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Copper(I)-catalyzed intramolecular photocycloadditions of dicyclopentadiene derivatives linked by removable tethers

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Abstract

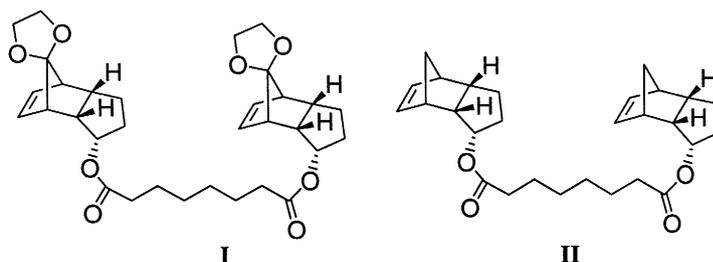
Cu(I)-catalyzed intramolecular [2+2] photocycloadditions of two dicyclopentadiene derivatives linked by an alkyl chain have been studied. These reactions are regio- and stereoselective and proceed considerably faster than the corresponding intermolecular reactions. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: intramolecular photocycloaddition; copper catalyzed; dicyclopentadiene; polycyclic compounds.

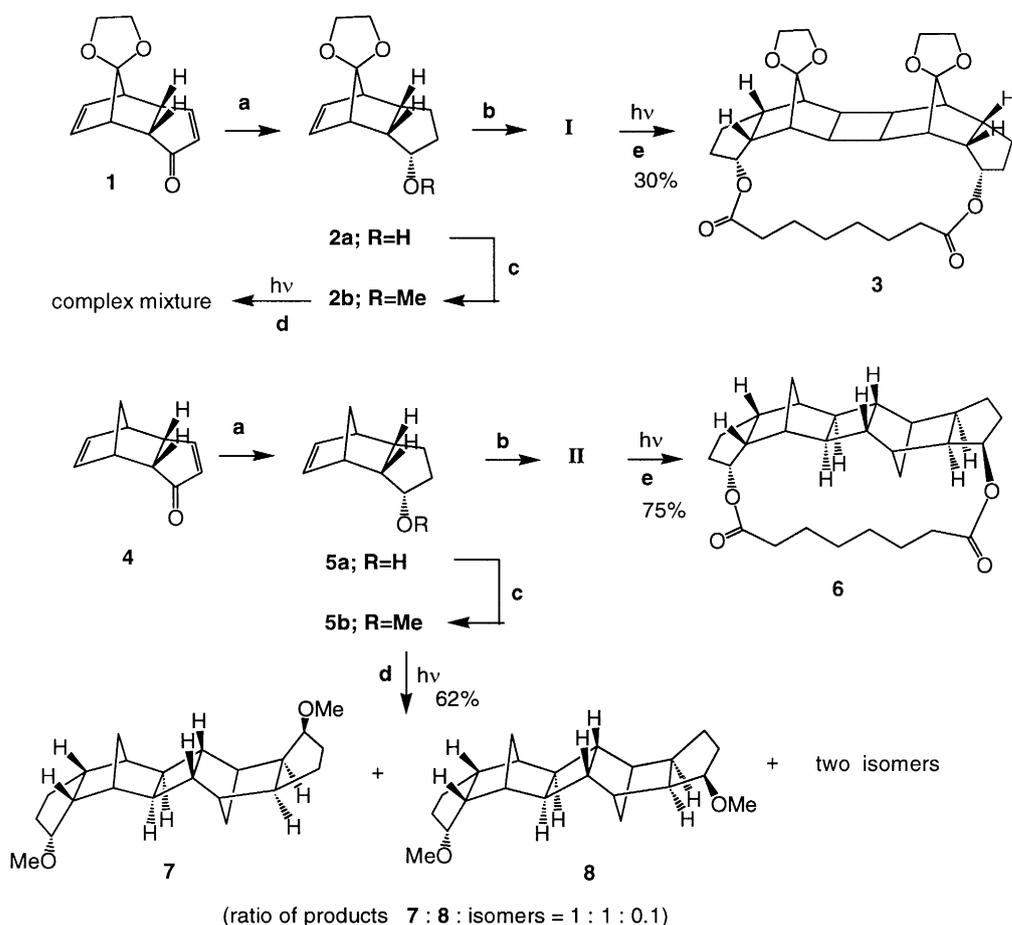
The Cu(I)-catalyzed [2+2] photocycloaddition of strained alkenes is a valuable methodology for the synthesis of carbocyclic compounds.¹ The photodimerizations of norbornenes,² *endo*-dicyclopentadienes^{2b} and other polycyclic derivatives³ have been thoroughly studied, because of the perspective to build, in one step and from simple molecules, complex and useful organic frameworks incorporating cyclobutane rings. Such dimerizations were conducted intermolecularly and often produced several isomers. Intramolecular [2+2] photocycloadditions⁴ are usually regio- and stereoselective and yield isomers not observed in the corresponding intermolecular reactions, for example *cis,syn,cis*-fused cyclobutane rings. Similarly, intramolecular photocycloadditions of polycyclic compounds could provide selective routes to polycarbocyclic molecules and to hitherto unknown isomers. However, this particular application has never been reported.

