Theoretical Study of the Ruthenium-Catalyzed Cyclocotrimerization of Alkynes with Isocyanates and Isothiocyanates: Chemoselective Formation of Pyridine-2-one and Thiopyrane-2-imine

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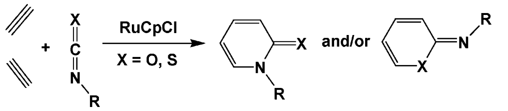
The cyclocotrimerization of acetylene with isocyanate HNCO and isothiocyanate HNCS, mediated by CpRuCl, is theoretically investigated on the basis of DFT/B3LYP calculations. By these means, the experimental result can be rationalized as to why, with HNCO, a nitrogen-heterocycle is formed, but with HNCS a sulfur-heterocycle is formed. According to the proposed mechanism, the key reaction step is the addition of a double bond to a metallacyclopentatriene formed by oxidative coupling of two acetylene ligands coordinated to CpRuCl, giving a bicyclic carbene intermediate. This double-bond-addition is initiated by η^1 attack at the ruthenium center, and it is just the attacking atom that is going to be incorporated into the cycle. Thus, the chemoselectivity originates from the fact that, for HNCO, N attack is preferred over O, but for HNCS, S attack is preferred over N. The onward reaction is a reductive elimination to give a coordinatively unsaturated metallaheteronorbornene intermediate finally rearranging to a ligated heterocycle. Completion of the cycles is achieved by an exothermic displacement of the respective heterocyclic product by two acetylene molecules which regenerates the bisacetylene complex.

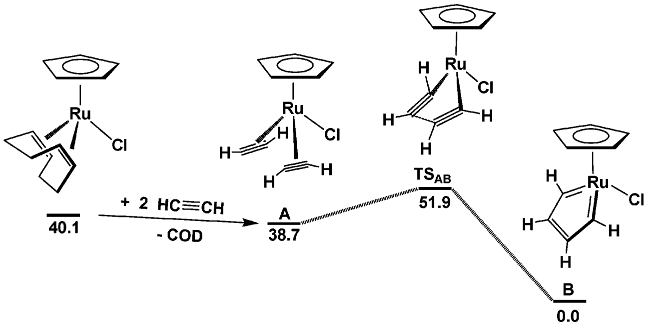
Introduction

The cyclocotrimerization of two alkynes with unsaturated organic compounds containing C═X bonds (X = O, S, N, etc.) is a synthetically useful and metal economic process for obtaining a variety of six-membered heterocyclic systems.[1−4] Transition metal complexes which catalyze such reactions, however, are rare particularly if X = S because the strong coordination of organosulfur compounds tends to deactivate the mediator. Among the catalysts which do not suffer from such drawbacks, the ruthenium complex RuCp*(COD)Cl appears to exhibit highly catalytic efficiency as recently found by Itoh and co-workers.[5,6] The coupling of diynes with ambidentate molecules RN═C═X (X = O, S) is particularly intriguing because there are two different kinds of ring closures possible leading either to pyridine-2-ones and pyridine-2-thiones or to pyrane-2-imines and thiopyrane-2-imines according to Scheme 1.

SCHEME 1



SCHEME 2



Experimentally, it was found that in the case of X = O exclusively pyridine-2-ones are formed, whereas in the case of X = S the chemoselectivity is reversed which gives thiopyrane-2-imines.

While the detailed mechanism of these conversions is not yet fully established, the initial steps should be identical to those calculated previously for the cyclocotrimerization of two molecules acetylene with another acetylene, ethylene, or CX_2 (X = O, S, Se), using RuCp(COD)Cl as the precatalyst.[7,8] These common steps are displayed in Scheme 2. Accordingly, the reaction is

