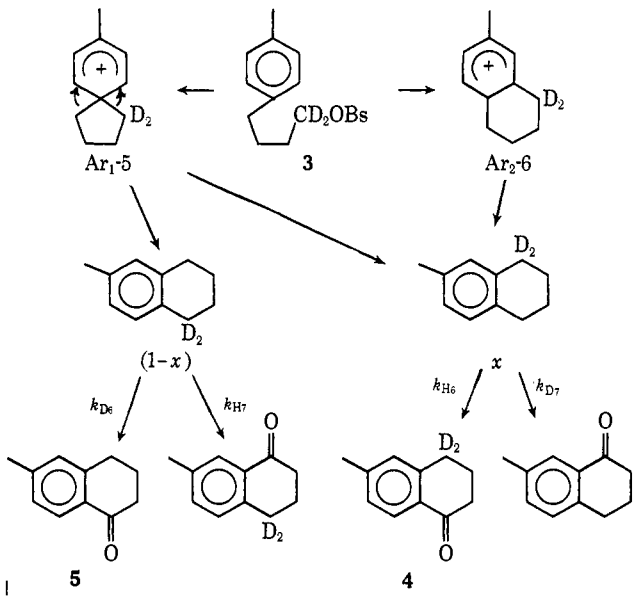
Scheme I[a]



[a] $x = (Ar_2\text{-}6) + (Ar_1\text{-}5)/2$; $1 - x = (Ar_1\text{-}5)/2$.

$$x\gamma/(1 - x) = [\mathbf{4}]/[\mathbf{5}] = d_2/d_0 \quad (1)$$

$$(1 - x)\gamma/x = d_4/d_0 \quad (2)$$

where $\gamma = (1 + k_{H7}/k_{D6})/(1 + k_{D7}/k_{H6})$.

Equations 1 and 2 were solved for x, the value of which shows that only 17 ± 1.5% of the cyclization to tetralin proceeded by the Ar_1-5 pathway.[12]

The relative rates (k_{Ar_1-5}/k_{Ar_2-6}), corrected for the statistical factor, are 5.6 and 0.41 for the para methoxy and para methyl systems, respectively. The former result, in particular, indicates a selectivity far less than that expected for an electrophilic aromatic substitution by such a poor electrophile as $RCH_2OSO_2C_6H_4Br$.[14] It is evident that either the Ar_2-6 transition state is sterically more favorable (as would appear from molecular models) or that attack at an alkylated aromatic carbon atom is more difficult than at an unsubstituted one. It is seen, however, that the difference between the two transition states is too small to explain the specificity of cycloacylation. We suggest that the Ar_1-5 intermediate may form during cycloacylation but that ring opening is preferred to rearrangement. Rearrangement would require either the unlikely migration of the carbonyl group or migration of the alkyl group leaving a positive charge adjacent to the carbonyl group.

(12) Two assumptions concerning isotope effects are made. The first is that the α-isotope effect for Ar_1-5 and Ar_2-6 can be neglected. The second is that the α-isotope effect for the rearrangement of the Ar_1-5 intermediate makes a negligible contribution to x. Calculations using a value of 1.2[13] for the latter quantity indicate that the second assumption is valid.

(13) W. M. Schubert and P. H. LeFevre, *J. Amer. Chem. Soc.*, **91**, 7746 (1969).

(14) Using $\sigma^+_{p\text{-MeO}}$ for Ar_1-5 and $\sigma^+_{m\text{-MeO}} + \sigma^+_{p\text{-CH}_3}$ ($\sigma^+_{p\text{-CH}_3}$ is an approximation to the effect of the ortho methylene group) for Ar_2-6, one obtains $\rho^+ \sim -1.5$, which is substantially lower than the most unselective electrophilic aromatic substitutions.[15]

(15) L. M. Stock and H. C. Brown, *J. Amer. Chem. Soc.*, **81**, 3323 (1959).

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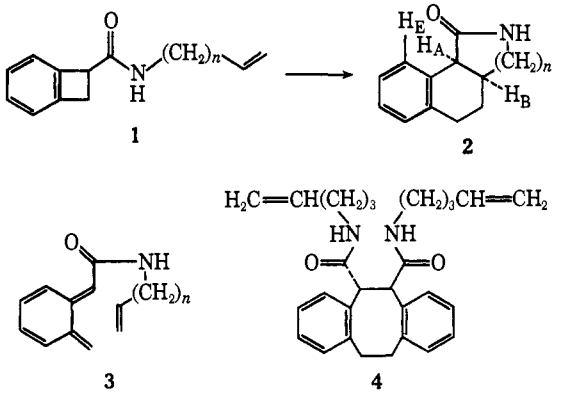
Intramolecular Cycloadditions of *o*-Quinodimethanes[1]

Sir:

As part of a general program directed toward stereoselective syntheses of annelated heterocyclic systems,[2] thermal rearrangements of benzocyclobutenes, typified by **1**,[3] have been examined. After heating a



