Note

Photochemical Oxidative Dimerization of Capsaicin in an Aqueous Solution

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Capsaicin (CAP) is a pungent principle of hot red peppers, which are used as an important spice for enhancing the palatability of food, and medicinally as a counterirritant. There have been studies showing that CAP caused the induction of a warming action,¹⁾ promotion of the peristaltic reflex,²⁾ and an increase in gastric acid secretion.³⁾ CAP can be used as a constituent of drinks⁴⁾ with vitamins such as riboflavin (RF) and ascorbic acid (Asc).⁵⁾ In this paper, we present the oxidative dimerization⁶⁾ of CAP by the action of a RF/RFH₂ photo-redox system (RFH₂: 1,5-dihydroriboflavin) in which RF acted as a photocatalyst.^{7,8)}

Commercially available CAP was purified by preparative reverse-phase HPLC (CAPCELL PAK C-18 (AG), 5 μ m; 10 mm $\times$ 250 mm and 10 mm $\times$ 20 mm) with elution by MeOH–H₂O (60:40). Pure CAP was collected from those fractions with $k' = 7.6$. RF (4 mg, 0.01 mmol) in 400 ml of 0.05 M citrate buffer (pH 5.0) and ethyl alcohol solution of CAP (30 mg, 0.1 mmol) in a 9:1 ratio was irradiated with a 400 W high-pressure mercury lamp (Riko UVL-400HA) through a copper nitrate solution filter (≥ 334 nm) at $30 \pm 2^\circ\text{C}$. After 20 min of irradiation, finely dispersed solids had formed, which were collected by filtration, washed with water and ethyl acetate–hexane (4:1), and then recrystallized from benzene–ethyl acetate–ethanol (1:3:1) in an 18 mg yield (60%), mp 160–161°C (**1**). IR ν_{max} (KBr) cm^{-1} : 3345, 3300, 2955, 1640, 1550 and 1265. FD-MS m/z : 608 (M^+ , 100%). Anal. Found: C, 70.88; H, 8.32; N, 4.76. Calcd. for $\text{C}_{36}\text{H}_{52}\text{N}_2\text{O}_6$: C, 71.02; H, 8.61; N, 4.60%. The elemental and FD-MS analysis of **1** corresponded to $\text{C}_{36}\text{H}_{52}\text{N}_2\text{O}_6$, i.e., two molecules of CAP minus two hydrogen atoms. The ^1H -NMR signals for the 8-methylnon-(*E*)-6-enamide moiety of **1**, which is the same as that of CAP,⁹⁾ were assigned on the basis of ^1H - ^1H COSY data (Table I). The coupling constants for the two aromatic protons (H-2 (δ 6.79, d, $J = 2.0$) and H-6 (δ 6.83, d, $J = 2.0$)) in **1** revealed the presence of meta ring protons. NOEs were observed with the two aromatic protons (H-2 and H-6) upon irradiating the benzylic protons (H-8) at δ 4.36 (Fig. 1). The spatial proximity among the methoxy protons (H-7, δ 3.90 (s)) and aromatic proton (H-6) was also clarified by NOE experiments.

Table I. ^1H -(400 MHz) AND ^{13}C -(100 MHz) NMR SPECTRAL ASSIGNMENTS OF COMPOUND **1**

Chemical shifts (δ) are expressed in ppm in CDCl_3 , and multiplicities and J -values in Hz; a Bruker AM-400 spectrometer was used.

C (and/or H)	^{13}C	^1H
1	130.3 (s)	
2	122.8 (d)	6.79 (d, 2.0)
3	124.0 (s)	
4	142.2 (s)	
5	147.4 (s)	
6	110.3 (d)	6.83 (d, 2.0)
7	56.2 (q)	3.90 (s)
8	43.6 (t)	4.36 (d, 5.7)
9	172.7 (s)	
10	36.7 (t)	2.19 (t, 7.6)
11	25.3 (t)	1.64 (m)
12	29.3 (t)	1.37 (m)
13	32.2 (t)	1.98 (dt, 5.7, 7.5)
14	126.5 (d)	5.30 (dt, 15.4, 5.7)
15	138.0 (d)	5.37 (dd, 5.6, 15.4)
16	31.0 (d)	2.23 (m)
17	22.7 (q)	0.94 (d, 6.8)
18	22.7 (q)	0.94 (d, 6.8)
NH		5.88 (br. t, 5.7)
OH		6.11 (br. s)

Fig. 1. Structure of **1**.

— represents NOE (%).

^{13}C -NMR signals of **1** were assigned on the basis of their chemical shifts, ^1H - ^{13}C COSY data, and by the ^1H - ^{13}C long-range COSY NMR spectrum of **1**. Cross peaks between C-8 (δ 43.6 (t)) and the two kinds of protons (H-2 and H-6), and between C-4 (δ 142.2 (s)) and the same two protons were observed in the ^1H - ^{13}C long-range COSY NMR spectrum of **1**. Accordingly, the 3,3'-bi-4-hydroxy-5-methoxybenzyl moiety, which is also the partial structure of dehydrodieugenol,¹⁰⁾ should exist. From these observations, the structure of **1** was determined to be N,N'-(3,3'-bi-4-hydroxy-5-methoxybenzyl)di-8-methylnon-(*E*)-6-enamide (Fig. 1). The ^1H - and ^{13}C -NMR signals of **1** were reasonably assigned as shown in Table I.

Photochemical oxidative dimerization of CAP did not proceed either in the presence of Asc or in the absence of oxygen.

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