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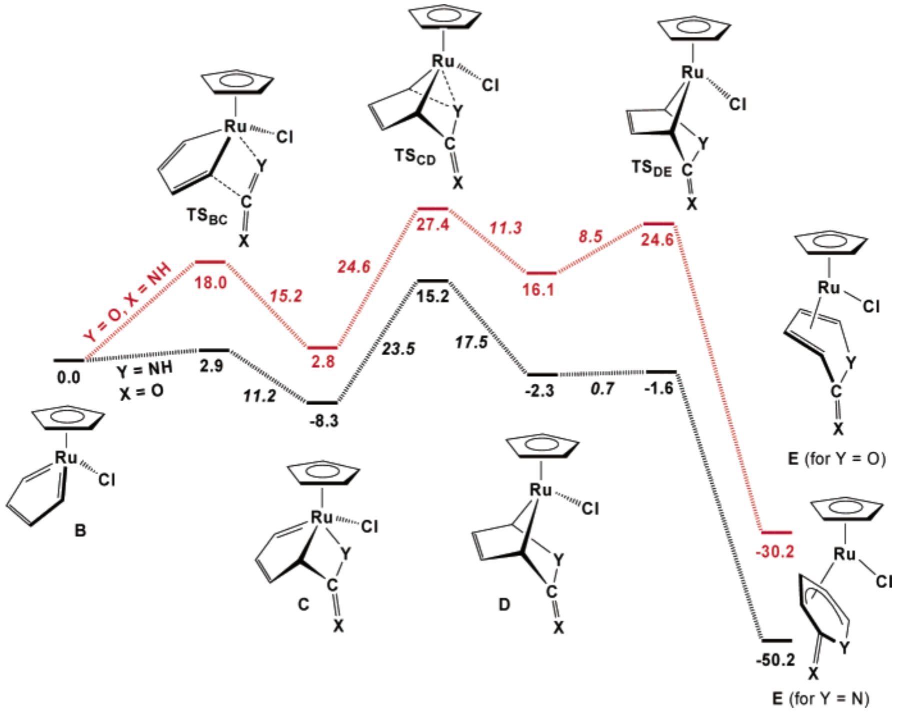
SCHEME 3



initiated by the replacement of labile COD by two molecules of acetylene to give the bisacetylene complex **A** which then transforms into the metallacyclopentatriene **B** as the result of oxidative coupling. Complex **B** would seem to be the common key intermediate. Featuring a biscarbene functionality, it is capable of inserting a multiple bond into a Ru═C bond.

In the present work, we continue our theoretical studies based on DFT/B3LYP calculations.[9,10] We will investigate the modes of addition of isocyanates and isothiocyanates X═C═NH (X = O, S) to **B**. It will be interesting to identify further intermediates and to see whether the experimentally observed chemoselectivity is rationalized.

Results and Discussion

Reaction of HN═C═O with B. The energy profile for the two alternatives, viz. orientation of N (black lines) or O (red lines) toward the ruthenium center, is shown in Scheme 3. The corresponding equilibrium structures and transition states are depicted in Figures 1 and 2. The initial η^1-Y (Y = N or O) coordination at ruthenium is stabilized by an additional (only slightly delayed) C−C bond formation (in $\mathbf{TS_{BC}}$, the C···C distance is still very long (2.24 for Y = N, and 2.17 Å for Y = O). Overall, there is Y═C addition to a Ru═C bond that leads to the primary bicyclic carbene intermediate **C**. This contrasts somewhat with the previously analyzed acetylene addition to **B**, in which case HC≡CH becomes η^2 bonded to the center without appreciable ligand−ligand interactions. In the present situation, the addition of the N═C bond is preferred energetically over O═C in that the first case is exothermic by 8.3 kcal/mol, but the latter case requires 2.8 kcal/mol and is slightly endothermic. These differences, however, are not reflected by the bond lengths (for Y = N, Ru−Y (2.06) and C−C (1.57 Å), and for Y = O, Ru−Y (2.07) and C−C (1.54 Å)). Moreover, the formation of **C** is strongly favored kinetically in the case of N═C bond addition, requiring only 2.9 kcal/mol, while the activation energy for O═C addition is 18.0 kcal/mol. The onward reaction of **C** to the metallaheteronorbornene **D** is essentially a reductive elimination in which a vacant coordination site is created.

