

Some Novel Reactions of Benzoxazole Derivatives with
Dimethyl Acetylenedicarboxylate¹

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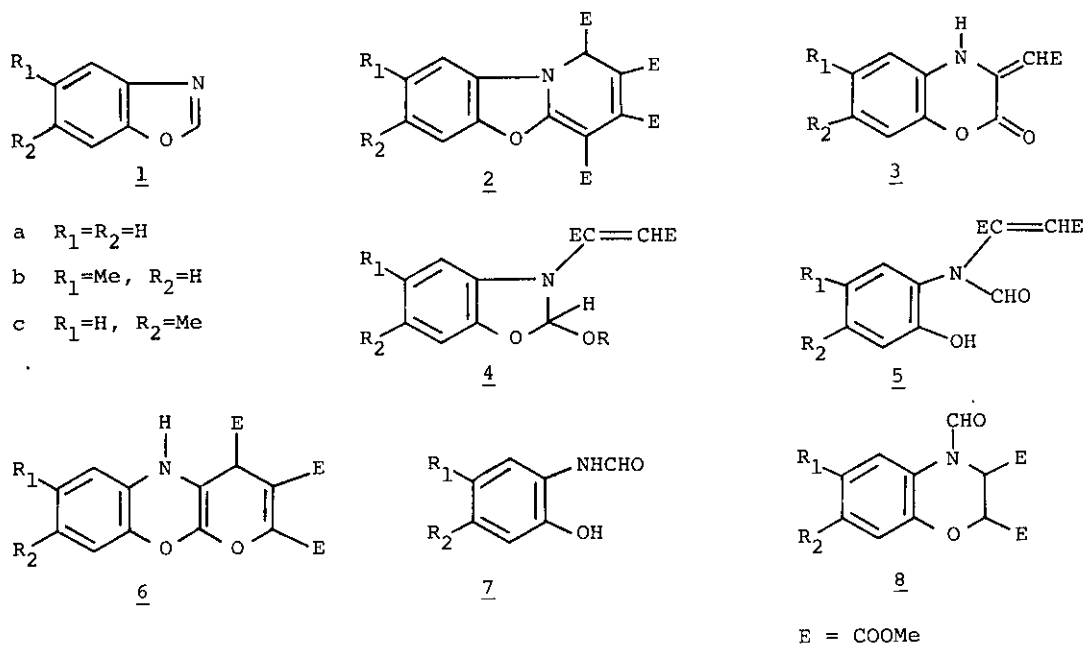
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Abstract - Benzoxazole derivatives(1) and dimethyl acetylene-
dicarboxylate(DMAD) gave novel tricyclic compound(6) through
the [2+4] cycloaddition of 3 and DMAD together with a solvent
addition product(4) and a ring-opened compound(5) in alcoholic
solvent at room temperature.

The reaction of benzoxazole(1a) with dimethyl acetylenedicarboxylate(DMAD) under
heating on a steam bath overnight have yielded 2 and 3.² During the course of
our work on heterocyclic compounds,³ we obtained new results on treating
benzoxazole derivatives(1) with DMAD at room temperature in the dark. We wish to
report here these novel addition reactions and also discuss plausible mechanisms
for the reactions.

After treatment of 1b in dry t-BuOH with three molar quantities of DMAD for
7 days at room temperature in the dark, three addition products were isolated
from the mixture by preparative TLC(Wakogel 13-5F, EtOAc:Benzenes = 1:9); 3b [
mp 148-149°, 1.7%, C₁₂H₁₁NO₄, ^{m/e} 233(M⁺)], 4b [R = t-Bu, mp 101-102°, 44.6%,
C₁₈H₂₃NO₆, ^{m/e} 349(M⁺), ¹H nmr (CDCl₃) δ 1.27(9H, s, O-t-Bu) 2.18(3H, s, C-CH₃)
3.61(3H, s, O-CH₃) 3.84(3H, s, O-CH₃) 5.47(1H, s, -CH-) 6.67(4H, =CH- and
aromatic protons), The ¹³C nmr (CDCl₃) showed sixteen signals.] and 4b [R = H,
oil, 8.2%, ^{m/e} 293(M⁺), ¹H nmr (CDCl₃) δ 2.29(3H, s, C-CH₃) 3.68(3H, s, O-CH₃)
3.96(3H, s, O-CH₃) 5.44(1H, s, -CH-) 6.70-7.40(4H, =CH- and aromatic protons)
8.24(1H, -OH)]. The structure of 3b was determined in comparison with the
spectral data of 3a which was synthesized from 2-aminophenol and DMAD.⁴ When
this reaction was carried out in MeOH, EtOH or iso-PROH instead of t-BuOH, the



