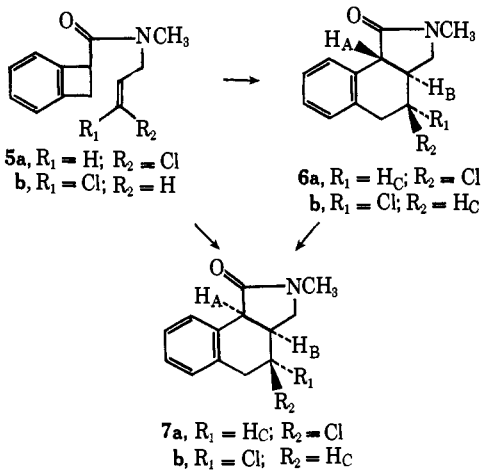
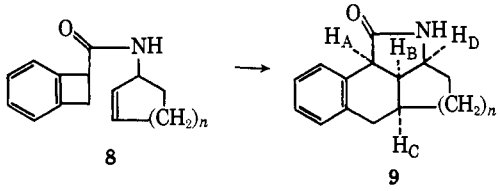
on the distance between the reaction partners. The concertedness of this cycloaddition step was tested as follows.

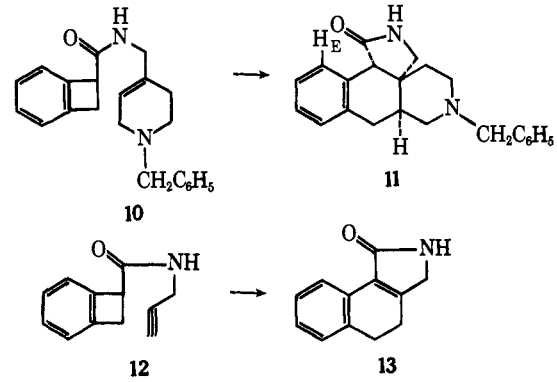


Thermolysis of the *cis*-3-chloroallylamide (**5a**)[4,8] in boiling bromobenzene gave the products **6a**[4] (mp 118–119°; nmr J_{AB} = 13 Hz, J_{BC} = 2 Hz) and **7a**[4] (mp 116–116.5°; nmr J_{AB} = 9 Hz, J_{BC} = 4.5 Hz) in 73% yield, whereas the trans amide **5b**[4,8] under similiar conditions 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).

W. Oppolzer
Pharmaceutical Chemical Laboratories, Sandoz Ltd.
4002 Basel, Switzerland
Received March 25, 1971

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.

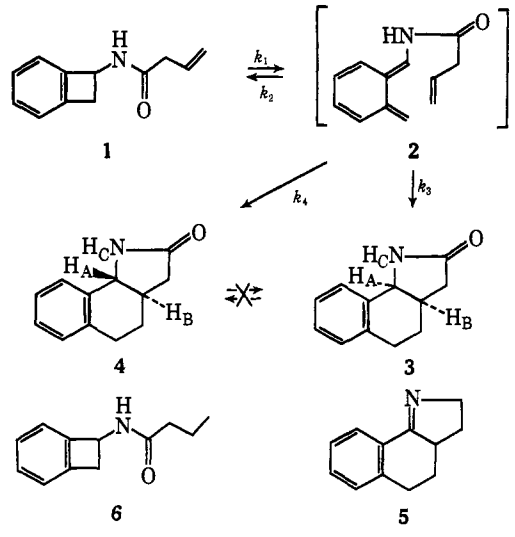
The amide **1**[2] (prepared by acylation of 1-aminobenzocyclobutene[3] with vinylacetyl chloride in aqueous potassium hydroxide, 50–90% yield) was isomerized completely in boiling toluene within 16 hr to give the two stereoisomeric benz[*g*]indoles **3**[2] (mp 162–164°; nmr ($CDCl_3$) δ_{H_A} = 4.76 (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).

but both afforded the same oily pyrroline **5**[2] on reduction with AlH_3 in tetrahydrofuran[4] and subsequent oxidation of the resulting pyrrolidines with $KMnO_4$ in acetone.[5]



The reaction **1** → **3** + **4** is analogous to the related transformations of olefinic 1-benzocyclobutene carboxamides[1,6] and probably proceeds by way of a reversible opening of the four-membered ring to form an *o*-quinodimethane intermediate **2**, which is then trapped by irreversible intramolecular cycloaddition processes. In order to test this hypothesis the thermal reorganization of optically pure butenylamide **1**[2,7] ($[\alpha]_{365\ nm}^{20°(CH_3OH)}$ +81.9°) in boiling toluene at 748 mm (0.5% solution) was monitored polarimetrically, as well as by nmr analysis. The experimental results are indicated by Figure 1.