To this end, we initiated the study of Cu(I)-catalyzed intramolecular photocycloadditions of dicyclopentadiene derivatives linked by removable tethers to determine the regio- and stereoselectivity of such reactions and also to examine whether the configuration of the cyclobutane ring formed in the cycloaddition is controlled by the tether's length and rigidity. Herein we report the study of the first two substrates, **I** and **II**, made of *endo*-dicyclopentadiene derivatives tethered at the oxygen atom by a six-membered alkyl chain.

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The synthesis and photoreactions of **I** and **II** are illustrated in Scheme 1. Reduction of the enone moiety in *endo*-dicyclopentadienones **1**⁵ and **4**⁶ using NaBH₄ produced the corresponding α -alcohols **2a** and **5a**, leaving only the 'norbornene' double bond available for the cycloaddition. Reaction of two moles of **2** or **5** with one mole of suberic acid dichloride provided esters **I** or **II**, respectively. All photocycloadditions shown in Scheme 1, inter- and intramolecular, were carried out in THF and occurred only in the presence of a catalytic amount of CuOTf.⁷



Scheme 1. *Reagents and conditions*: (a) NaBH₄, MeOH, 0–5°C, 80%. (b) ClC(CH₂)₆COCl, pyridine, C₆H₆, Δ , 10–12 h, 75%, diastereomeric mixture; the photolysis was performed on one isolated diastereomer (**II**). (c) CH₃I, NaH, THF, 82%. (d) hv, THF, CuOTf, 1 week. (e) hv, THF, CuOTf, 3 h

In the photocycloaddition reactions of **2b** and **I**, we observed that the ketal group was cleaved during prolonged irradiation, and it is likely that the resulting ketone participated in photoreactions leading to

a complex mixture of products. However, there was a distinct difference between the intermolecular and intramolecular processes. In the intermolecular reaction of **2b** the ketal cleavage was faster than the cycloaddition and no photodimers were recovered. The intramolecular photocycloaddition of **I** proceeded in 30% conversion in 3 h, yielding dimer **3** as a mixture of two isomers (1:1). Further irradiation led to ketal deprotection and degradation processes. Although NMR spectral data and FAB-MS clearly indicated formation of **3**, determination of the stereochemistry was not possible as the two isomers could not be separated.

Conversely, the photocycloadditions of substrates **5b** and **II** proceeded in high yields. Irradiation of **5b** for 7 days afforded unreacted starting material and four photodimers: *exo-trans-exo* regioisomers **7** and **8** in 1:1 ratio and a small amount of two additional isomers.⁸ The photoadducts **7** and **8** were separated by column chromatography and their single-crystal X-ray structures clearly established the *exo-trans-exo* configuration of the cyclobutane ring. The intramolecular photocycloaddition of one isolated diastereomer **II**, which was complete only in 3 h, led to the *exo-trans-exo* **6**, isolated in 75% yield.⁸ The ¹H NMR spectrum of the crude reaction mixture indicated the presence of only traces of other isomers. The *exo-trans-exo* stereochemistry in **6** was unambiguously deduced through single-crystal X-ray diffraction analysis⁹ and is shown in Fig. 1. The tether, both in **3** and **6**, was readily cleaved upon reduction with LiAlH₄.

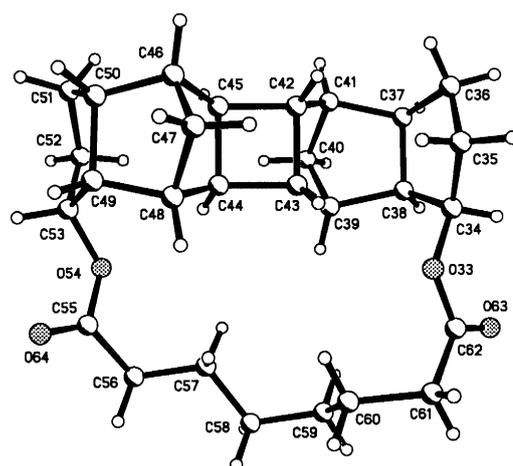


Fig. 1. A perspective drawing of the (*R,R*) diastereomer of **6**, showing one conformer of three seen in the crystal structure. All three show the identical *exo-trans-exo* fused ring system seen here, but differ in their torsion angles along the tether-chain

Since the tether in **I** and **II** is a long and flexible alkyl chain, we did not expect a change in the configuration of the cyclobutane ring with respect to the intermolecular reaction. We are currently investigating how the stereochemistry of the reaction is controlled by variations in the tether's length and rigidity.

In summary, the intramolecular photocycloadditions of **I** and **II** in the presence of CuOTf, proceeded considerably faster than the corresponding intermolecular reactions and are regio- and stereoselective. A study of intramolecular cycloadditions of a variety of functionalized dicyclopentadienes linked by removable tethers that can produce synthetically useful polycyclic cages is in progress.