The second step, **C** → **D**, is endothermic for both alternatives. The activation energy will be guided, on one hand, by the strength of the Y−Ru bond to be broken and, on the other hand, by the capability of Y to simultaneously bind to a carbon and to share a lone-pair with the vacant coordination site. This implies a rather complex dependence on the size of Y. A comparison of the energies necessary to form $\mathbf{TS_{CD}}$ in Scheme 3 with those calculated for the corresponding step in the reaction of **B** with CY_2 (Y = O, S, Se) reported previously[7] has a bearing on this point. While the barrier is highest if Y is a second-period element, it decreases in the order O (28.1) > S (17.7) > Se (14.6 kcal). The 28.1 kcal for the CO_2 system is similar to the values shown in Scheme 3 (23.5 kcal for N and 24.6 kcal for O). This may be considered in the context of the atomic radii increasing in the order O (0.66) < N (0.70) < S (1.02) < Se (1.20 Å).[11] It may be noted that in the similar reaction

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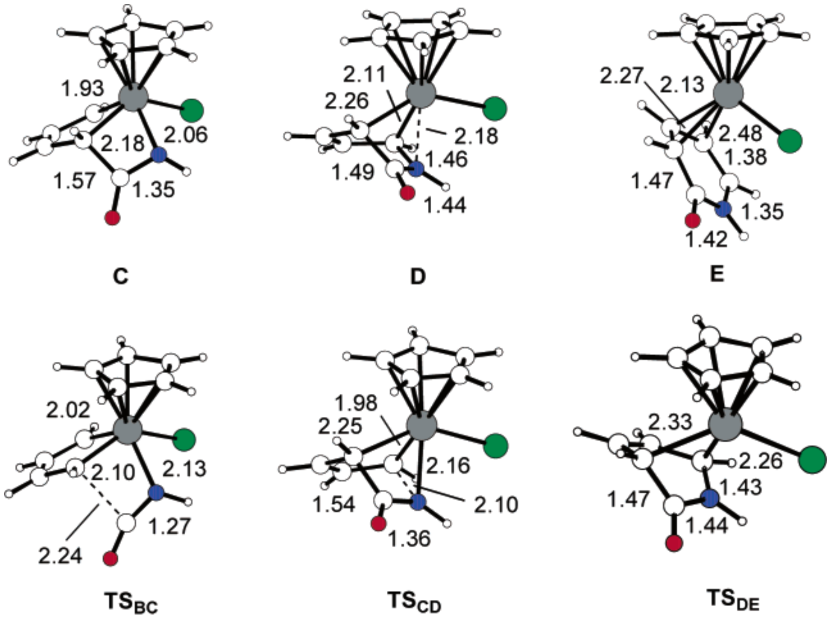


FIGURE 1. Optimized B3LYP geometries of the equilibrium structures and transition states (distances in Å) for the reaction of **B** with HN=C=O via N=C bond insertion.

