THE REACTION OF 2-SUBSTITUTED QUINOLINE 1-OXIDES WITH DIMETHYL ACETYLENEDICARBOXYLATE: FORMATION OF 1-BENZAZEPINE DERIVATIVES

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Abstract — The 1,3-dipolar cycloaddition of 2-phenylquinoline 1-oxide (1) and quinaldine 1-oxide (3) with dimethyl acetylenedicarboxylate gives ring expanded products, 2-phenyl- (2) and 2-methyl-3H-3-methoxalyl-3-methoxycarbonyl-1-benzazepines (5), respectively. The reaction of quinaldonitrile 1-oxide (4) yields 1H-2-cyano-3-methoxycarbonyl-1-benzazepine (6) accompanied by further demethoxalylation.

In the course of our continuing investigation of the 1,3-dipolar cycloaddition of substituted quinoline 1-oxides with dimethyl acetylenedicarboxylate (DMAD)[2], an interesting ring expansion was observed in the reaction of some 2-substituted quinoline 1-oxides.

A solution of 2-phenylquinoline 1-oxide (1) and DMAD (1.2 equiv.) in dichloromethane was kept at room temperature for 3 days to give 3H-3-methoxalyl-3-methoxycarbonyl-2-phenyl-1-benzazepine (2), colorless prisms, mp 94-96°C, in a high yield of 87.8%. Its structure was deduced from the elemental analyses, the IR and PMR spectroscopies[3], and established by an X-ray diffraction study[4].

Subsequently the reaction of quinaldine 1-oxide (3) as well as that of quinaldonitrile 1-oxide (4) with DMAD was found to yield also a ring expanded product. While treatment of 3 with DMAD at room temperature caused only resinification, the reaction proceeded at -10°C in dichloromethane, though very slowly, and the 3H-1-bezazepine (5) of the same type as 2 was obtained as an oil in 81.4% yield after 2 weeks' reaction. Although purification of 5 was not effected because of its

high instability, its structure could be confirmed by spectral data.

In contrast to the case of 3, the reaction of 4 with DMAD in dichloromethane did not occur at all at low temperature. When heated in DMF at 100°C, however, the reaction proceeded and 1H-2-cyano-3-methoxycarbonyl-1-benzazepine (6), orange needles, mp 122-125°C (dec.), was isolated in 28.2% yield after 1 h's reaction. These reactions are formulated in Chart 1.

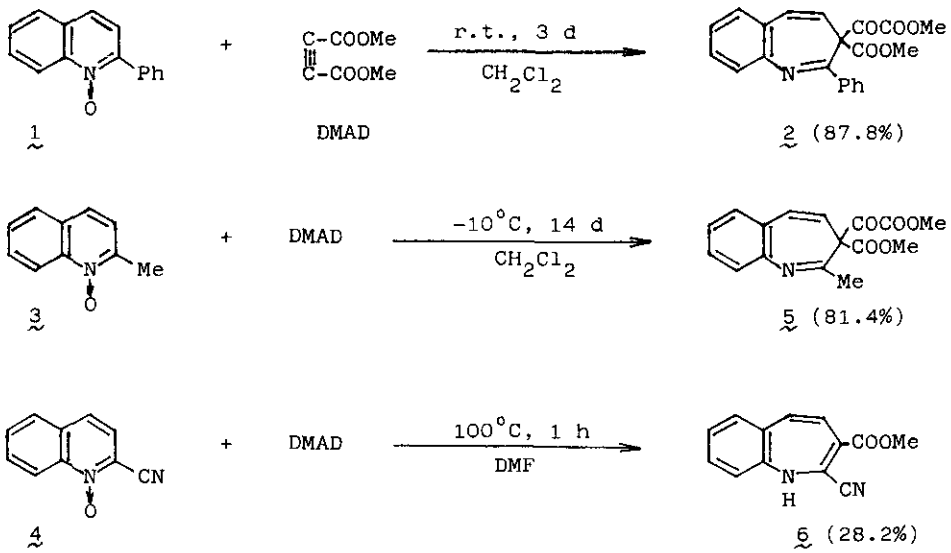

Chart 1

The formation of 1-benzazepines (2, 5 and 6) is very significant in view of no precedent for the expansion of a pyridine ring to an azepine system in the 1,3-dipolar cycloaddition of aromatic N-oxides. The formation of 2 and 5 can be well rationalized by the following mechanism. The initially formed primary cycloadduct (A) readily undergoes a 3,5-sigmatropic shift leading to a 2,3-dihydroquinoline (B) followed by its valence isomerization to give a 3H-1-benzazepine, 2 or 5. Since heating is required for the reaction of 4 to proceed, the 3H-1-benzazepine (C) similarly formed undergoes thermal demethoxalylation to give the thermodynamically more stable 1H-1-bezazepine derivative 6 (Chart 2).

It is also noticeable that these results present direct evidence for the intermediacy of the 2,3-dihydroquinoline (B) of an azanorcaradiene type as well as of the analogous dihydropyridine which was postulated in a variety of 1,3-dipolar cycloadditions of quinoline and pyridine N-oxides[2c,5].

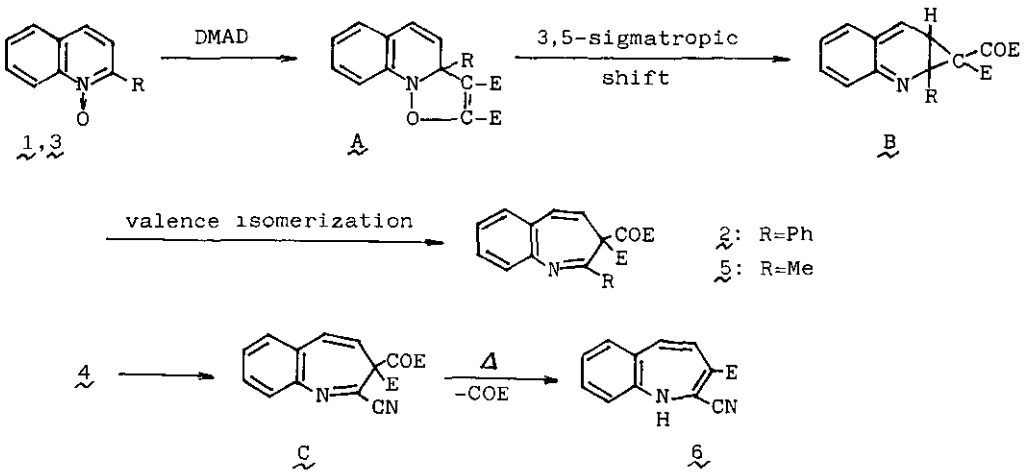

Chart 2

REFERENCES AND NOTE

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3. IR (Nujol) cm^{-1}: 1735, 1760 (C=O). PMR ($CDCl_3$) δ : 3.41 (3H, s, $COOCH_3$), 3.58 (3H, s, $COOCH_3$), 6.59 (1H, d, $J_{4,5}$=10 Hz, C_4- or C_5-H), 6.99 (1H, d, $J_{4,5}$=10 Hz, C_4- or C_5-H), 7.10-7.60 (9H, m, Ar-H).

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