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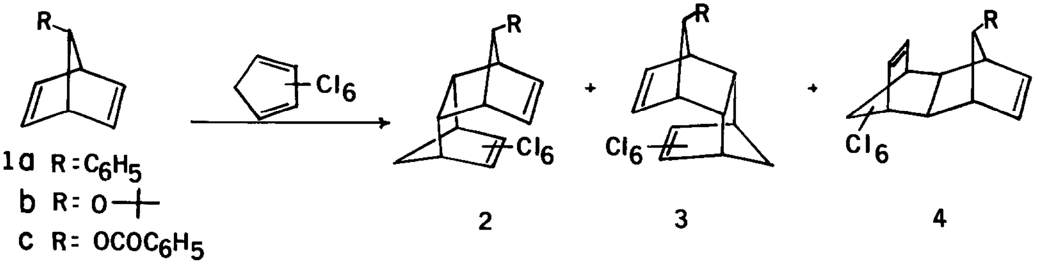
ENDO ADDITION OF CHLOROSULFONYL ISOCYANATE TO NORBORNADIENES

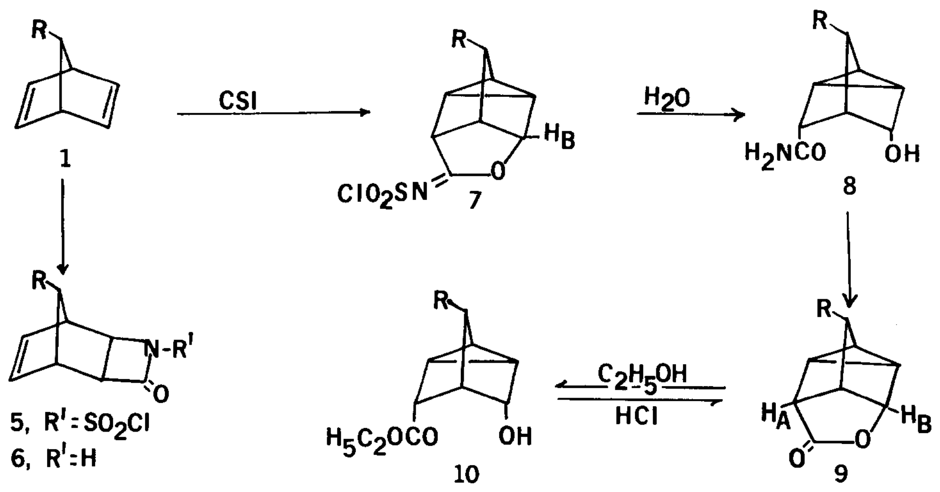
Paul H. Mazzocchi*, Theodore Halchak and Herman L. Ammon
Department of Chemistry
University of Maryland
College Park, Maryland 20742

SUMMARY The addition of chlorosulfonyl isocyanate to several 7-substituted norbornadienes affords *endo* and *exo* addition products.

Recently there has been a great deal of interest in additions to 7-substituted norbornadienes.[1] With respect to inverse electron demand Diels-Alder[1a-c] additions, the preponderance of *syn*-*endo* adducts obtained with certain 7-substituents (i.e. **3b**) has been explained by specific activation of the *syn* double bond by the substituent.[1a]



The addition of chlorosulfonyl isocyanate (CSI) to norbornene and norbornadiene has been shown to occur exclusively by *exo* addition to give the *exo* adducts in 86% and 94% yield respectively.[2] We initiated a study of the effects of 7-substituents in norbornadiene on the mode of CSI addition and we now report our initial results. These constitute the first case of *endo* addition of CSI to norbornadienes. Addition of 7-phenylnorbornadiene (**1a**) to CSI in $CHCl_3$ and subsequent treatment with Na_2SO_3-KOH[3] gave a 37% yield of the exo-β-lactam 6a: NMR($CDCl_3$) δ3.3 (m, 3H), 3.75 (m, 2H), 6.2 (m, 2H), and 7.2-7.4 (m, 5H), IR($CHCl_3$) 1770 cm^{-1}.[4,5] A second crystalline product was isolated from the aqueous phase and was preliminarily characterized as the amide alcohol **8a**:



NMR(DMSO-d$_6$) δ1.3-2.1 (m, 3H), 2.2-2.4 (m, 2), 3.0 (s, 1H), 7.4 (s, 5H), and 4.8-6.7 (broad, exchangeable, 3H), IR(KBr) 3650, 3490, 3360, 3200, 1690 and 1460 cm^{-1}; mass spectral parent ion and base peaks at m/e 229 and m/e 167 respectively. The yield after several recrystallizations (H_2O) was 15%.

Confirmation of the structure and *endo* orientation of the amide-alcohol was provided by brief treatment of **8a** with HCl-EtOH which resulted in its smooth conversion to the lactone **9a**:[6] NMR(CDCl$_3$) 1.7-2.0 (m, 3H), 2.55-2.75 (m, 2H), 3.4 (s, 1H), 4.95 (m, HB), 7.35 (s, 5H); IR(CDCl$_3$) 1785 cm^{-1}.

