

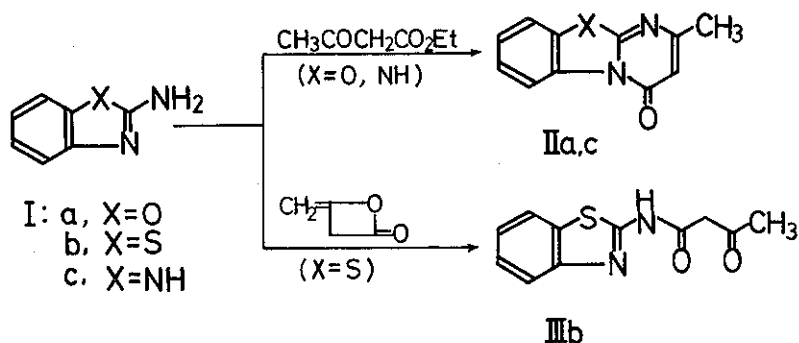
Reaction of 2-Aminobenzoxazole with
Diketene¹⁾

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2-Aminobenzoxazole reacts with diketene to give the related N-acetoacetyl, and pyrimido-[1,2-a]benzoxazol-4-one derivatives in good yield. Ring closure reaction of the N-acetoacetyl derivative (IIIa), and other reactions are described.

Antaki et al.²⁾ reported that 2-aminobenzoxazole (Ia, X=O) and 2-aminobenzimidazole (Ic, X=NH) reacted with ethyl acetoacetate to give 2-methyl-4H-pyrimido[2,1-b]benzoxazol-4-one (IIa, X=O) and 2-methyl-4H,10H-pyrimido[1,2-a]benzimidazol-4-one (IIc, X=NH), respectively. Ried et al.³⁾ reported the similar reaction of 2-aminobenzimidazole (Ic) with β -diketones to give the pyrimido[1,2-a]-benzimidazole derivatives. On the other hand, Allen et al.⁴⁾ investigated the reaction of 2-aminobenzothiazole (Ib, X=S) with diketene, and obtained 2-acetoacetamidobenzothiazole (IIIb) in quantitative yield.

While investigating on some potential uses of diketene, our interest was focused on the reaction of 2-aminobenzoxazole (Ia) and 2-aminobenzimidazole (Ic) with diketene, which is the subject of the present paper.

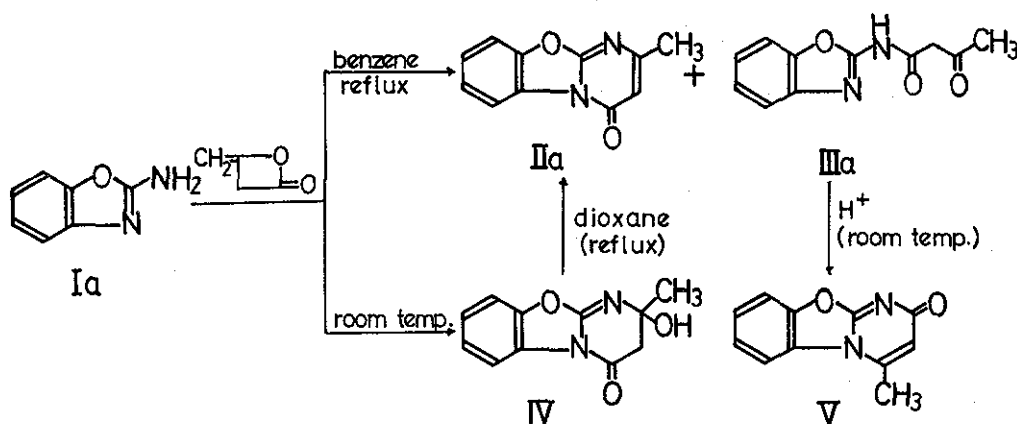


A mixture of 2-aminobenzoxazole and a slight excess of diketene in benzene was refluxed for 2 hr, and condensed in vacuo to give an oily residue, which was purified by recrystallization from ether giving colorless prisms of mp 144-145° (lit. mp 146°²), C₁₁H₈O₂N₂ (IIa), in 17% yield. The residual solid insoluble in boiling ether was recrystallized from benzene to give colorless prisms of mp 138-139°, C₁₁H₁₀O₃N₂ (IIIa), in 23% yield.