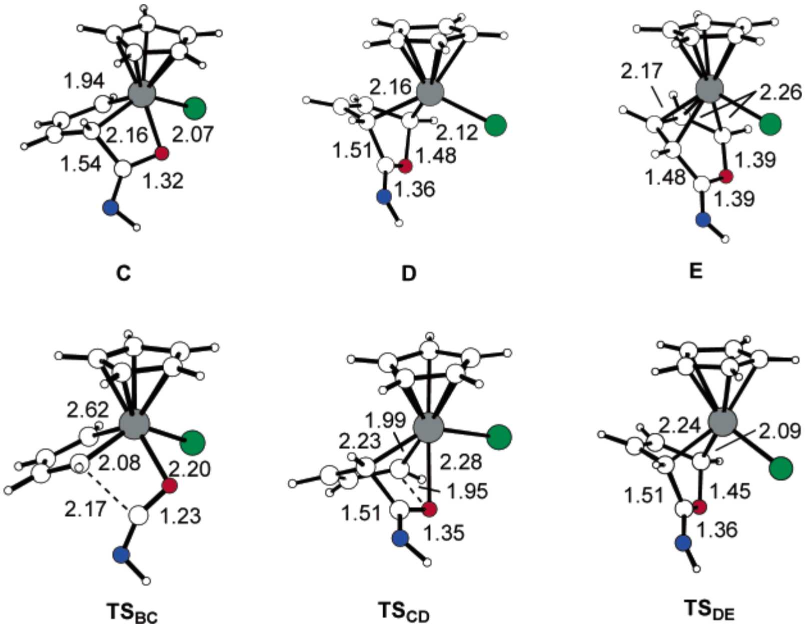
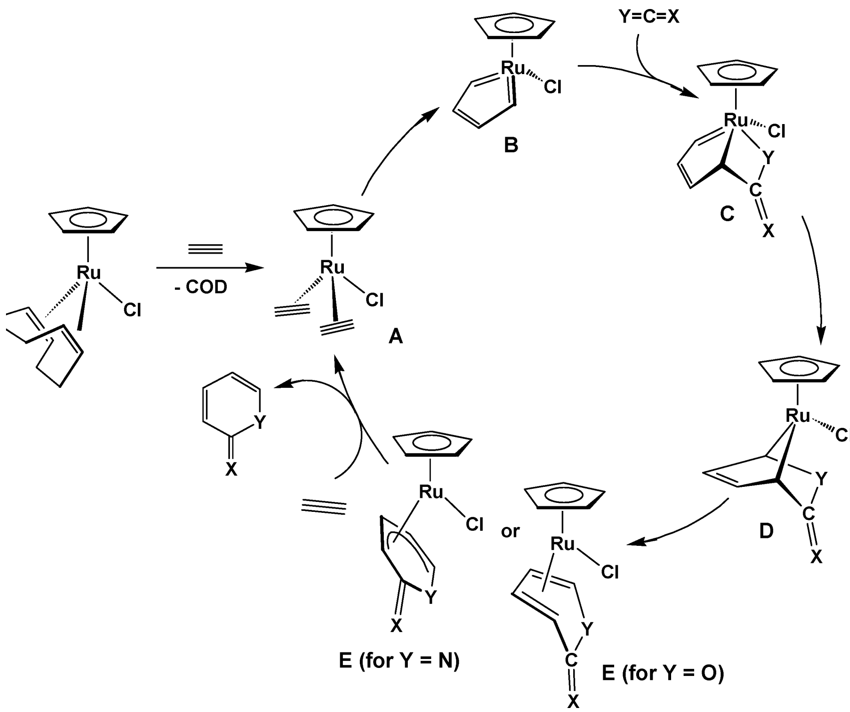


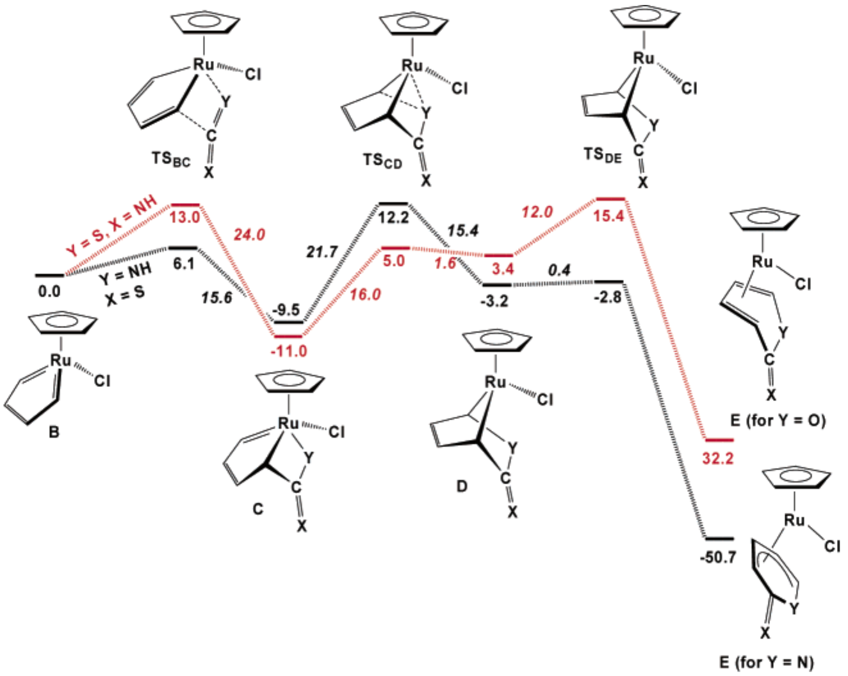
FIGURE 2. Optimized B3LYP geometries of the equilibrium structures and transition states (distances in Å) for the reaction of **B** with HN=C=O via O=C bond insertion.

