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PHOTOCYCLOADDITION OF 4-METHOXYQUINOLIN-2(1H)-ONE AND RELATED COMPOUNDS TO ALLENE: SYNTHESIS OF 1-METHYLENE-1,2-DIHYDROCYCLOBUTA[*c*]QUINOLIN-3(4H)-ONE AND RELATED COMPOUNDS[1]

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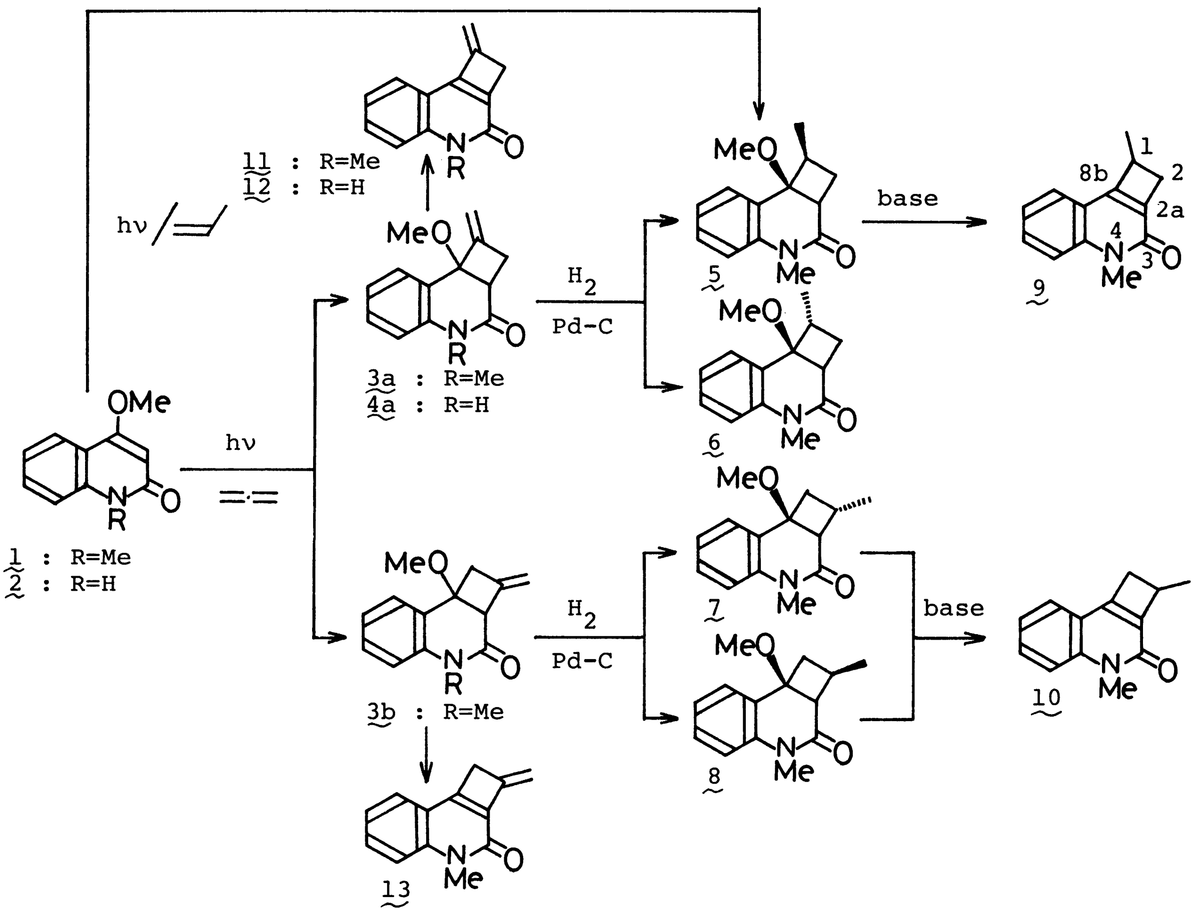
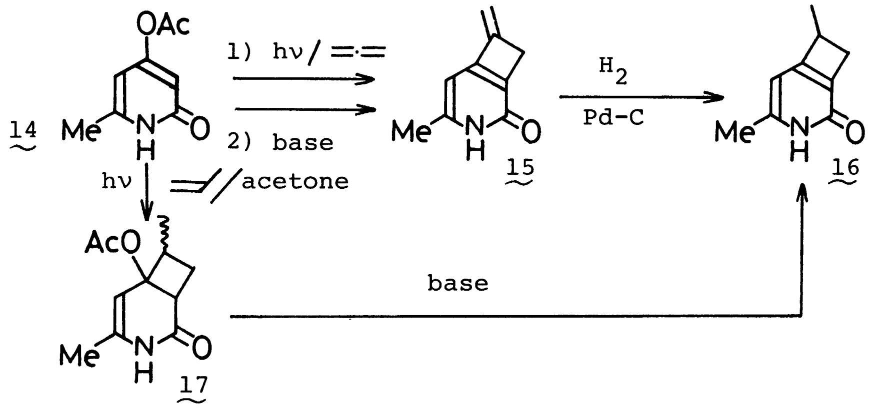
Photocycloaddition of 4-methoxy-2-pyridones and -quinolones to allene gives the head-to-tail adduct as the predominant product, which by base treatment affords the title compounds.