The ir and nmr spectral data of IIa and IIIa are as follows:
IIa, ir $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3040, 1710 (sh), 1693, 1642, 1612, 1538.
nmr (CDCl₃) ppm: 2.39 (3H, s, -CH₃), 6.20 (1H, s, C₃-H), 7.26-7.56 (3H, m, C₇, C₈, C₉-H), 8.20-8.48 (1H, m, C₆-H). IIIa; ir $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3440 (sh), 3240 (sh), 3025, 1725, 1705 (sh), 1625, 1585.
nmr (CDCl₃) ppm: 2.05 (0.8H, s, CH₃-C(OH)=C), 2.36 (2.2H, s,

CH₃-CO-), 3.92 (1.3H, s, -CH₂-), 5.82 (0.3H, br. s, -CH=C(OH)CH₃), 7.30-7.60 (5H, m, ring H, NH), 12.10-12.90 (0.4H, br, enol OH). Keto:enol=2.75:1.

Under the similar reaction condition, the use of 2-aminobenzoxazole (Ia) in excess resulted in the formation of IIIa in 46% yield. Reversely, in the case of the use of diketene in excess, IIa was afforded in 72% yield.



However, when the reaction was carried out at room temperature, the cyclic adduct (IV) was obtained. Namely, 2-aminobenzoxazole (Ia) was added in excess diketene with ice-cooling. The reaction mixture was stirred at room temperature until 2-aminobenzoxazole was completely dissolved, during which time an exothermic reaction was regulated with water-cooling. Crystals precipitated were collected, and purified by recrystallization from ether to give colorless needles of mp 95-96°, C₁₁H₁₀O₃N₂ (IV), in 59% yield.

ir $\overset{\text{CHCl}_3}{\underset{\text{max}}{>}}$ cm^{-1} : 3280 (br), 2990, 1720 (sh), 1706, 1478. nmr (CDCl_3) ppm: 1.64 (3H, s, $-\text{CH}_3$), 2.86 (2H, ABq, $J=16.2$ Hz, $-\text{CH}_2-$), 5.00-5.40 (1H, br, $-\text{OH}$), 7.02-7.30 (3H, m, $\text{C}_7, \text{C}_8, \text{C}_9$ -H), 7.66-7.95 (1H, m, C_6 -H). Refluxing of IV in dioxane gave IIa in 44% yield. On the basis of these data, the structure of IV was assigned as 2-hydroxy-2-methyl-2H-3,4-dihydropyrimido[2,1-b]benzoxazol-4-one.

Stirring a solution of 2-acetoacetamidobenzoxazole (IIIa) in 5% HCl at room temperature gave rise to colorless prisms (from acetone) of mp $284-286^\circ$, $\text{C}_{11}\text{H}_8\text{O}_2\text{N}_2\cdot\text{H}_2\text{O}$ (V-monohydrate), in 36% yield. This was characterized as 4-methyl-2H-pyrimido[2,1-b]-benzoxazol-2-one on the basis of spectral data as follows: ir $\overset{\text{KBr}}{\underset{\text{max}}{>}}$ cm^{-1} : 3360-3080, 1730 (sh), 1675, 1620, 1608. nmr ($\text{CF}_3\text{CO}_2\text{H}$) ppm: 2.10 (3H, s, $-\text{CH}_3$), 6.14 (1H, s, C_3 -H), 6.98-7.60 (4H, m, benzene ring H).

Reaction of 2-aminobenzimidazole (Ic) with diketene gave a sole product, which was identified as IIc by the comparison with an authentic specimen prepared from Ic and ethyl acetoacetate according to the literature.²⁾

REFERENCES

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