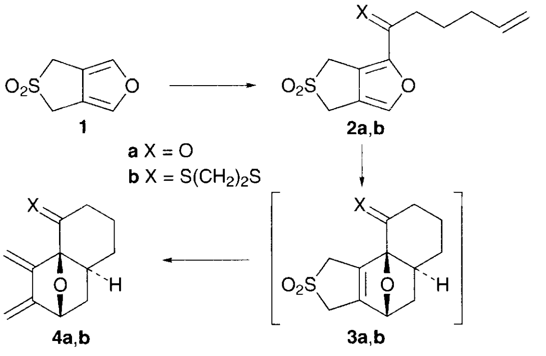
A Novel Approach to Functionalized Polycyclic Systems; New Aspects of the Diels–Alder Reactions of 2-Acyl Derivative of 4*H*,6*H*-Thieno[3,4-*c*]furan 5,5-Dioxide

Shojiro Maki, Katsuhiro Konno and Hiroaki Takayama*

Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-01, Japan

The intramolecular Diels–Alder reaction of the 2-acyl derivative of 4*H*, 6*H*-thieno[3,4-*c*]furan 5,5-dioxide **2a** is achieved by the use of molecular sieves as additive to give the corresponding cycloadduct **4a** in high yield. Addition of dienophiles to this reaction media afforded the polycyclic compounds **5** and **7a–c** *via* tandem cycloaddition in a single step.

The intramolecular Diels–Alder reaction of furan derivatives is one of the useful methods for construction of polycyclic ring systems, which has been demonstrated in complex natural product synthesis.[1] However, the intramolecular Diels–Alder reaction of 2-acylfuran derivatives using a furan moiety as a diene has never been realized due to the deactivating effect of the 2-acyl group coupled with the low reactivity of furan as a diene. Accordingly, the 2-acyl group must be protected by acetal or cyanohydrin to yield the corresponding cycloadduct.[2] In our studies on the chemistry of 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide **1**, a novel approach to functionalized polycyclic systems,[3,4] is realizable for compounds **2** which are readily accessible from **1**; heating **2a** in refluxing xylene gave no cycloadduct, but the corresponding dithioacetal **2b** smoothly afforded the cycloadduct **4b** *via* **3b** in high yield under the same conditions (Scheme 1).[3] In continuing work, however, we have found that the intramolecular Diels–Alder reaction of **2a** can be achieved by the use of *molecular sieves* as additive. Furthermore, subsequent intermolecular Diels–Alder reaction of the resulting cycloadduct **4a** proceeds well in a one pot operation by the addition of dienophiles to this reaction media (tandem cycloaddition). Reported herein are these new aspects of the Diels–Alder reaction of **2a**.

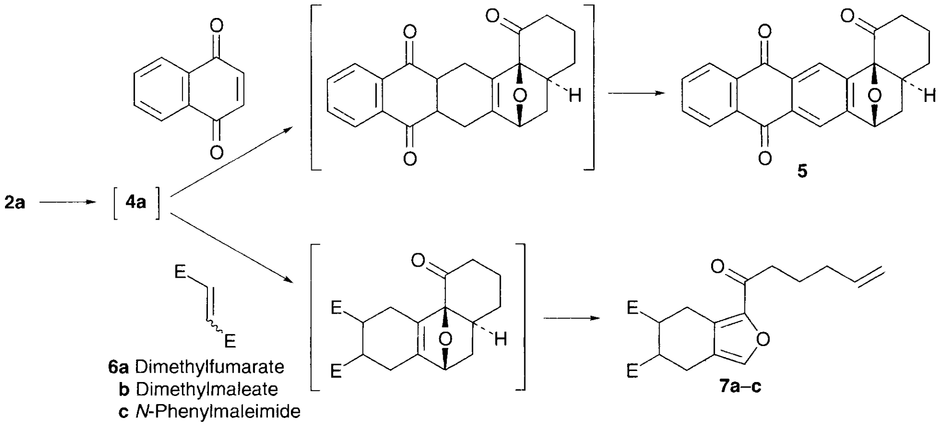


Scheme 1

Heating **2a** in refluxing toluene in the presence of molecular sieves 4 Å (MS-4 Å) for 120 h produced the cycloadduct **4a** in 90% yield.† Using MS-13X or Celite instead of MS-4 Å gave similar results, but silica gel or camphorsulfonic acid had no effect. This remarkable effect of using molecular sieves and Celite is noteworthy. Although it is not clear how they are involved in the reaction pathway, they appear to accelerate the formation of the intermediate **3a** in some way, and once formed, SO_2 extrusion (the cheletropic reaction) immediately takes place to make the equilibrium favorable for product formation, which is a key feature of Diels–Alder reactions for **1** and **2** as noted previously.[3]

Addition of dienophiles to the above reaction media prompted sequential intra- and inter-molecular Diels–Alder reaction (tandem cycloaddition). Heating **2a** in refluxing toluene in the presence of MS -4 Å and 1,4-naphthoquinone for 24 h afforded the hexacyclic compound **5** in 18% isolated yield (80% conversion yield).† Obviously, this was a result of tandem cycloaddition, followed by autooxidation as shown in Scheme 2. This reaction sequence would be useful method for rapid access to the pentacyclic benzo[*a*]naphthacenequinone framework of benanomycins and pradimicin antibiotics and related natural products of biological interest.[5] With other dienophiles such as dimethylfumarate **6a**, dimethylmaleate **6b** and *N*-phenylmaleimide **6c**, the reaction took a somewhat different pathway and the products under the same conditions were the bicyclic furans **7a** (87%), **7b** (50%) and **7c** (81%),† respectively. In these cases, retro-cycloaddition occured after tandem cycloaddition.[6]

Thus, by the use of molecular sieves as additive, the intramolecular Diels–Alder reaction of **2a** was greatly accelerated, and the polycyclic compounds **5** and **7a–c** were synthesized from **2a** in a single step. In addition to those reported previously,[3,4] this study further demonstrates the versatility of **1**



Scheme 2

as a building block for the construction of functionalized polycyclic systems.

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Footnote

† All new compounds gave satisfactory spectral and analytical data.

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