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The photochemical reaction between 9-vinyladenine (**2**) and diethyl fumarate (**4**) gave an unusual photoadduct, epimers **4** and **5**, probably derived from attack of the vinyl group on N-3 and reaction of diethyl fumarate on N-9 and N-6.

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During our work related to the synthesis of Cyclobut-A (**1**) [1], a new antiviral agent active against human immunodeficiency virus (HIV) [2], we have examined the possibility to obtain the four-membered ring of Cyclobut-A by a photochemical (2+2) cycloaddition between 9-vinyladenine (**2**) and diethyl fumarate (**3**) [3]. 9-Vinyladenine can be prepared from adenine by reaction with sodium hydride and 1-bromo-2-chloroethane [4] to 9-chloroethyladenine [5], and subsequent conversion to 9-vinyladenine using sodium methoxide [6].

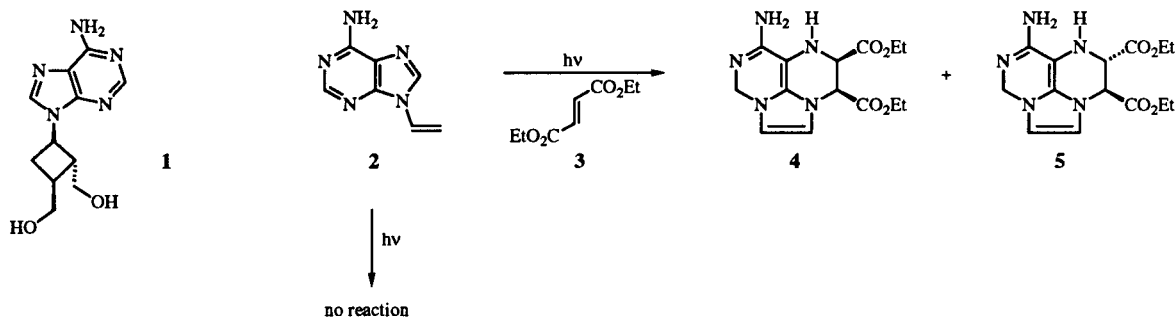
Photochemical irradiation of **2** in the presence of diethyl fumarate and acetonitrile at 254 nm in a Rayonet apparatus for 71 hours showed the formation of two reaction products on tlc. Chromatographic purification of the reaction mixture gave 1:1 mixture of two compounds **4** and **5** in quantitative yields.

The ¹H-nmr spectra of **4** and **5** (DMSO-d₆) showed two AB systems. The first showed absorptions at δ 6.73 and at 6.36 ppm (*J* = 15.7 Hz), while the second absorbed at δ 6.24 and at 5.71 ppm (*J* = 12.0 Hz). These signals can be assigned to the olefinic protons in **4** and **5**. Probably, the first AB system (*J* = 15.7 Hz) can be attributed to **4**. Other signals in the ¹H-nmr spectra were recorded at the same chemical shifts for **4** and **5**. In particular, the ¹H-nmr spectra showed signals at δ 4.1 (q, OCH₂CH₃), 3.8 (NH signals), 3.44 (m, N-CH₂-N), 2.36 (m, CH-CO₂Et), and 1.2 ppm (t, OCH₂CH₃). The mass spectra showed peaks at *m/z* 307,

149, 128, 117, 101, 99, 89 and 71. Nevertheless, the molecular weight of **4** and **5** was obtained performing the spectra at 5 eV. Under these conditions only peaks at *m/z* 321, 307, and 293 were obtained. These data are in agreement with the proposed structure.

It is noteworthy that no reaction occurred when the irradiation was performed without diethyl fumarate. This behaviour probably involves the attack of the excited adenine derivative on fumarate to have any reaction. Furthermore, both adenine and 9-ethyladenine did not react under the same reaction conditions. Therefore, the reaction requires the presence of the vinyl group to occur.