Previously, we have succeeded in the synthesis of 1,2-dihydrocyclobuta[*c*]quinolin-3(4H)-ones from 4-methoxy-2-quinolone by initial photoaddition of the latter to an olefin followed by elimination of methanol.[2] One of the characteristic features of this two-step procedure is the regioselectivity in the first step to give only the head-to-tail adduct. Predominant formation of the head-to-tail adduct is also found in the photoaddition of cyclic alkenones to electron-rich olefins.[3] However, the photocycloaddition of allene to these enones is attended by unusual regioselectivity and the head-to-head adduct is the predominant product.[4] We therefore attempted the extension of our two-step procedure using allene instead of olefins. This study would provide not only what kind of regioselectivity exists in the photoaddition step, but also a simple route to 1-methylene or 2-methylene derivative of the cyclobutane-fused heteroaromatics. The latter success would broaden the use of these cyclobutenes as synthons for polycyclic heteroaromatic compounds[5] due to the possession of functionality on the cyclobutene ring.

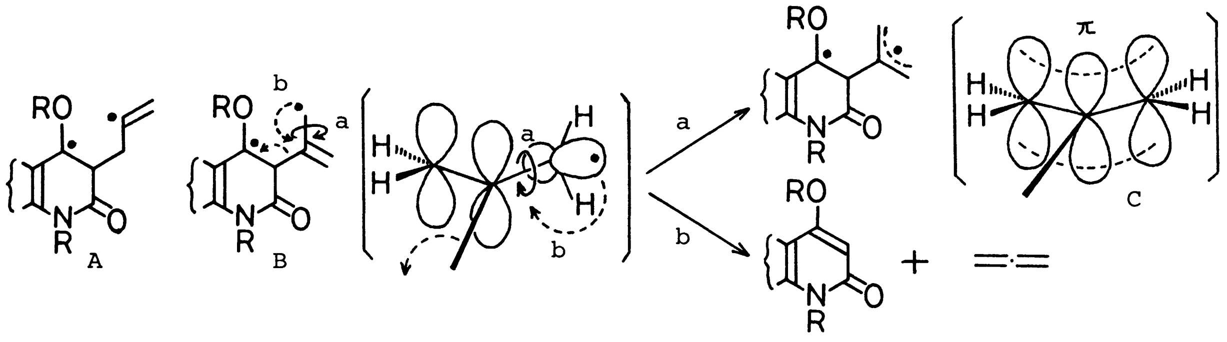
Irradiation[6] of 4-methoxy-1-methylquinolin-2-one (**1**) in methanol in the presence of an excess of allene followed by silica gel column chromatography afforded two kinds of 2+2 adducts:[7] **3a** (mp 80.5-82°C, 59.6%) and **3b** (oil, 9.7%). Catalytic hydrogenation (H_2, Pd/C) of the major adduct (**3a**) afforded the corresponding dihydro derivatives: **5** (mp 66-67°C, 59.6%) and **6** (mp 124-128°C, 23.7%).[8] Both isomers show in their NMR spectra their 2a-proton signals as triplet (2a-H of **5**: δ 3.39 with J=9.4 Hz and that of **6**: δ 3.20 with J=8.8 Hz). This fact as well as almost exclusive formation of **5** from photoaddition of **1** to propene[9] demonstrated unambiguously the head-to-tail structure for the major adduct (**3a**). Catalytic hydrogenation of the minor adduct (**3b**) gave again the mixture of two stereoisomers[10] (**7** and **8** in a ratio of *ca*. 3:1) in 91% yield. Without separation, the mixture was treated with base (KOH/MeOH, reflux) to give the expected cyclobutene derivative [**10**, mp 98-99°C, NMR ($CDCl_3$): δ 1.44 (3H, d, J=6.8 Hz), 2.63 (1H, dd, J=13.2 and 1.2 Hz), 3.1-3.8 (2H, m), 3.62 (3H, s), 6.8-7.6 (4H, m)]