with Y = alkene, an agostic interaction tends to counterbalance unsaturation. In the present case, the transition state $\mathbf{TS_{CD}}$ largely resembles **D** having a nitrogen and oxygen atom in a pyramidal environment, with the C−Y bond partly formed and the Ru−Y bond already weakened (ca. 0.1 Å longer than in **C**). In **D**, the C−Y bond approaches a normal bond, although on the long side (1.47 for N and 1.48 Å for O). They become typical C−N and C−O bonds (1.35 and 1.39 Å) in the final species **E**, when the Ru−Y bond has completely vanished. It is noteworthy that the structure of **E** differs in the two cases. For Y = N, the transformation of **D** starts by a pivoting of the butadiene moiety, moving it from di-σ to η^3-coordination with the pyridine-2-one ligand being already planar. For Y = O, the conversion of **D** involves rearrangement of a di-σ coordinated metallaoxonorbornene to an η^4-bound pyrane-2-imine. The differential behavior appears to be a substituent effect in that the oxo substituent can form a relatively stable oxyanion, giving rise to resonance-stabilization. This reduces the activation energy (0.7 kcal for pyridine-2-one and 8.5 kcal for pyrane-2-imine formation). Subsequent completion of the cycle is achieved by the displacement of the heterocyclic product by two acetylene molecules regenerating **A** (Scheme 4), which is exothermic by 14.5 kcal for pyridine-2-one and 12.8 kcal for pyrane-2-imine.

SCHEME 4



SCHEME 5



Reaction of HN═C═S with B. The energetic profiles of the two alternative pathways initiated by S → Ru and N → Ru attack are contrasted in Scheme 5 with the geometries of the entities depicted in Figures 3 and 4. While, as expected, the overall picture parallels largely the case above, some peculiarities are obvious. At first, the step **B** → **C** is exothermic for both interaction modes. Interestingly, the formation of **C** is slightly more exothermic for Y = S despite a twice as high activation energy as compared to Y = N. This means, according to the principle of microscopic reversibility, that, for **C**, once it is formed the reverse reaction is much more disfavored thermodynamically if Y = S. Consequently, S═C addition is preferred over N═C, in accord with the experimental result. Likewise, for the same reason as noted above, the subsequent reductive elimination to give the metallaheteronorbornene **D** is more facile in this case.

The final transformation of **D** into **E** takes place analogously to the case described above, noting the same structural differences of the products **E** and similar differences in the activation barriers for the two pathways. Completion of the cycles is achieved by substituting

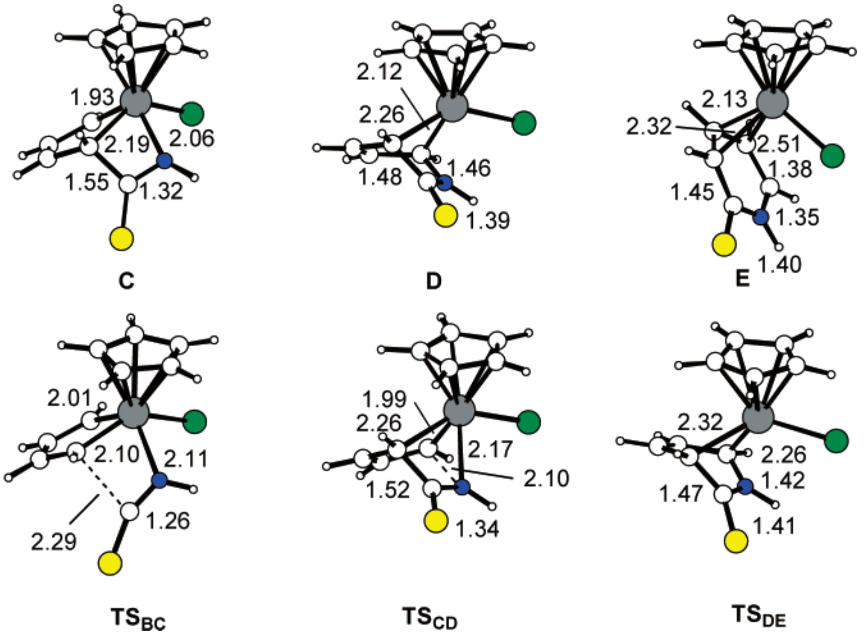


FIGURE 3. Optimized B3LYP geometries of the equilibrium structures and transition states (distances in Å) for the reaction of **B** with HN=C=S via N=C bond insertion.

