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A Novel Intramolecular Cyclization Product of (+)-Catechin under Radical Reaction

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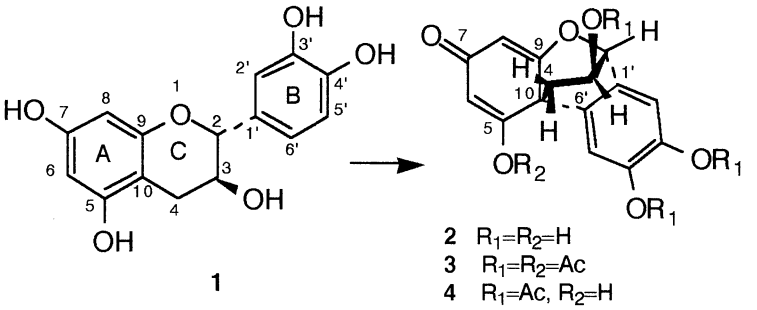
From (+)-catechin under radical reaction with 2,2'-azobis(2-methylpropionitrile), a novel intramolecular cyclization product was isolated and its structure has been characterized to be 2,4',5',12-tetrahydroxy-9,10-benzo-7-oxatricyclo[6.2.2.0^{1,6}]dodeca-2,5,9-trien-4-one by the spectroscopic analyses and the chemical transformation.

In the course of our works on the antioxidative mechanism of natural antioxidants,[1-3] we have reported two major oxidation products of (+)-catechin (**1**) during the autoxidation of unsaturated lipid under photoirradiation. Successively, the reaction products of **1** undergoing a radical scavenging reaction with 2,2'-azobis(2-methylpropionitrile) (AIBN), have been studied and the major product (**2**) has been found to be an intramolecular cyclized derivative of **1** having a unique structure. In this paper we wish to report the isolation and identification of **2**. (+)-Catechin (**1**) (1.0 g) and AIBN (1.13 g) were dissolved in ethyl acetate-methanol (8:2) and the mixture was irradiated with fluorescent lamps (30 W x 2) at 40 °C for 10 days. The solvent was removed in vacuo, the resulting residue was chromatographed on a Sephadex LH-20 column by eluting with ethanol-hexane (7:3). The fraction containing **2** was further purified by preparative HPLC using an ODS column, and **2** was obtained as a white amorphous powder (93 mg) in 9.3% yield.[4] Compound **2** was found to have a molecular formula $C_{15}H_{12}O_6$, based on the FD-MS [m/z; 288 (M^+)] and the elemental analysis (Found : C, 58.83; H, 4.87%. Calcd for $C_{15}H_{12}O_6 \cdot H_2O$: C, 58.83; H, 4.61%). The peak assignments of the ^{1}H and ^{13}C NMR spectra were determined based on 2D NMR (COSY and COLOC) spectra. From the data in ^{1}H and ^{13}C NMR spectra of **2**, the fact could be deduced that the B ring of **1**, the aromatic ring moiety, and the C ring of **1**, the six-membered hetero ring, were maintained in **2**. And, the only two aromatic protons as singlet peaks, showed the presence of a substituent on the 6'-position carbon in the B ring. But, the conformation of the C ring of **2** was not similar to that of **1**, because the ^{1}H-^{1}H coupling constants in the C ring of **2** were different from the corresponding ones of **1**. Furthermore, the ^{1}H and ^{13}C NMR spectra showed a trisubstituted olefin signals [δ_C 175.1(s), 99.2(d); δ_H 5.40(s)]. In the COLOC of **2**,[5] long-range interactions ($^{2}J_{C\text{-}9,\ H\text{-}8}$, $^{3}J_{C\text{-}9,\ H\text{-}2}$, $^{3}J_{C\text{-}9,\ H\text{-}4\alpha}$ and $^{3}J_{C\text{-}9,\ H\text{-}4\beta}$) were observed between C-9 and H-8, C-9 and H-2, C-9 and H-4α, and also C-9 and H-4β, respectively. The signal at δ_C 190.6(s) in the ^{13}C NMR spectrum was considered



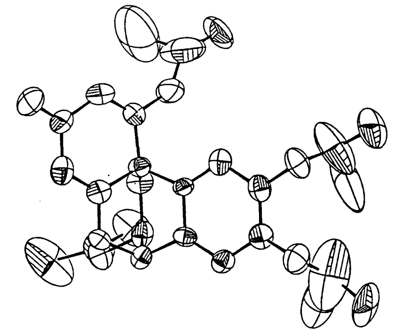


Fig. 1. Perspective drawing of **3**.

