



Reactivity increase of dienophiles by change of the ester substituents into the acid chlorides: cycloaddition reaction of the diacid chloride of 3,10-hexacyclo[10.2.1.1^{5,8}.0^{2,11}.0^{3,10}.0^{4,9}] hexadeca-6,13-diene-3,10-dicarboxylic acid with quadricyclane



Davor Margetić^{a,*}, Anamarija Briš^a, Ronald N. Warrener^b, Douglas N. Butler^b

^aLaboratory for Physical–Organic Chemistry, Division of Organic Chemistry and Biochemistry, Ruder Bošković Institute, 10001 Zagreb, Croatia

^bCentre for Molecular Architecture, Central Queensland University, Rockhampton, Queensland 4702, Australia

ARTICLE INFO

Article history:

Received 15 February 2013

Received in revised form 6 June 2013

Accepted 17 June 2013

Available online 24 June 2013

Keywords:

Polynorbornanes

Acid chloride

Polycycles

Quadricyclane

DFT calculations

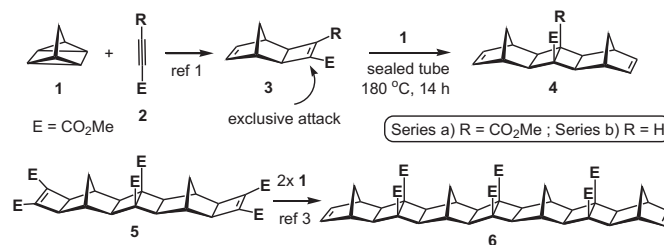
ABSTRACT

Conversion of the ester substituents on the cyclobutene π -bond of dimethyl tricyclo[4.2.1.0^{2,5}]nona-3,7-diene-3,4-dicarboxylate to the corresponding acid chloride increases the cycloaddition reactivity toward quadricyclane so dramatically that the reaction temperature can be dropped from 180 °C (preparation of title 3,10-diester) to room temperature (preparation of the title 3,10-diacid chloride). The cycloadduct product, an acid chloride of the title ring system, is extremely docile and can be recrystallized unchanged from hot methanol.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

In 1965, Claiborne Smith reported that heating dimethyl acetylene dicarboxylate (DMAD) **2a** with quadricyclane **1** yielded dimethyl tricyclo[4.2.1.0^{2,5}]nona-3,7-diene-3,4-dicarboxylate **3a**.¹ This was an important finding as it was first example of the bis-homo Diels–Alder reaction of quadricyclane and this reaction has since been used² to produce a wide variety of substituted tricyclo[4.2.1.0^{2,5}]nona-3,7-dienes. Some years later, we reported³ that further reaction of Smith's diene **3a** with quadricyclane **1** yielded **4a**, the 3,10-bis(methoxycarbonyl) derivative of the title ring system. This reaction required rather forcing conditions (180 °C, sealed tube), and, while we have been able to produce the 14 σ -system **6** by [π 2+ σ 2+ σ 2] reaction of quadricyclane with the bis-cyclobutene 1,2-diester **5** (Scheme 1),³ the reaction becomes impractical due to product insolubility when applied to higher members thereby limiting the ultimate length of the molecular rack formed via these sequential processes.



Scheme 1. Construction of polynorbornanes by quadricyclane addition to cyclobutene esters.

