BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 2044—2046 (1969)

Synthesis and Spectrophotometric Observations of Ethyl *p*-(Acetylsalicylylamino)-benzoate*1

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(Received September 10, 1968)

Ethyl *p*-(acetylsalicylylamino)-benzoate (AB) has been synthesized in a water medium.[1] This paper will describe a new simple method of synthesizing AB and will present its ultraviolet, infrared, fluorometric, and phosphorometric spectra.

Acetylsalicylic acid (1 g) and ethyl *p*-aminobenzoate (1 g) were dissolved in 40 m*l* of ethyl acetate, and then dicyclohexylcarbodiimide (1 g) in 5 m*l* of ethyl acetate was gradually stirred into the mixed solution at room temperature. As the reaction proceed, dicyclohexylurea was obtained as the precipitate. The reaction mixture was then allowed to stand at room temperature for 16 hr. The precipitated dicyclohexylurea was filtered off, and the filtrate was evaporated to dryness *in vacuo* below 40°C. The oily residue was dissolved in 5 m*l* of methanol, and 5 m*l* of ether and 100 m*l* of petroleum ether were added to the solution. Crystals were obtained after the solution had been kept in a refrigerator. This crystalline material was recrystallized from methanol, ether, and then petroleum ether; fine needles were thus obtained. The yield was 900 mg. Melting point: 140°C (uncorrected, this is identical with that in Reference 1).

Found: C, 66.03; H, 5.40; N, 4.45%. Calcd

*1 This is an anaesthetica.

1) D. Curtis, U. S. Pat. 2352691 (1944).

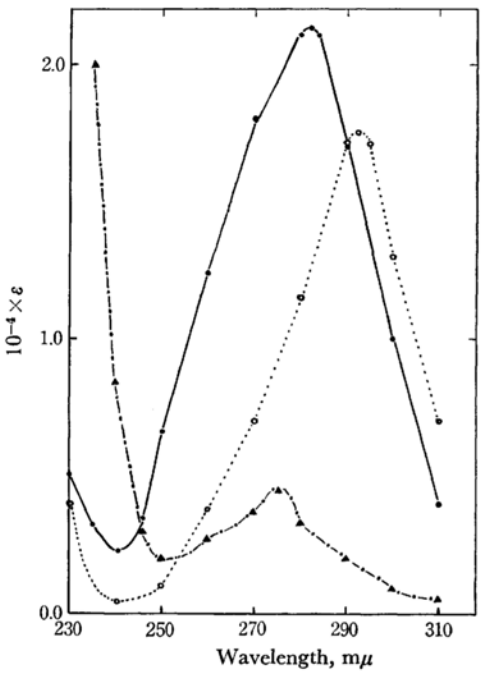

Fig. 1a. Ultraviolet spectra of AB, ethyl *p*-aminobenzoate and acetylsalicylic acid.
●——● AB
○·····○ Ethyl *p*-aminobenzoate
▲—·—·▲ Acetylsalicylic acid
Each concentration in methanol was 5×10^{-5}M.

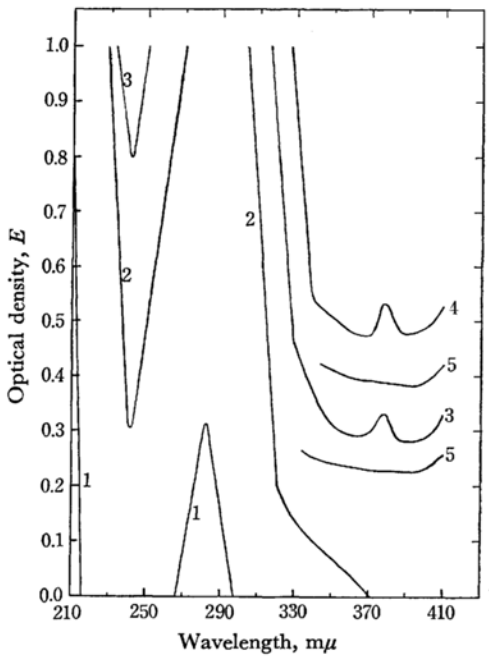

Fig. 1b. Ultraviolet spectrum of AB.
The concentration of AB in methanol was 5×10^{-5}M.
Curves 1, 2, 3 and 4 were determined at different sensitivities of spectrophotometer.
Curve 5 is methanol.

for $C_{18}H_{17}O_5N$: C, 66.06; H, 5.20; N, 4.28%.

One mg of AB is soluble in 5 m*l* of water at 100°C and in methanol, ethanol, and ether, and insoluble in petroleum ether. The ferric chloride reaction[2] was negative with this compound.