5% solution in toluene of the propenylamide **1**, $n = 1$[4] (prepared from benzocyclobutene-1-carboxylic acid chloride[5] and allylamine), in an autoclave at 190° for 16 hr the *cis*-benz[*e*]isoindole **2**, $n = 1$[4] (mp 171–172°; nmr $J_{AB} = 8$ Hz), crystallized from the cooled solution in 85% yield. Thermolysis of the homologous butenylamide **1**, $n = 2$,[4] in boiling *o*-dichlorobenzene (8% solution) afforded the *cis*-benz[*h*]isoquinoline **2**, $n = 2$[4,6] (mp 112–113°; nmr $J_{AB} = 5$ Hz; 85%). When a 0.5% solution of the pentenylamide **1**, $n = 3$,[4] in *o*-dichlorobenzene was refluxed for 16 hr the expected naphth[1,2-*c*]azepine **2**, $n = 3$[4] (mp 195–197°; nmr ($CDCl_3$) $J_{AB} = 8$ Hz, $\delta_{HE} \leq 7.2$ ppm), was isolated together with the dimer **4**[4] (mp 159–161°) in yields of 20 and 6%, respectively. This supports the hypothesis that *o*-quinodimethanes of type **3** are intermediates in the reaction[7] and suggests that the activation entropy in the intramolecular cycloaddition **3** → **2** depends strongly

(1) Presented in part at the IUPAC Symposium Cycloaddition Reactions, Munich, Germany, Sept 7–10, 1970.

(2) W. Oppolzer and K. Keller, *Tetrahedron Lett.*, 1117, 4313 (1970); W. Oppolzer and H. P. Weber, *ibid.*, 1121, 3034 (1970); W. Oppolzer, *ibid.*, 3091 (1970).

(3) 1-Substituted benzocyclobutenes are readily available; for a recent review, see I. L. Klundt, *Chem. Rev.*, 70, 471 (1970).

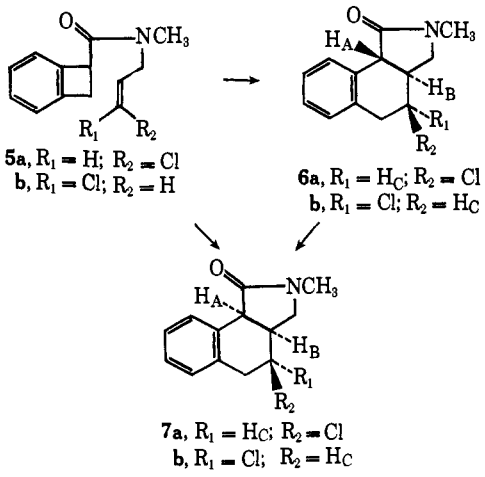
(4) Elemental analytical data and ir and nmr spectra in excellent agreement with the assigned structure were obtained for this substance.

(5) J. A. Skorcz and J. E. Robertson *J. Med. Chem.*, **8**, 255 (1965).

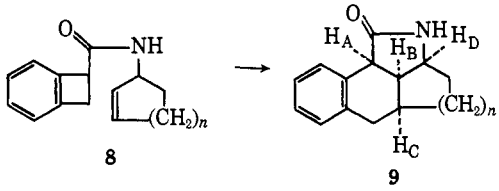
(6) The product was correlated chemically with a reference compound, the structure of which has been established by X-ray crystallographic analysis; J. M. Bastian and H. P. Weber, private communication.

(7) (a) Direct evidence for the intermediacy of *o*-quinodimethanes in this type of reaction is reported in the subsequent communication. (b) For the occurrence of *o*-quinodimethane intermediates during the intermolecular reactions of 1,2-diphenylbenzocyclobutenes with typical dienophiles, see R. Huisgen and H. Seidl, *Tetrahedron Lett.*, 3381 (1964); G. Quinkert, K. Opitz, W. W. Wiersdorff, and M. Finke, *Justus Liebigs Ann. Chem.*, **693**, 44 (1966).

on the distance between the reaction partners. The concertedness of this cycloaddition step was tested as follows.