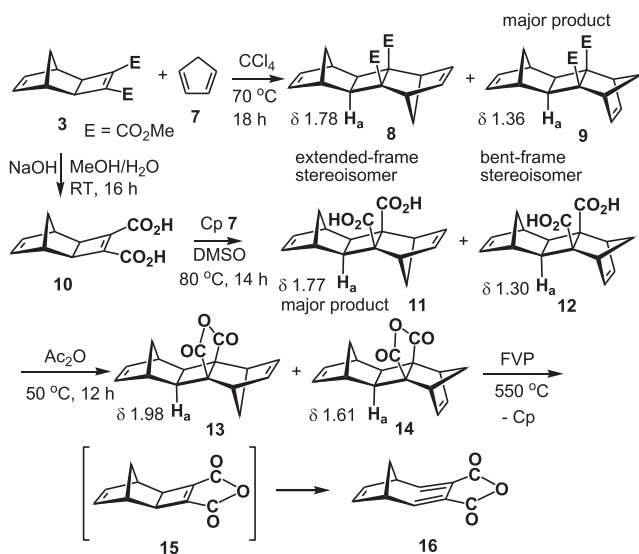
Other researchers have shown that a combination of heat and high pressure (100 °C, 10 kbar, 65 h) can be used to form the monoester derivative **4b** by reaction of quadricyclane **1** with methyl propiolate **2b**.⁴ We find that high pressure alone (up to 14 kbar) fails to induce significant reaction between DMAD and quadricyclane and only trace amounts of **4a** are observed.

2. Results and discussion

We reasoned that the dienophilicity of the cyclobutene component in Smith's diene **3a** was the limiting factor in formation of the hexacyclic system **4**, so we sought ways to remedy this problem. Hydrolysis of **3a** to the cyclobutene-1,2-diacid **10** was reported by

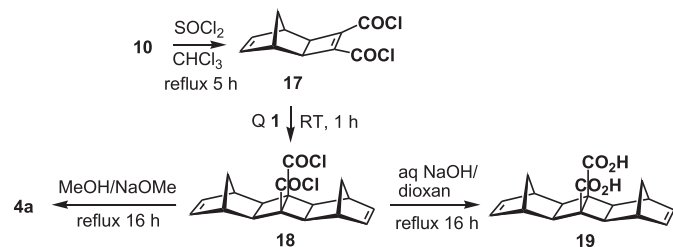
* Corresponding author. Tel.: +385 1 456 1008; fax: +385 1 468 0195; e-mail address: margetid@irb.hr (D. Margetić).

us earlier,³ and while the stereoselectivity of the reaction with cyclopentadiene changed from that favoring the bent-frame isomer **9** to one favoring the extended-frame isomer **11**,^{5,6} it did not improve the dienophilicity. Our next approach was to attempt to convert the diacid to the corresponding anhydride, on the assumption that the annulated maleic anhydride so formed would improve the dienophilicity by increasing the ring strain at the π -centre.⁷ This could not be achieved directly by William's in situ method⁸ and the indirect method outlined in Scheme 2 was devised. The diacid **10**/cyclopentadiene **7** mixture of stereoisomeric adducts **11** and **12** were heated with acetic anhydride to yield a mixture of anhydrides **13** and **14**, which were not separated as both adducts should give the same product in the next step. Retro-Diels–Alder elimination of cyclopentadiene from **13/14** was conducted under flash vacuum pyrolysis conditions (packed quartz tube, 550 °C, 0.04 mbar). However, the anhydride product from this reaction was the muconate derivative **16**, rather than the cyclobutene anhydride **15**. There is a good precedent for ring-opening of these types of cyclobutenes to 1,3-dienes under FVP conditions.⁹



Scheme 2. Synthetic route to **16**.

We next turned to the acid chloride of Smith's diene, since it was well established in Diels–Alder chemistry that acid chlorides are far more reactive dienophiles than their esters or acids, especially in the fumarate series.¹⁰ As shown in Scheme 3, conversion of diacid **10** to the acid chloride **17** was achieved by reaction with thionyl chloride. The key reaction of **17** with quadricyclane occurred exothermically in ether at room temperature and led to the formation of the hexacyclic bis-(acid chloride) **18** in excellent yield.



Scheme 3. Synthesis of **18** and functional transformations.