corresponding analogs(3a,b,c) were also obtained respectively. It can be presumed that 3 is the Michael type addition product of aminophenol and/or 1 with DMAD as shown in scheme 2.

The spectral data described above have distinctly represented that the main product(4b, R = t-Bu) is the 1:1:1 molar adduct of 1b, DMAD and t-BuOH. Such a solvent adduct has been obtained by R. M. Acheson et al⁵ on refluxing benzimidazole with DMAD in benzene containing MeOH. The similar solvent adducts (4a,b,c) were also obtained in other alcohols(e.g. MeOH, iso-PrOH) but could not be obtained in refluxing alcohols. It may be assumed that after Michael type addition of 1 with DMAD, the second molecule of DMAD reacts with an intermediate (A) to afford the tricyclic compound 2 at elevated temperature whereas at room temperature, solvent itself reacts prior to further addition of DMAD to give the solvent adduct 4.

4b (R = H) was also prepared on treating of 1b with DMAD in t-BuOH containing H₂O in 7.9% yield together with novel ring-opened 1:1:1 molar adduct(5b, oil, 31.3%) and N-formyl-2-aminophenol derivative(7b, mp 111-113°, 44%). The principal formation of 5b and 7b in solvent containing H₂O indicates that H₂O may preferentially attack at C₂ position of benzoxazole to cause a following ring opening reaction. 4b (R = H) is very labile to be easily converted to 5b by allowing to stand at room temperature but 4c (R = H, mp 123-128°) could be obtained in crystalline form.

A reaction of 1b with DMAD in MeOH according to similar conditions described above gave three kinds of products; 3b (72.5%), 5b [3.6%, ^m/_e 293(M⁺), ¹H nmr (CDCl₃) δ 3.75(3H, s, O-CH₃) 3.79(3H, s, O-CH₃) 6.80-7.33(4H, =CH- and aromatic protons) 8.03(1H, -OH) 8.20(1H, -CHO)] and 6b [mp 138-140°, 5.0%, C₁₈H₁₇NO₈, ^m/_e 375(M⁺), ¹H nmr (CDCl₃) δ 3.69(3H, s, O-CH₃) 3.71(3H, s, O-CH₃) 3.80(3H, s, O-CH₃) 6.71-7.24(4H, -CH- and aromatic protons) 11.71(1H, -NH-), In the ¹³C nmr (CDCl₃) spectrum eighteen signals were observed.].

5b was readily converted into 8b [mp 84-85°, ^m/_e 293(M⁺)] with Et₃N in benzene at r.t. which was also obtained in EtOH 1.8% yield. The structure of 8b could not be characterized until now but is presumed to be an analogous structure of the product of benzothiazole with DMAD in MeOH.⁶

The structure of 6b was assigned on the basis of spectral data described above. It is reasonable to assume that the Diels-Alder cycloaddition between 3b and DMAD caused in the reaction mixture. This assumption was clearly supported

by preparation of 6b in good yield by treatment of 3b with DMAD in refluxing t-BuOH for 2 days. A corresponding compound(6c, mp 149-151°) was also prepared by treating of 1c with DMAD in MeOH at room temperature.

We could not obtain the cycloaddition product 2 in all experiments and throughly recovered the starting material 1 in dry solvents(e.g. toluene, benzene, DMF) in the place of dry alcohols. Thus, it was proved that these addition reactions of benzoxazole derivatives with DMAD proceed only in alcoholic solvents at room temperature and the presence of H₂O, however, tends to open the oxazole ring preferentially. It has been already reported that benzothiazole with DMAD in MeOH and DMF at room temperature afforded different results.⁶

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