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CYCLOADDITIONS OF 1,2-DIHYDROCYCLOBUTA[c]QUINOLIN-3(4H)ONES TO OLEFINS: NEW AZA-ANALOGUES OF *ortho*-QUINODIMETHANES[1]

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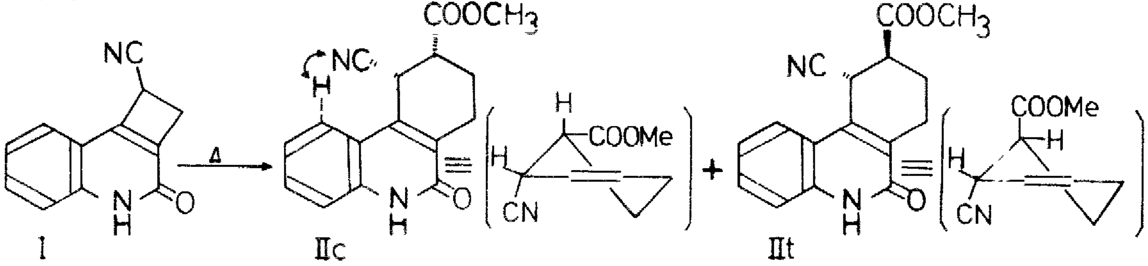
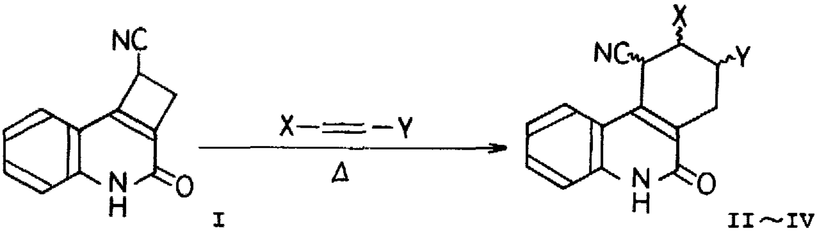
Summary An usefulness of 1,2-dihydrocyclobuta[c]quinolin-3(4H)ones as synthons for organic synthesis for aza-analogues of benzocyclobutenes was demonstrated by their inter- and intramolecular cycloadditions to olefins.

Benzocyclobutenes have been effectively utilized as starting materials for the synthesis of polycyclic ring systems.[2,3] The key reaction in these syntheses is an intra- and intermolecular cycloaddition of *o*-quinodimethanes, generated *in situ* by the thermolysis of benzocyclobutenes, to olefins or imines. In this paper, we report cycloaddition reactions of 1,2-dihydrocyclobuta[c]quinolin-3(4H)ones with olefins.

A 20 mM solution of 1-cyano-1,2-dihydrocyclobuta[c]quinolin-3(4H)one[1b] (I) in xylene containing 30 mol. equiv. of methyl acrylate was heated at 100° until all of the starting materials were consumed (*ca.* 15 hr). Evaporation of the solvent gave a crystalline adduct (II: mp 200-212°) in 90% yield. Though the product showed only one spot on t.l c., PMR spectrum showed it to be a mixture of two stereoisomers both having a head-to-head structure (IIt and IIc in *ca.* 2 1 ratio). Heating of II in pyridine-d_5 at 100° for 15 hr afforded the equilibration mixture in which IIc [δ. 3.59, s (Me), and 5.08, d, J=4.0 Hz (CHCN)] predominated over IIt [δ: 3.77, s (Me), and 5.20, d, J=2.0 Hz (CHCN)].[4] This clearly indicates that cycloaddition reaction proceeded under kinetic control, being the major stereoisomer (IIt) less stable thermodynamically than the minor one (IIc). The smaller coupling constants in these doublets indicate *quasi*-





I **II**~**IV**

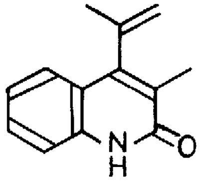
alkene X	Y	cycloadduct[a,b] (mp)	ratio of *cis*- and *trans*-isomers[c] in the product as formed		after equilibration[d]	
COOMe	H	**II** (200-212°)	*trans*/*cis*	*ca*. 2	*trans*/*cis*	*ca*. 3/4
COOMe	COOMe	**III** (240-242°)	*trans*/*cis*	*ca*. 3	———	
(COOMe (Me	H	**IV** (262-265°)	*trans*/*cis*	*ca*. 1.5	*trans*/*cis*	*ca*. 1/3

a) The compound (**I**) was warmed at 100° in xylene in the presence of 30 mol. excess of alkenes.
b) The adducts were obtained in 90-95% yields.
c) *Cis* and *trans* refer to the relation between CN and X functions, and *cis* isomer is thermodynamically more stable than the *trans*-isomer.
d) The equilibration was reached after 15-20 hr's heating (100°) in pyridine-d_5. The ratios were determined by NMR spectra.

