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LETTERS

A Novel "Type-Two" Intramolecular Diels–Alder Reaction Leading to Three-Atom-Bridged Tricyclic Pyrazoles

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Abstract: (Acryloyloxy)butylated pyrazolo-3-sulfolenes are thermolyzed to the corresponding *o*-quinodimethanes which undergo simultaneous "type-two" intramolecular Diels–Alder reactions to form two- and three-atom-bridged tricyclic pyrazoles.

"Type-two" intramolecular Diels–Alder (T2-IMDA) reactions have been well studied in the past two decades[1] and are useful in the synthesis of natural products.[2] The bridge-head double bond containing product from a T2-IMDA reaction is conceivably more strained than the fused bicyclic product from a "type-one" IMDA reaction, and thus T2-IMDA reactions usually do not proceed as easily.[1b] Almost all known T2-IMDA reactions produce bicyclic systems containing one-atom bridge (eq 1). More difficulties are expected for T2-IMDA reactions leading to systems containing bridges with more atoms because of constraints on the molecules. So far, there is only one report on the construction of a two-atom-bridged tricyclic system by a T2-IMDA reaction (eq 2).[3] It is therefore desirable to determine if T2-IMDA reactions could be used for the construction of multicyclic molecules containing a bridge with three or more atoms (eq 3).

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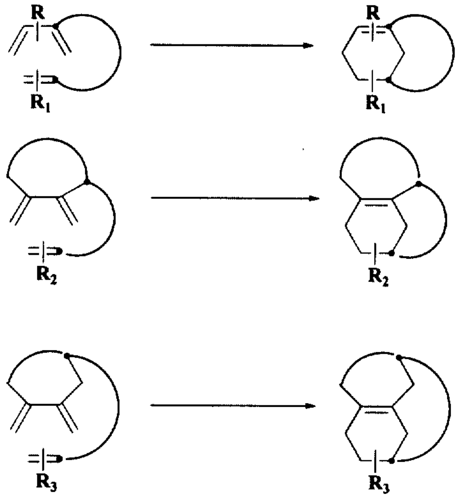
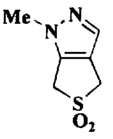


(eq 1)

(eq 2)

(eq 3)

Various heteroaromatic *o*-quinodimethanes are known to undergo inter- and intramolecular Diels–Alder reactions successfully.[4] The thermal reaction of an inseparable mixture (3:1) of *N*4-methylated and *N*5-methylated pyrazolo-3-sulfolenes **1** and **2** with *N*-phenylmaleimide gave a 3:1 mixture of the [4+2] cycloadducts **3** and **4**.[5] Therefore, pyrazolo-*o*-quinodimethane is an ideal diene moiety for our study because the dienophile can be linked to either of the two nitrogen atoms of the pyrazole ring. The T2-IMDA reactions shown in (eq 2) and (eq 3) can be examined from the same starting material.



1

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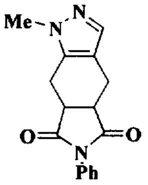

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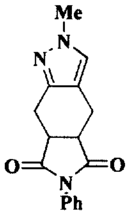