Adenine is a poor photoreactive compound, considering all the classes of purines that can react with oxygen [7] or with alcohols [8-10] to give the corresponding photoadducts. Furthermore, halo derivatives can react with benzene to give the corresponding arylation products [11]. Therefore the above described reaction represents one of the few photoreactions of adenine derivatives. Clearly the reaction involves both an attack of the vinyl group on the N-3 position of adenine and a reaction of diethyl fumarate on the N-6 and the N-9 positions. It is not clear how the molecule can lose a carbon atom on the imidazole ring. No other reaction product derived from this carbon atom was recovered from the reaction mixture.



EXPERIMENTAL

9-Chloroethyladenine.

Adenine (10 g) was dissolved in DMF (100 ml) and treated with sodium hydride (3.6 g). After 1 hour, 1-bromo-2-chloroethane (11 g) in DMF (20 ml) was added. After 3 hours the mixture was poured in saturated ammonium chloride and extracted with diethyl ether. The neutral extracts were dried (sodium sulfate). Removal of the solvent yielded a crude product that was chromatographed on silica gel. Elution with chloroform/methanol 1:1 gave pure 9-chloroethyladenine (2.9 g, 20%); ¹H-nmr (DMSO-d₆): δ 8.16 (s, 1 H), 8.14 (s, 1 H), 7.26 (s, 2 H), 4.49 (t, 2 H, J = 5.9 Hz), 4.06 (t, 2 H, J = 5.9 Hz).

9-Vinyladenine.

To a solution of 9-chloroethyladenine (0.6 g) in dioxane (50 ml) was added a methanol solution of sodium methoxide prepared from 4 ml of methanol and 0.4 g of sodium. After stirring at room temperature for 24 hours, water was added until the solution became clear and then treated with Dowex 50 (H⁺) until neutrality, and then evaporated to dryness. Column chromatography (elution with chloroform/methanol 2:1) gave pure 9-vinyladenine (0.29 g, 60%); ¹H-nmr (DMSO-d₆): δ 8.48 (s, 1 H), 8.19 (s, 1 H), 7.37 (s, 2 H), 7.29 (dd, 1 H, J₁ = 16 Hz, J₂ = 9.3 Hz), 6.06 (d, 1 H, J = 16 Hz), 5.11 (d, 1 H, J = 9.3 Hz).

Irradiation of 9-vinyladenine.

A mixture of 9-vinyladenine (100 mg) and diethyl fumarate (10 ml) in acetonitrile (10 ml) was irradiated in a quartz tube with magnetic stirring by using a Rayonet apparatus equipped with an 8 W low pressure mercury lamp whose output was centered at 254 nm. After 71 hours, the solvent was evaporated and the crude product was chromatographed on silica gel. Elution with chloroform/methanol 2:1 gave 100 mg of **4** and 98 mg of **5**.

Compound **4** had ¹H-nmr (DMSO-d₆): δ 6.73 (1 H, d, J = 15.7 Hz), 6.36 (1 H, d, J = 15.7 Hz), 4.1 (4 H, q, J = 7 Hz), 3.8 (3 H, bs), 3.44 (2 H, m), 2.36 (2 H, m), 1.2 (6 H, t, J = 7 Hz); ms: m/z 307 (4%), 294 (14), 167 (6), 149 (43), 146 (16), 145 (9), 129 (6), 128 (17), 127 (9), 117 (88), 101 (50), 100 (16), 99 (34), 89 (66), 71 (100).

Anal. Calcd. for C₁₄H₁₉N₅O₄: C, 52.33; H, 5.96; N, 21.79. Found: C, 52.5; H, 6.2; N, 21.6.

Compound **5** had ¹H-nmr (DMSO-d₆): δ 6.24 (1 H, d, J = 12 Hz), 5.71 (1 H, d, J = 12 Hz), 4.1 (4 H, q, J = 7 Hz), 3.8 (3 H, bs), 3.4 (2 H, m), 2.4 (2 H, m), 1.2 (6 H, t, J = 7 Hz); ms: m/z 307 (4%), 294 (14), 167 (6), 149 (43), 146 (16), 145 (9), 129 (6), 128 (17), 127 (9), 117 (88), 101 (50), 100 (16), 99 (34), 89 (66), 71 (100).

Anal. Calcd for C₁₄H₁₉N₅O₄: C, 52.33; H, 5.96; N, 21.79. Found: C, 52.4; H, 6.4; N, 21.7.

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