The rate of disappearance of the optically active butenylamide **1** is first order, giving directly the rate constant $k_1 = 1.37 \times 10^{-4}$ sec^{-1} for the step **1** → **2**. Under identical conditions a first-order rate constant $k_1' = 1.94 \times 10^{-4}$ sec^{-1} was measured for the racemization[8] of optically pure butyramide **6**[2,7] ($[\alpha]_{365\ nm}^{20°(CH_3OH)}$ +107.5°). Hence it appears that the olefinic double bond of the butenylamide **1** is not involved to any major extent in the opening of the benzocyclobutene. Further evidence for an achiral intermediate such as **2** is provided by the racemic nature of the products **3** and **4**, isolated at an early stage of the reaction (after 60 min).

Figure 1 also gives information concerning the relative rates of the forward and reverse reactions; if one applies the steady-state approximation[9] to the intermediate **2**, assuming that $k_1 \ll k_2$, the ratios $k_3/k_2 = 3.55$ and $k_4/k_2 = 0.75$ may be derived.[10]

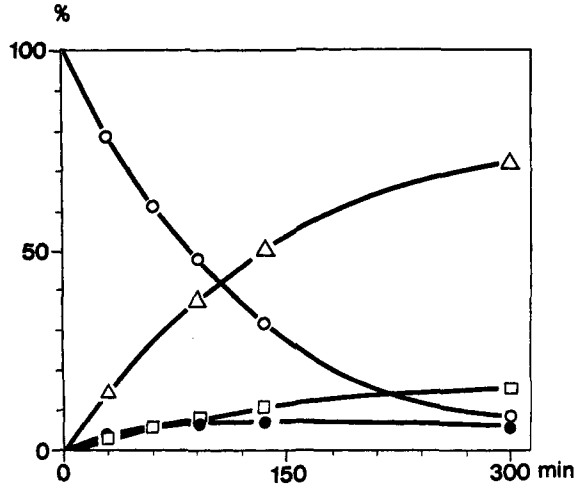
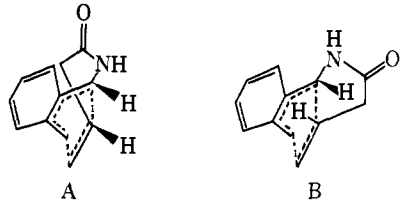


Figure 1. Kinetics of the rearrangement of optically active **1** in refluxing toluene (0.5% solution, 748 mm): ○, concentration of optically active **1**; ●, concentration of racemic **1**; △, concentration of **3**; □, concentration of **4**.

Consequently, the transition state of the addition **2** → **3** is 1.0 kcal/mol lower and that of the addition **2** → **4** 0.2 kcal/mol higher than the barrier of the ring opening **1** → **2**.

On the assumption that the four-membered ring in **1** opens preferentially to form the sterically favored trans-substituted *o*-quinodimethane **2**, it can be shown by inspection of appropriate models that the subsequent synchronous cycloaddition step[11] has to be regiospecific, giving exclusively annelated products.[12] Thus the endo transition state A should lead to the cis-fused product **3** and the exo transition state **B** to the trans-fused product **4**.



(4) N. M. Yoon and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 2927 (1968).

(5) O. Bayer in "Methoden der Organischen Chemie," 4th ed, Vol. VII/1, Georg Thieme Verlag, Stuttgart, 1954, p 206.

(6) Rearrangements of the corresponding benzocyclobutenylcarboxamides require considerably higher temperatures to proceed at a comparable rate; see ref 1.

(7) Prepared by acylation of optically active aminobenzocyclobutene, separated from its enantiomer by three crystallizations of the corresponding *d*-mandelate (mp 159–160°; $[\alpha]_{546\ nm}^{20°(CH_3OH)}$ +55.1°) from benzene–methanol (3:1).

(8) On heating **6** in refluxing toluene (0.5% solution) for 16 hr its nmr spectrum remained unchanged.

(9) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 195.

(10) Comparable rate ratios were derived from Figure 1 using a "kinetics" computer program; Dr. K. Frei, Sandoz Ltd., personal communication.

(11) For stereochemical results supporting the concertedness of intramolecular *o*-quinodimethane–olefin cycloadditions, see ref 1.

(12) This is a general explanation for the regioselectivity observed in numerous examples of intramolecular benzocyclobutene–olefin additions.

W. Oppolzer

Pharmaceutical Chemical Laboratories, Sandoz Ltd.
4002 Basle, Switzerland

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