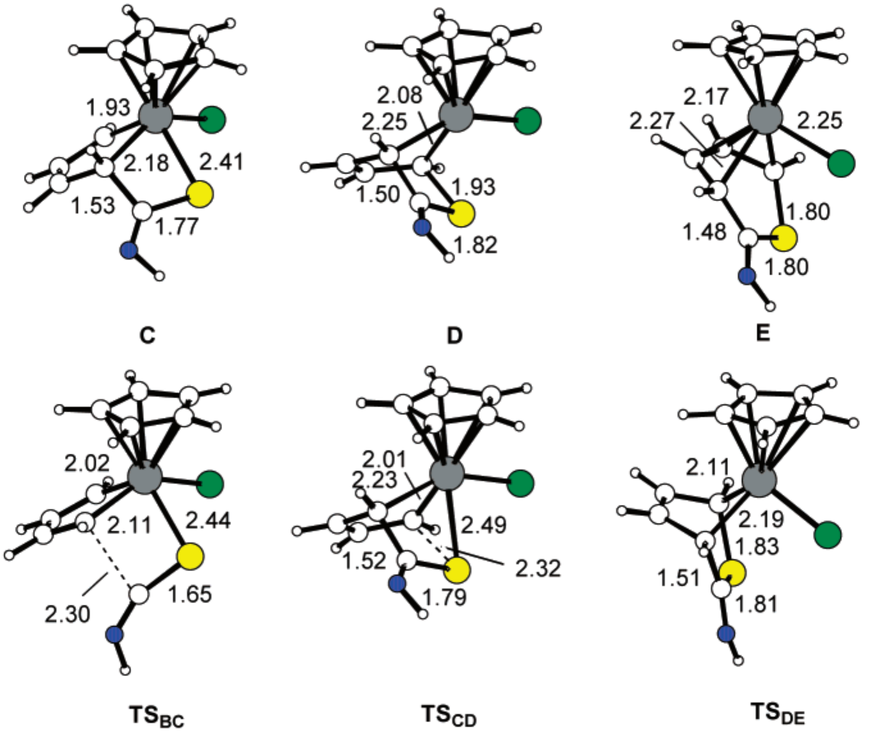


FIGURE 4. Optimized B3LYP geometries of the equilibrium structures and transition states (distances in Å) for the reaction of **B** with HN=C=S via S=C bond insertion.

two acetylenes for the heterocycles, the process of which is exothermic by 17.7 and 14.2 kcal/mol, respectively, for pyridine-2-thione and thiopyrane-2-imine (Scheme 4).

Conclusion

It is gratifying to see how theoretical studies using DFT/B3LYP calculations can aid in understanding the fundamental transformations involved in the cyclocotrimerization of alkynes with HN=C=O and HN=C=S catalyzed by the CpRuCl fragment. Specifically, the experimentally observed chemoselectivity, leading to pyridine-2-one in the former case, and thiopyrane-2-imine in the latter, is well reproduced. The course of the reactions is characterized by three not so trivial intermediates, viz. a metallacyclopentatriene, a bicyclic carbene, and a coordinatively unsaturated metallaheteronorbornene. Along these lines and in combination with our previous work,[7,8] the understanding of the mechanism of the synthetically important cyclocotrimerization for obtaining six-membered heterocyclic systems is hopefully advanced.

Computational Details

All calculations were performed using the Gaussian98 software package on the Silicon Graphics Origin 2000 of the Vienna University of Technology.[12] The geometry and energy of the model complexes and the transition states were optimized at the B3LYP level[13] with the Stuttgart/Dresden ECP (SDD) basis set[14] to describe the electrons of the Ru atom. For the H, C, N, and O atoms, the 6-31g** basis set was employed.[15] A vibrational analysis was performed to confirm that the structures of the model compounds have no imaginary frequency. The transition state structure was relaxed after applying a small perturbation to ensure that it is connected to the corresponding reactant and product. A vibrational analysis was also performed to confirm that it has only one imaginary frequency. The geometries were optimized without constraints (C_1 symmetry).

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Supporting Information Available: Computational details for all structures (Cartesian coordinates, energies, and the number of imaginary frequencies). This material is available free of charge via the Internet at http://pubs.acs.org.

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