The hexacyclic acid chloride **18** is an unusual product in its own right, as it could be recrystallized unchanged from hot methanol

solution, which is not the expected result for an acid chloride. This acid chloride is extremely docile and only by boiling in MeOH/NaOMe overnight, the known hexacyclic diester **4a**³ was formed. Further, conversion to the hexacyclic diacid **19** required boiling of **18** in aqueous sodium hydroxide/dioxan for extended periods. We ascribe this docile behavior to the sterically crowded environment of the acid chloride groups in this ring system where the carbocyclic framework hinders approach of the nucleophilic reagent to the carbonyl centers of the acid chlorides.

We have also conducted computational study on the stereospecificities of the DA reactions¹¹ of cyclopentadiene with dienophiles **3**, **10**, **15**, and **17** and find that the formation of extended product is favored in the case of **10** (Table 1). Increased reactivity of diacid chloride **17** observed experimentally is associated with significantly lower LUMO energy level (reduced FMO gap). As a consequence, the activation energy is smaller by 3.8 kcal mol⁻¹ than for reaction of ester **3**. Data collected in Table 1 shows that experimentally observed stereochemical outcomes are readily predicted by the B3LYP/6-31G* method. Moreover, these calculations support our rationale that the presence of the intramolecular hydrogen bonding in transition states involving diacid **10** reverses stereochemical outcome. Anhydride **15** was predicted to have the smallest activation energy, as the consequence of imposed ring strain.

Table 1
Calculated transition state energies for the DA reactions of cyclopentadiene with **3**, **10**, **15**, and **17** and their LUMO energy levels

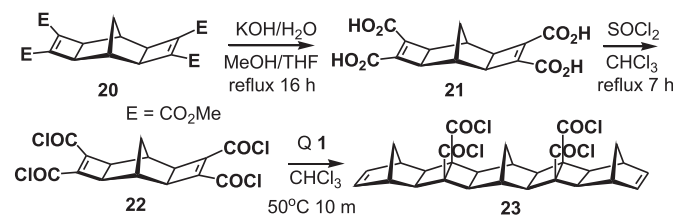
Dienophile	R	LUMO (eV) ^{a,b}	E _{TS(extended)} (kcal mol ⁻¹) ^c	E _{TS(bent)} (kcal mol ⁻¹) ^c
3	CO ₂ Me	1.7	35.6	33.7
10	CO ₂ H	0.7	32.1	32.5
15	Anhydride	1.0	27.3	27.8
17	COCl	0.2	31.8	30.6

^a RHF/6-31G*//B3LYP/6-31G*.

^b HOMO_{CPD} = -8.1 eV.

^c B3LYP/6-31G*.

The opportunity to exploit this new finding is enhanced by our ability to conduct the process in tandem using the doubly activated bis-cyclobutene **22** (Scheme 4). This compound is readily available in two steps from the known tetraester **20**.¹² Reaction was again rapid and was complete at room temperature over 30 min to furnish the 10 σ -rod **23** (in 93% yield), which can be recrystallized from CHCl₃/MeOH without change.



Scheme 4. Synthesis of tetraacid chloride **21** and Q cycloaddition.

The high reactivity of cyclobutene-1,2-di(acid chlorides) toward quadricyclane is general and the carbocyclic frame of the bridged systems could be readily extended by 3 σ -bonds by reaction at room temperature. For example, inclusion of the 1,4-dimethoxynaphthalene chromophore can be accommodated and the extension process has been applied to the linear-framed substrate **24** to give **25** (Scheme 5). Reaction was conducted at room temperature and produced the scaffold acid chloride in essentially quantitative yield. The acid chloride group was finally converted to the corresponding ester **26** by reaction with sodium methoxide in methanol at reflux. Literature procedure requires quadricyclane reaction of corresponding diester by heating in sealed tube at 180 °C for 17 h.¹³

Download English Version:

<https://daneshyari.com/en/article/5218465>

Download Persian Version:

<https://daneshyari.com/article/5218465>

[Daneshyari.com](https://daneshyari.com)