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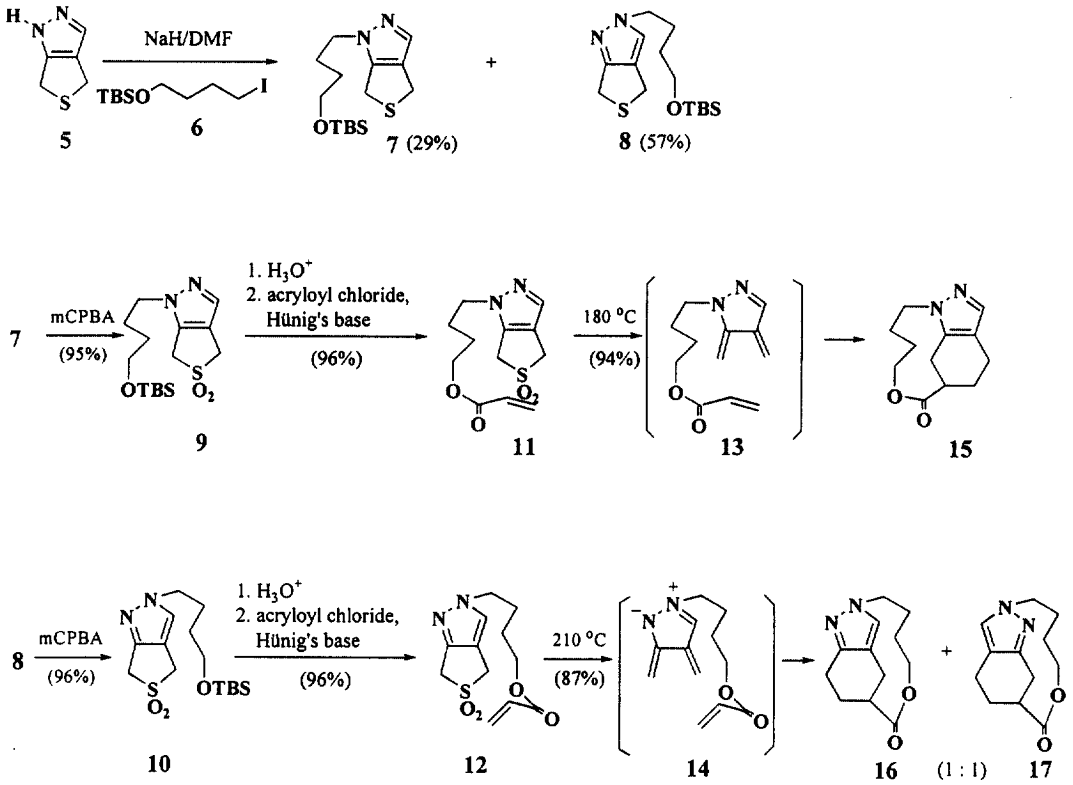
Pyrazole-fused dihydrothiophene **5**[6] was treated with NaH and then the siloxybutyl iodide **6**[7] to give an isomeric mixture of the *N*-substituted products **7** and **8** which could be separated by column chromatography (Scheme 1). Compound **7** and **8** were each oxidized with *m*-chloroperbenzoic acid (mCPBA) to the corresponding fused 3-sulfolenes **9** and **10**.

Desilylation of **9** and **10** and subsequent esterification with acryloyl chloride gave **11** and **12**, respectively, in good yield. When compound **11** was thermolyzed at 180 °C in benzene (0.005 M) in a sealed tube for 4 h, extrusion of SO_2 produced the intermediate *o*-quinodimethane **13** which underwent T2-IMDA reaction to give the two-atom-bridged tricyclic compound **15** in 94% yield.

Scheme 1



Although it was reported that both **1** and **2** lose SO_2 at 200 °C[5], compound **12** appeared to be more thermally stable than **11**. No reaction took place when **12** was thermolyzed in benzene (0.005 M) in a sealed tube at 180 °C for 6 h. Thermolysis at 190 °C for 6 h gave mainly recovered starting material along with trace amount (< 5%) of the desired cycloadducts. The difficulty encountered here was not unexpected because the generation of the zwitterionic *o*-quinodimethane **14** should be less favorable than the formation of the neutral species **13**.[8]

Thermolysis of **12** at 210 °C for 4 h brought about complete extrusion of SO_2. The T2-IMDA reaction of the transient intermediate **14** led to the formation of the three-atom-bridged tricyclic heterocyles **16** and **17** in a 1:1 ratio.

The high yield in the formation of **15–17** and the efficient synthesis of the precursors **11** and **12** make T2-IMDA reactions useful for the construction of bridged multicyclic systems which are otherwise difficult to prepare. The scope and limitations of this novel T2-IMDA reaction are under study.

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