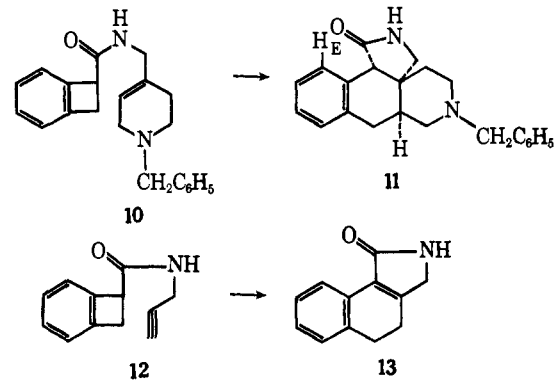


Thermolysis of the *cis*-3-chloroallylamide (**5a**)[4,8] in boiling bromobenzene gave the products **6a**[4] (mp 118–119°; nmr J_{AB} = 13 Hz, J_{BC} = 2 Hz) and **7a**[4] (mp 116–116.5°; nmr J_{AB} = 9 Hz, J_{BC} = 4.5 Hz) in 73% yield, whereas the trans amide **5b**[4,8] under similiar conditions afforded the stereoisomers **6b**[4] (mp 132–133°; nmr J_{AB} = 13 Hz, J_{BC} = 11 Hz) and **7b**[4] (mp 126–126.5° nmr J_{AB} = 8 Hz, J_{BC} = 10 Hz) in 77% yield. According to nmr and glc analysis the conversions **5a** → **6a** + **7a** and **5b** → **6b** + **7b** are stereospecific to within 0.5%. Thus the observed stereochemical relationships are in keeping with the operation of a symmetry-controlled [$_{\pi}4_s$ + $_{\pi}2_s$] process.[9] In boiling *o*-dichlorobenzene (containing traces of *p*-toluenesulfonic acid) compounds **5a** and **6a** were cleanly converted to the cis-fused product **7a**, whereas the compounds **5b** and **6b** gave exclusively the product **7b**. Consequently, these results represent the stereocontrolled formation of three centers of chirality in a single synthetic operation.



The analogous stereospecific transformations of the cyclic olefins **8**, n = 1,[4] and **8**, n = 2,[4] to the tetracyclic products **9**, n = 1[4] (mp 199–200°; nmr J_{AB} = 9.5 Hz, J_{BC} = J_{BD} = 7–8 Hz; 70%), and **9**, n = 2[4] (mp 175–177°; nmr J_{AB} = 8.5 Hz, J_{BD} ≤ 7 Hz, 72%), respectively, illustrate an approach to condensed ring systems with stereochemical control over four adjacent centers of chirality.

The flexibility of this method is further exemplified by the transformations **10** → **11** and **12** → **13**. Thus, heating a 1% solution of **10**[4,10] in toluene at 250° for 8 hr afforded **11**[4] (mp 216–217°; nmr ($CDCl_3$) δ_{H_E} = 7.5 ppm, 64%); refluxing an 8% solution of **12**[4] in bromobenzene for 16 hr gave **13**[4] (mp 174–176°; 95%). These experiments indicate that trisubstituted olefinic double bonds, as well as carbon–carbon triple bonds, can participate in intramolecular *o*-quinodimethane cycloadditions. Finally it should be mentioned that all the reported reactions proceeded in a highly regioselective manner.



Besides providing a simple and efficient route to a variety of new ring systems, the described method may prove of value in the synthesis of certain natural products.[11]

(8) The corresponding amines were prepared by the reaction of methylamine with pure *cis*- and *trans*-1,3-dichloropropene, kindly provided by Dr. M. Kohler, Sandoz Ltd.

(9) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(10) Prepared in 70% overall yield by alkylation of *N*-(4-pyridylmethyl)benzocyclobutenyl-1-carboxamide with benzyl bromide and subsequent reduction of the resulting pyridinium bromide with sodium borohydride in methanol at 0°.

(11) For an application of intramolecular *o*-quinodimethane cycloadditions to the synthesis of *dl*-chelidonine, see W. Oppolzer and K. Keller, *J. Amer. Chem. Soc.*, **93**, 3835 (1971).

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The Thermal Rearrangement of *N*-(1-Benzocyclobutenyl)vinylacetamide. Kinetics and Mechanism

Sir:

Thermal rearrangements of olefinic 1-benzocyclobutene derivatives exhibit a high degree of regio- and stereoselectivity.[1] These features can be accounted for in terms of a scheme involving *o*-quinodimethane intermediates. The mechanistic implications of such a scheme have now been tested in the following way.

The amide **1**[2] (prepared by acylation of 1-aminobenzocyclobutene[3] with vinylacetyl chloride in aqueous potassium hydroxide, 50–90% yield) was isomerized completely in boiling toluene within 16 hr to give the two stereoisomeric benz[*g*]indoles **3**[2] (mp 162–164°; nmr ($CDCl_3$) δ_{H_A} = 4.76 (d, J = 6.5 Hz), δ_{H_C} ≤ 7.4 ppm) and **4**[2] (mp 194–195°; nmr ($CDCl_3$) δ_{H_A} = 4.26 (d, J = 8.5 Hz), δ_{H_C} = 8.35 ppm) in the ratio 4.7:1 (96% yield). The isomers **3** and **4** were not interconverted on heating in boiling toluene for 20 hr

(1) W. Oppolzer, *J. Amer. Chem. Soc.*, **93**, 3833 (1971).

(2) Elemental analyses, as well as ir and nmr spectra, were in excellent agreement with this structure.

(3) J. A. Skorcz and J. E. Robertson, *J. Med. Chem.*, **8**, 255 (1965).