2 to have an α,β-unsaturated ketone, which was also supported by the absorption band ν 1705 and 1673 cm^{-1}. These observations could be suspected that the aromatic carbon on C-5 or C-7 in the A ring of **1** was converted to the ketone by a dehydrogenation. Moreover, the signal at δ_C 49.6(s), assigned to an alkane carbon, indicated that the aromatic carbon corresponding C-10 of **1** was converted to sp^3 carbon. Furthermore, in the ^{13}C NMR spectrum of **2**, 14 signals were observed and one signal was not observed. These fact deduced that **2** had a keto-enol moiety. Acetylation of **2** (112 mg) with acetic anhydride/pyridine afforded two acetyl derivatives. From the data of the SIMS, one of them was a tetra-*O*-acetyl derivative (**3**) (45.5 mg) [m/z; 457 $(MH)^+$] and the other was a tri-*O*-acetyl derivative (**4**) (61.5 mg) [m/z; 415 $(MH)^+$]. The NMR spectra of **3** showed two trisubstituted olefin signals [δ_C 157.6(s), 120.1(d); δ_H 6.52 (d, *J*=1.3 Hz) and δ_C 169.4(s), 102.8(d); δ_H 5.76 (d, *J*=1.3 Hz)], and in comparison with that of **4** the signal at δ_C 157.6(C-5) was identified with the carbon bearing the acetoxyl group. Moreover, in the COLOC of **3**, long-range interactions ($^3J_{C\text{-}10,\,H\text{-}3}$, $^3J_{C\text{-}10,\,H\text{-}6}$, $^3J_{C\text{-}10,\,H\text{-}8}$ and $^3J_{C\text{-}10,\,H\text{-}5'}$) were observed between C-10 and H-3, C-10 and H-6, C-10 and H-8, and also C-10 and H-5', respectively. To confirm the structure and the absolute configuration, an X-ray crystallographic analysis of **3** was carried out. Figure 1 shows a perspective drawing of the structure of **3**.[6] Thus, the structure of **2** was finally determined as shown in scheme and can be represented by 2,4',5',12-tetrahydroxy-9,10-benzo-7-oxatricyclo[6.2.2.$0^{1,6}$]dodeca-2,5,9-trien-4-one. Investigations of other products, especially a keto-enol tautomer of **2**, and the antioxidative mechanism of **1** will be reported in the nearest further as a full paper.

References

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4) **2**: Mp 139.5-140.5 °C (decomp.); $[\alpha]_D^{25}$ +218.0° (*c* 0.0337, MeOH); UV (MeOH) λmax nm (ε) 211 (22,600), 248 (21,300), 286 (7,280), 350sh (790); IR ν (KBr) 3510, 3200, 2710, 1705, 1673 cm^{-1}; ^1H NMR (270 MHz, MeOH-*d4*) δ 1.29 (dd, *J*=13.4, 2.6 Hz, H-4α), 2.55 (dd, *J*=13.4, 9.3 Hz, H-4β), 3.95 (ddd, *J*=9.3, 2.6, 1.5 Hz, H-3), 5.31 (d, *J*=1.5 Hz, H-2), 5.40 (s, H-8), 6.71 (s, H-5'), 6.80 (s, H-2'); ^{13}C NMR (67.8 MHz, MeOH-*d4*) δ 37.4 (t, C-4), 49.6 (s, C-10), 67.7 (d, C-3), 82.6 (d, C-2), 99.2 (d, C-8), 112.2 (d, C-5'), 112.9 (d, C-2'), 127.0 (s, C-1'), 127.4 (s, C-6'), 146.0 (s, C-4'), 147.6 (s, C-3'), 175.1 (s, C-9), 176.6 (s, C-5), 190.6 (s, C-7).

5) The number of the carbon skeleton of **2** in this text is applied correspondingly to that of **1**.

6) Crystal data will be described in detail elsewhere.

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