Treatment of **1c** with CSI and aqueous workup afforded the corresponding lactone **9c** (IR(CDCl$_3$) 1785 and 1725 cm^{-1}),[7] in addition to the β-lactam **5c**. A tentative assignment of the orientation of the bridge substituent with respect to the lactone carbonyl in **9a** and **9c** was made by comparing the chemical shifts of Ha in **9a** vs **9c**. Proton H_A is deshielded by the bridge carbonyl group by approximately 0.2 ppm in **9c** (δ2.9) vs **9a** (δ~2.65) whereas the H_B chemical shifts are quite similar.

This assignment was confirmed by a single crystal x-ray determination on **9a** (Fig. 1). Data were collected on a Picker FACS-I diffractometer with graphite crystal monochromatized MoK radiation (λ = 0.71069) Å The crystal data are: monoclinic, $P2_1/n$; a = 5.967(1), b = 8.402(1), c = 20.769(4) Å, β = 93.66-(2)°; Z = 4. Intensities were measured with the θ-2θ scan method to a maximum 2θ of 50°. 1276 of the 1822 unique reflections were more than 3σ above background. The structure was solved by direct methods and refined by the full matrix least squares technique. The final R ($\Sigma|F_o-F_c|/\Sigma F_o$) and weighted R ($[\Sigma w(F_o-F_c)^2/\Sigma wF_o^2]^{1/2}$) factors are 0.038 and 0.037.

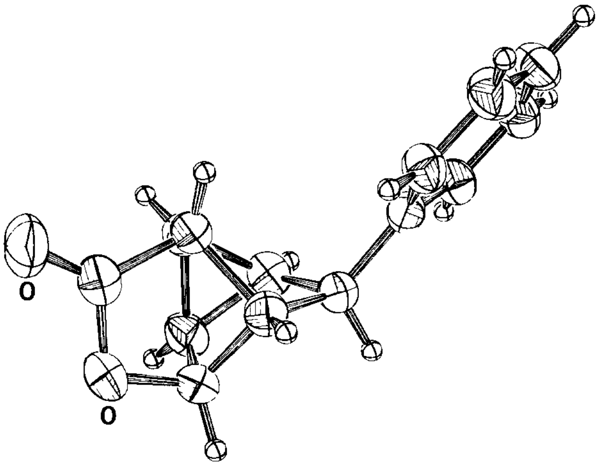


Figure I ORTEP Drawing of lactone 9a

Evidence for the intermediacy of 7 was provided by examination of the infrared spectrum of the reaction mixture (1a + CSI) which showed strong 1610 (C=N) and 1820 (C=O) cm^{-1} absorption from 7a and 5a respectively. These bands appear immediately on CSI addition and their relative intensities do not change on standing.

Speculation on the nature of the transition states leading to 7a and 5a must be consistent with the fact that the 5a/7a ratio of 2 is essentially invariant[8] in solvents of widely different dielectric constants (CCl_4, $CHCl_3$, EtBr, CH_3CN) but the rate of CSI addition to 1a is quite solvent dependent ($k_{CH_3CN}/k_{CCl_4} \simeq 10$). These results suggest that the transition states involved in these reactions are polar and that the polarities of the transition states leading to 7 and 5 are quite similar.

A reasonable mechanistic hypothesis involves either initial *exo* or *endo* attack by the electron deficient carbonyl carbon of CSI at a double bond, and would result in the required polarized transition state. The preponderance of lactone 9 over the isomeric (unisolated) lactone which would result from initial *anti*-*endo* attack, indicates that there is some preference for *syn*-*endo* over *anti*-*endo* attack.[1a]

Clearly 7-substitution results in a dramatic increase in the yield of *endo* addition products. This could result from either a significant increase in the rate of *endo* addition or a decrease in the rate of *exo* addition. We hope to be able to answer this question when we have finished our investigations on the stereochemistry and kinetics of CSI additions to a series of norbornadienes with *p*-substituted 7-phenyl substituents (F, H, CH_3, OCH_3).

Acknowledgement

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References and Footnotes

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4. All new compounds gave acceptable elemental analysis (C,H,N).

5. The *exo* stereochemistry follows from the analysis of the NMR couplings. See *ref.* 2.

6. Prolonged treatment of **9a** with EtOH-HCl afforded the alcohol ester **10**.

7. This material was originally isolated by Moriconi and Crawford (ref. 2) but its structure was not assigned. They reported an 11% yield of **5c** and we have isolated **9c** in 10% yield.

8. Determined by NMR using the olefin proton and H_B resonance in **5** and **7** respectively. H_B was assigned to a resonance at 5.2δ. An additional peak (1/3 the intensity of the 5.2δ peak) at 5.0δ was observed in all cases and was tentatively assigned to the isomeric imino lactone formed via initial *anti-endo* attack. This material may have been lost during work-up. In support of this hypothesis preliminary experiments with 7-(p-methoxyphenyl)norbornadiene indicate that in this case we isolate a mixture of isomeric lactones in a 3:1 ratio. We are presently working on the separation of these materials.

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