in quantitative yield. The dihydro derivative (5) was treated with base as above to give the cyclobutene [9, mp 101.5-102.5°C, NMR ($CDCl_3$): δ 1.46 (3H, d, J=7.0 Hz), 2.62 (1H, dd, J=13.0 and 1.6 Hz), 3.29 (1H, dd, J=13.0 and 4.2 Hz), 3.3-3.8 (1H, m), 3.61 (3H, s), 6.8-7.7 (4H, m)] in almost quantitative yield. Though both cyclobutenes (9 and 10) show almost the same NMR spectra, it is obvious from their formation that 9 is 1-methyl-1,2-dihydrocyclobuta[c]quinolin-3(4H)-one and 10 is the corresponding 2-methyl derivative.[11] Hence, the structures of two methylenecyclobutenes (11, mp 148.5-149°C and 13, mp 135-136.5°C) obtained from the adducts (3a and 3b) in quantitative yields by the same base treatment were also determined unequivocally. The same regioselectivity in the photoaddition step is also observed for 4-methoxy-2-quinolone (2) and -2-pyridone series. Thus, only the head-to-tail adduct (4a, mp 151.5-153.5°C, 77.2%) was formed from 2 and allene,12) which by base treatment afforded 12 (mp >300°C) in quantitative yield. A cyclobutene [16, mp 144-145°C, NMR (CDCl$_3$): δ 1.31 (3H, d, J=6.8 Hz), 2.32 (3H, s), 2.4-2.8 (1H, m), 3.0-3.5 (2H, m), 5.85 (1H, s), 12.6 (1H, bs)] was obtained from 4-acetoxy-6-methyl-2-pyridone13) (14) by the application of the two-step procedure, followed by catalytic hydrogenation. The following independent synthesis of 16 revealed that 15 is 5-methyl-1-methylene-1,2-dihydrocyclobuta[*c*]pyridin-3(4H)-one. Thus, 14 was irradiated in acetone in the presence of propene to give a 2+2 adduct (17, mp 154.5-156°C, 62%) as the sole detectable product.14) Its head-to-tail structure was readily deduced by the appearance of 2a-proton as a triplet (δ 3.28 with J=9.6 Hz) in the NMR spectrum. By base treatment, 17 afforded 16 in quantitative yield.

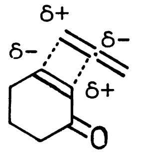
The preferencial formation of the head-to-tail adduct over the head-to-head isomer seems to deserve comments, because the similar photoaddition of cycloalkenone to allene gave the head-to-head adduct predominantly.4) One reasonable explanation is to assume that the addition proceeds in a stepwise manner *via* a biradical as in the case of the addition to olefins.5) We consider that the biradical (A) should be more stable than the biradical (B), because in order to attain allyl radical stabilization as in C, *p*-orbital carrying an odd electron in B must rotate 90° around the σ-bond. The more attractive explanation is that the biradical (B) is actually formed preferentially over A.15) However, the former reverts mostly to the original components (heteroaromatics and allene) by the fission of the newly formed σ-bond rather than the above mentioned 90° rotation. In our case this reverse process may be assisted by the gain of aromaticity in one component (*e.g.*, 1), while in aliphatic series the rates of two processes (a and b) are reversed due to the absence of such stabilization.



Thus, we have established the synthesis of 1-methylene derivatives of 1,2-dihydrocyclobuta[*c*]pyridin- and -quinolin-3(4H)-ones. The modification of the methylene function in them to other functions (*e.g.*, C=O, epoxide, *etc.*) as well as extension of the present method to other heteroaromatics is now under investigation.

References

1) Part XV of "Cycloadditions in Syntheses." Part XIV, C. Kaneko, T. Naito, and T. Ohashi, Heterocycles, **20**, 1275 (1983).
2) C. Kaneko and T. Naito, Chem. Pharm. Bull., **27**, 2254 (1979); H. Fujii, K. Shiba, and C. Kaneko, J. Chem. Soc., Chem. Commun., **1980**, 537.
3) S. W. Baldwin, "Organic Photochemistry," ed by A. Padwa, M. Dekker, New York (1981), Vol.5, p.123.
4) Ref. 3, p.150.
5) C. Kaneko and T. Naito, Heterocycles, **19**, 2183 (1982).
6) Irradiation was carried out using 5-10 mM solution of heteroaromatics at ≥300 nm (Ushio 450 W high-pressure mercury lamp, Pyrex filter) at room temperature. Prior to irradiation, allene was bubbled through the solution about 10 min.
7) The structures of the products were supported by acceptable combustion data and/or mass spectra and other spectral data.
8) Stereochemistry of the products (**5**, δ of 1-Me: 1.27 d and **6**, δ of 1-Me: 0.86 d) was deduced from NMR spectra. Only the shielding (up-field shift) of 1-methyl groups by the benzene ring is expected for the product having *cis* relationship between these two groups. Hence, the product showing the 1-methyl signal at δ 0.86 is assigned as **6**.
9) In this reaction, **5** and **6** were obtained in *ca*. 10:1 ratio.
10) Stereochemistries of **7** (δ of 2-Me: 0.86 d) and **8** (δ of 2-Me: 1.26 d) were assigned by NMR spectra. Only the 2-methyl group in **7** would be shielded by the carbonyl group.
11) Non-identity of both samples (**9** and **10**) is assured by mixed melting point determination (mp. 62-82°C) and from comparison of IR spectra.
12) The NMR spectrum of the mother liquor fraction of **4a** showed a broad singlet at δ 3.89, indicating the presence of a small amount of the head-to-head adduct (**4b**).
13) C. Kaneko, Y. Momose, and T. Naito, Chem. Lett., **1982**, 1361.
14) Stereochemistry of **17** is not yet determined.
15) The predominant formation of the head-to-head adduct in the cycloaddition of allene to excited enones (n-π*) is explained by the interaction depicted in formula D. See, E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra, J. Am. Chem. Soc., **86**, 5570 (1964).



(n-π*)
D

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