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7. General procedure for photocycloadditions: *Intramolecular*: 0.1 mmol of starting material was dissolved in 20 mL of dry THF and placed in a dry quartz tube shielded with a vycor filter. A catalytic amount (3–5 mol%) of CuOTf was added and the solution was irradiated with a 450 W Hanovia medium pressure Hg lamp. The reaction was monitored by TLC and NMR. After irradiation was complete, THF was removed in vacuo and the crude residue was purified by silica gel column chromatography to obtain the pure products. *Intermolecular*: Reactions were carried out in a similar manner with 0.5 mmol of starting material in 10 mL of THF. The reaction was monitored by TLC and GC–MS.
8. Selected data for **I**: $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.21 (m, 4H), 5.09 (m, 2H), 3.88 (m, 4H), 3.78 (m, 4H), 3.16 (m, 2H), 2.81 (m, 2H), 2.66 (m, 2H), 2.57 (m, 2H), 2.29 (t, 4H, $J=10$ Hz), 1.83 (m, 2H), 1.56–1.65 (m, 8H), 1.34–1.41 (m, 6H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 173.3, 135.4, 131.6, 127.3, 76.8, 64.8, 64.1, 50.7, 49.3, 46.6, 42.4, 34.4, 34.1, 28.8, 24.8, 24.5. Compound **II**: $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.06 (m, 4H), 4.97 (m, 2H), 2.92 (m, 2H), 2.76 (m, 2H), 2.69 (m, 2H), 2.59 (m, 2H), 2.26 (t, 4H, $J=8$ Hz), 1.72 (m, 2H), 1.41–1.62 (m, 8H), 1.24–1.36 (m, 12H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 173.3, 137.3, 134.0, 77.1, 52.0, 49.1, 46.9, 45.7, 44.5, 34.3, 32.7, 28.7, 24.8, 24.3. Compound **3** (mixture of two isomers): $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 5.17 (m, 2H), 5.11 (m, 2H), 3.88 (m, 12H), 3.79 (m, 6H), 3.70 (m, 2H), 3.59 (m, 2H), 3.42 (m, 2H), 2.45 (m, 4H), 1.59–2.05 (series of m, 52H); FABMS: 554 (M^+). Compound **6**: $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.93 (m, 2H), 2.67 (m, 2H), 2.50 (m, 2H), 2.35 (m, 2H), 2.17 (m, 4H), 2.09 (m, 2H), 2.01 (m, 2H), 1.85–1.93 (m, 6H), 1.60–1.67 (m, 8H), 1.37–1.42 (m, 8H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 173.3, 77.6, 45.3, 43.9, 43.0, 42.1, 40.4, 38.3, 37.2, 36.1, 32.2, 29.6, 26.0, 22.0; Compound **7**: $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 3.74 (m, 2H), 3.36 (s, 6H), 2.36 (m, 2H), 2.27 (m, 2H), 2.21 (m, 2H), 2.14 (d, 2H, $J=10$ Hz), 2.06 (d, 2H, $J=5$ Hz), 2.00 (d, 2H, $J=5$ Hz), 1.85 (m, 4H), 1.55 (m, 2H), 1.40 (m, 4H), 1.30 (d, 2H, $J=10$ Hz); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 84.5, 57.8, 45.1, 44.1, 42.6, 41.9, 40.2, 38.6, 37.3, 32.6, 22.7. Compound **8**: $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 3.74 (m, 2H), 3.36 (s, 6H), 2.33 (m, 2H), 2.20 (d, 2H, $J=5$ Hz), 2.14 (d, 2H, $J=10$ Hz), 2.11 (d, 2H, $J=5$ Hz), 1.94 (d, 2H, $J=5$ Hz), 1.83 (m, 4H), 1.55 (m, 4H), 1.37 (m, 4H), 1.30 (d, 2H, $J=10$ Hz); $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 84.4, 57.9, 45.0, 44.1, 42.7, 42.1, 40.7, 38.1, 37.4, 32.7, 22.6.
9. Crystal data for **6**: $\text{C}_{28}\text{H}_{38}\text{O}_4$, F.W.=438.58, monoclinic space group $P2_1$; $a=7.765(1)$, $b=17.781(2)$, $c=24.799(3)$ Å, $\beta=90.376(9)^\circ$, $V=3424.1(8)$ Å³, $Z=6$, and $D(\text{X-ray})=1.276$ mg mm⁻³. 7010 data measured to a 2θ max of 116° . $R=0.0640$, $wR2=0.1498$ for 4464 unique reflections with $I>2\sigma(I)$. X-Ray intensity data were measured on a Bruker diffractometer with CuK α radiation ($\lambda=1.54178$ Å) at $T=294$ K. Crystallographic data for **6**, **7** and **8** have been deposited with the Cambridge Crystallographic Data Center. Copies can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).