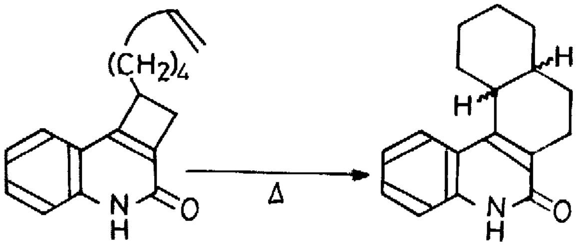
axial orientation of the cyano group in each isomer (**IIc** or **IIt**) and such configurations are reasonably expected from steric repulsions between the cyano group and the *peri*-hydrogen atom if the former takes *quasi*-equatorial orientation. Based on these data, stereo-structures of both isomers are deduced to be as shown in the formulae **IIt** and **IIc**. Other electron-deficient alkenes also reacted with **I** under the same condition to give mixtures of two stereoisomers, in which the major isomers were always thermodynamically less stable than the minor ones, and hence, treatments with pyridine at 100° as above reversed the proportions of the two isomers. In all products, head-to-head structures are assured from PMR spectra: the signal of the proton on the cyanated methine function in each isomer appeared as a doublet, without exception. The results of these cycloaddition reactions are summarized in the Table.

Contrary to the ease of cycloaddition reactions between **I** and electron-deficient alkenes, electron-rich alkenes (*e.g.*, allyl acetate, *cis*-2-butene-1,4-diol, *etc*.) did not react with **I** under these conditions, and only dimer[5] of **I** was obtained after a prolonged reaction time (*ca*. 100 hr for the complete consumption of **I**).

The above results showed clearly that 1,2-dihydrocyclobuta[c]quinolin-3-ones reacted with olefins in the same manner as benzocyclobutenes. A similarity of reactions between our system and benzocyclobutenes was further demonstrated by the following intramolecular rearrangement reaction. Thus, heating of 1,1-dimethyl-1,2-dihydrocyclobuta[c]quinolin-3(4H)one[1b] (**V**) under a comparable condition as the above cycloaddition reactions afforded 4-isopropenyl-3-methyl-2-qui-



VI

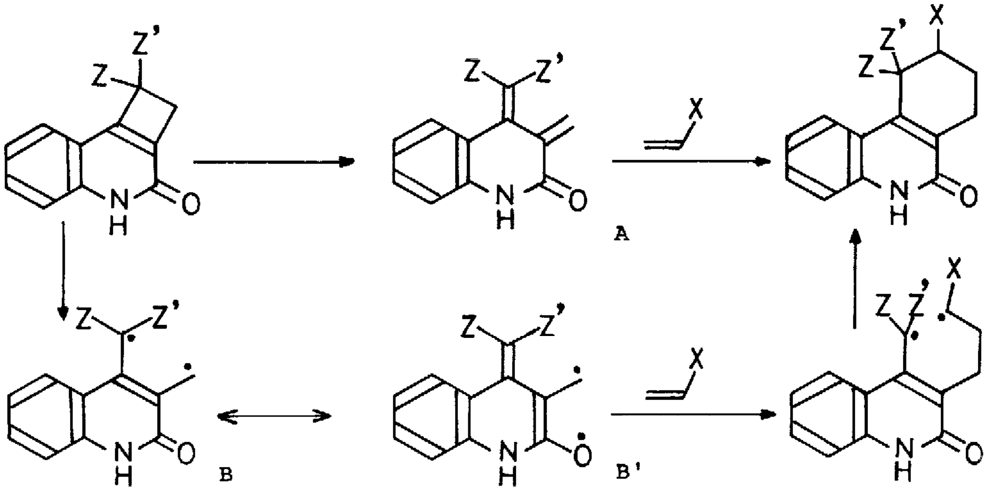


VII VIII

nolone [**VI**. mp 177.5-179°; δ(CDCl$_3$): 2.04, d, J=1.0 Hz (Me), 2.23, s (C$_3$-Me), 5.41, d, J=1.5 Hz, and 4.89, d,q, J=1.5 and 1.0 Hz: the olefinic proton being *trans* to the methyl group at 2.04; λ_{max}^{MeOH} nm (log ε)· 221 (4.54), 271 (3.87), 324.5 (3.90), and 338.5 (3.74)] in a quantitative yield. Quite recently, Kametani *et al.*[6] reported the same kind of isomerization reactions of 1,1-dialkylated benzocyclobutenes and proposed the mechanism involving an initial opening to *o*-quinodimethane species and subsequent [1,5]-sigmatropic hydrogen shift.