The ultraviolet spectrum of AB was determined in methanol using Beckman DU and Shimadzu MPS-50L spectrophotometers; the results are shown in Figs. 1a and 1b.

From the results, the λ_{max} of AB was located at 282.5 mμ (ε, 21400) and the λ_{min} at 241 mμ in methanol. AB may exist in the two forms of keto and enol isomers, shown below;

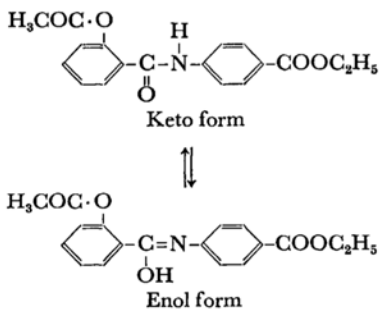

Figure 1b shows the presence of a band at 377.5 mμ, and the infrared spectrum of AB, as measured with a Hitachi infrared spectrophotometer, EPI-G type, showed characteristic absorption bands at 3320 cm^{-1} and 3070 cm^{-1} attributable to the *trans* form of the amide group,[3] as is shown in Fig. 2.

Consequently, it is probable that the steric structure of AB is mainly the keto form. If the band at 377.5 mμ is the enol form as shown in Fig. 1b, it is in a negligibly low concentration.

When AB was excited at 280 mμ or at 300 mμ

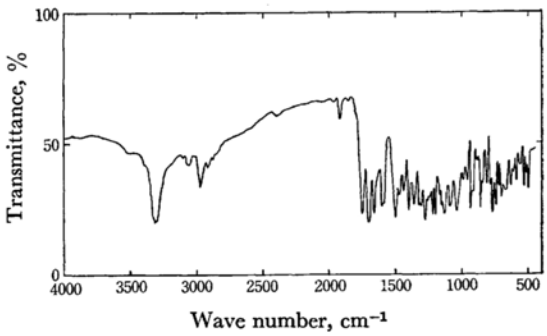

Fig. 2. Infrared spectrum of AB measured by the KBr tablet method.

2) Commentary of the Japanese Pharmacopoeia, 7th Ed. Nankodo Co., Tokyo (1962), p. 4.

3) K. Nakanishi, "Infrared Absorption Spectra," Nankodo Co., Tokyo (1967), p. 49.

in cyclohexane with a Hitachi fluorescence spectrophotometer, model MPF-2A, the maximum appeared in the fluorescence spectrum at 323 mμ as is shown in Fig. 3a, while the phosphorescence spectrum was observed at 77°K in ether : isopentane : alcohol (5 : 5 : 3, v/v); on the other hand, several peaks were observed between 400 mμ to 500 mμ. as Fig. 3b shows. This phenomenon may be inferred to be due to the effect of the temperature on the molecular distribution in the vibrational levels.

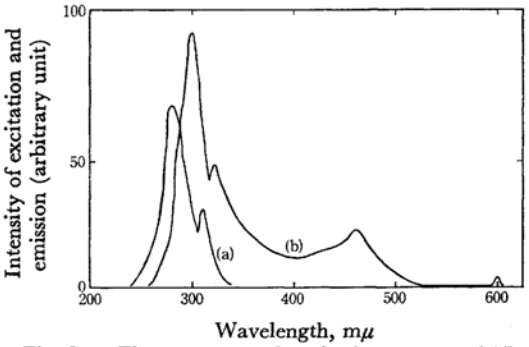

Fig. 3a. Fluorescence and excitation spectra of AB.
The concentration of AB in cyclohexane was 5 μg.
(a) Excitation spectrum
Emission at 310 mμ, slit width 1.29 mm, band path of wavelength 10 mμ.
(b) Fluorescence spectrum
Emission at 300 mμ, slit width 1.29 mm, band path of wavelength 10 mμ.
The peak at 300 mμ is due to the scattered light and the small peak at 600 mμ is also due to the scattered light.

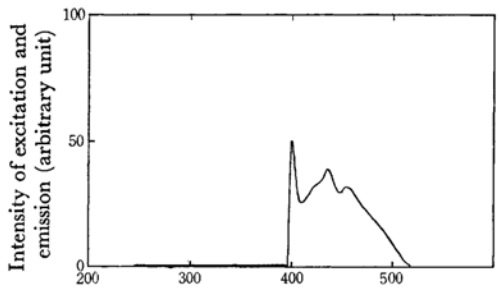

Fig. 3b. Phosphorescence spectrum of AB.
The concentration of AB in ether: isopentane : alcohol (5 : 5 : 3, v/v) was 5 μg.
The temperature of the solution of AB was 77°K.
Excitation at 280 mμ, slit width 2.58 mm, band path of wavelength 2 mμ.