt, J=9 and 7 Hz), 3.71 (1H, dt, J=9.5 and 7 Hz), 3.76 (1H, d, J=15.5 Hz), 3.80 (1H, d, J=15.5 Hz), 4.04 (1H, dd, J=9 and 3 Hz), 4.25 (1H, t, J=7 Hz), 4.44 (1H, br-dt, J=8 and 4 Hz), 6.73 (1H, d, J=8.5 Hz), 7.35 (2H, d, J=8 Hz), 7.45 (1H, br), 7.47 (2H, t, J=8 Hz), 7.58 (1H, tt, J=8 and 1 Hz), 7.77 (2H, dd, J=8 and 1 Hz), and 7.77 (2H, d, J=8 Hz); MS m/z 508 (MH^+). Found: C, 68.39; H, 7.33; N, 8.31%. Calcd for $C_{29}H_{37}N_3O_5$: C, 68.62; H, 7.35; N, 8.28%.

Determination of Relative Quantum Yield for Disappearance of Starting Benzophenones 1. A 300 W high pressure mercury projector lamp was used as a light source. A combination of Corning 7-54 glass filter and an aqueous K_2CrO_4 solution filter was used for isolation of 313 nm light.[11] An CH_3CN solution (10^{-4} mol dm^{-3}) of starting benzophenones **1** in a Pyrex tube under deareated conditions (freeze-pump-thaw) was irradiated; the conversion of **1** was less than 10%. The amount of **1** disappeared was determined by measuring the amount of **1** before and after irradiation by HPLC (Cosmosil $5C_{18}$ column) with 30% H_2O and 70% MeOH as eluents. 1-Methylnaphthalene was used for a standard. Each quantum yield was an average value of more than two experiments. The value in **1d** was a standard for determination of the relative quantum yield.

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