Finally, it is demonstrated that the cycloaddition of 1,2-dihydrocyclobuta[c]-quinolin-3-ones to electron-rich olefins becomes possible if these two functions are suitably located each other in one molecule due to an entropy assistance, whose significant participations are now well documented in the intramolecular cycloaddition reactions of benzocyclobutenes.[2,3] Thus, 1-(5-hexenyl)-1,2-dihydrocyclobuta[c]quinolin-3-one[7] (**VII**: mp 118.5-120°) afforded the cyclized adduct [**VIII**· mp 285-288°, λ_{max}^{MeOH} nm: 222, 272.5, 282, 324.5, and 338.5; δ(pyridine-d$_5$): 1.0-1.9, m (10H), 2.3-3.25, m (3H), 7.1-7.8, m (4H), and 12.65, bs (N*H*)] in a quantitative yield by heating for 6 hr in refluxed *o*-dichlorobenzene.

These experiments revealed that 1,2-dihydrocyclobuta[c]quinolin-3-ones, now readily available,[1a,1b] can serve as synthons in organic syntheses as aza-analogues of benzocyclobutenes. All of these reactions can be explained to proceed



through aza-*o*-quinodimethanes (**A**) as key intermediates, just like as now well documented participations of *o*-quinodimethanes in the reactions of benzocyclobutene series.[8] However, the regio-selective formation of the head-to-head adducts (*e.g.*, **IIt**) in the intermolecular cycloaddition reactions seem to indicate that a stepwise process through diradical intermediates (**B**$\longleftrightarrow$**B'**) is an another attractive mechanism for these reactions.[9]

References and notes

1. Part III of "Cycloadditions in Syntheses". a) Part I: C. Kaneko, T. Naito, and M. Somei, J. Chem. Soc., Chem. Commun., 804 (1979); b) Part II C. Kaneko and T. Naito, Chem. Pharm. Bull., 27, 2254 (1979).
2. W. Oppolzer, Synthesis, 793 (1978).
3. T. Kametani and K. Fukumoto, Heterocycles, 3, 29 (1975).
4. This base-catalized isomerization reaction was runned in a sealed NMR tube using pyridine-d_5 as a solvent and followed NMR spectroscopically.
5. The dimer was obtained as a solid mass (mp >300°); λ_{max}^{MeOH} nm: 230, 273, and 330; ν_{max}^{KBr} cm^{-1}: 3500, 2220, and 1650, and showed M^+ at m/e 392. Due to its insolubility, purification and structure determination were unsuccessful. The same dimer was formed from I in a high yield by heating in xylene (100°, *ca.* 100 hr) or in refluxed *o*-dichlorobenzene (*ca.* 30 min). Formation of the dimers from some benzocyclobutenes under comparable conditions as well as their structure determination have been reported: a) A.T. Blomquist, Y.C. Meinwald, C.G. Bottmley, and P.W.Martin, Tet.Lett., 13 (1960); b) T.Kametani, T. Takahashi, K. Ogasawara, and K. Fukumoto, Tetrahedron, 30, 1047 (1974).
6. T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, H. Nemoto, M. Ihara, K. Fukumoto, F. Sato, and H. Inoue, J. Org. Chem., 42, 2672 (1977).
7. According to the general method previously described,[1b] this compound (**VII**) was prepared by regioselective photo-cycloaddition of 4-methoxy-2-quinolone to 1,7-octadiene to form the head-to-tail adduct [**IX**: mp 107-108°, $\delta(CDCl_3)$: 3.30, t, J=9.0 Hz (C_{2a}-H)], followed by elimination of methanol by treatment with sodium methoxide in methanol (reflux; 2 hr).
8. *o*-Quinodimethane has been characterized at -190°: K.L. Tseng and J Michl, J. Am. Chem. Soc., 99, 4840 (1977).
9. The suggested diradical intermediate (**B**) is also in accordance with resonance stabilization (**B**$\longleftrightarrow$**B'**) which is not possible for the one derived from benzocyclobutenes. Though Fleming claimed against diradical intermediates in the cycloaddition reactions involving benzocyclobutenes,[a] a stepwise mechanism through diradical or ionic intermediate has also been suggested:[b] a) I. Fleming, F.L. Gianni, and T. Mah, Tet. Lett., 881 (1976); b) T. Kametani, Y. Kato, T. Honda, and K. Fukumoto, J. Chem. Soc., Perkin I, 2001 (1975).
10. All new compounds gave satisfactory combustion and/or mass spectrometric analysis and spectroscopic data consistent with the assigned structures.

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