Photorearrangement

DOI: 10.1002/anie.200701658

Photochemical Rearrangements of Norbornadiene Pauson–Khand Cycloadducts**

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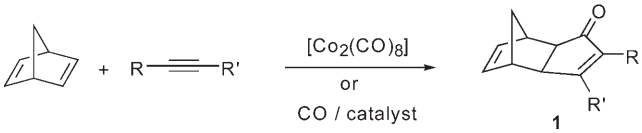
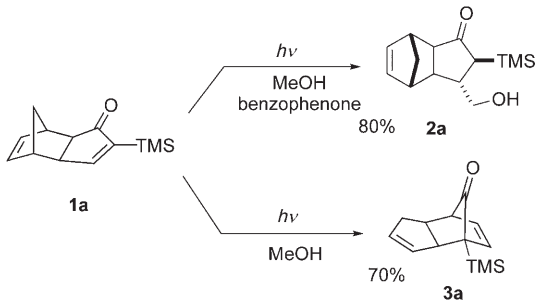
The intermolecular Pauson–Khand reaction[1] (PKR), that is, cobalt-catalyzed carbonylative cycloaddition between an alkyne and an alkene, is one of the most reliable reactions for the construction of cyclopentane derivatives. The scope of the PKR is extremely wide with respect to alkynes; most acetylenic compounds give good yields. With terminal alkynes the reaction affords α-substituted cyclopentenones with high selectivity. In contrast, the choice of alkene counterparts is more limited: only strained alkenes react. Cyclopentenes, cyclobutenes, and bicyclic cyclopentenes are the best substrates. Among them, norbornadiene cycloadducts **1** (Scheme 1) are the most accessible and useful.[2] Moreover, we have recently developed a practical asymmetric process for the preparation of norbornadiene PKR adducts based on the stoichiometric use of chiral bidentate P,S ligands.[3]



Scheme 1. Intermolecular Pauson–Khand cycloaddition between norbornadiene and alkynes.

Although PKR provides ready access to myriads of cyclopentenones, the photochemistry of the enone functional group of these substrates[4] has been almost completely ignored. Some years ago, we reported the rearrangement of cyclopropene PKR adducts to phenols,[5–6] but to date no other photochemical processes have been described for this type of compound. We present here a novel photochemical skeletal rearrangement of norbornadiene PKR adducts **1**.

While studying different procedures to introduce a hydroxymethyl group into PKR adduct **1a** (R = TMS), prepared in either racemic or optically active form from norbornadiene and trimethylsilylacetylene, we performed photochemical conjugate addition of methanol. Following the methodology developed by Fraser-Reid and co-workers,[7,8] **1a** was irradiated at 350 nm in methanol in the presence of 60 mol% of benzophenone as triplet sensitizer. We observed that, in addition to the desired product **2a**, rearranged byproduct **3a** was also formed, in 7% yield (Scheme 2). Interestingly, this unexpected byproduct could be converted to the main reaction product by irradiation without



Scheme 2. Photochemical reaction of **1a** in methanol. TMS = $SiMe_3$.

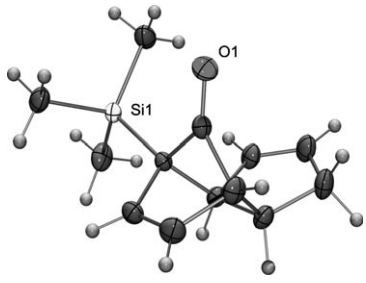


Figure 1. ORTEP view of the X-ray structure of **3a** (thermal ellipsoids shown at 50% probability).

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[**] We thank the Spanish MEC (Grants CTQ2005-00623 and CTQ2005-07790) and the Catalonian AGAUR (Grant 2005SGR00111) for financial support. X.V. thanks the DURSI for "Distinció per a la Promoció de la Recerca Universitaria". A.L. thanks the MEC for a fellowship.

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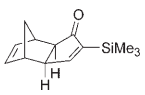
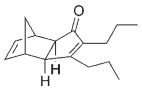
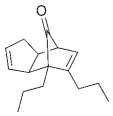
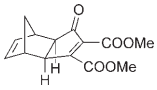
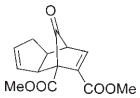
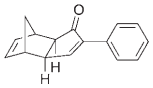
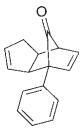
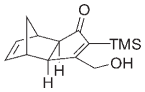
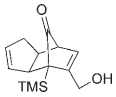
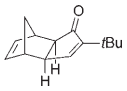
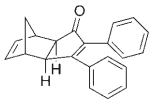
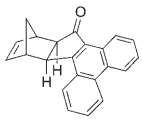
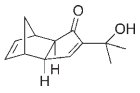
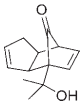
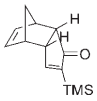
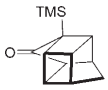
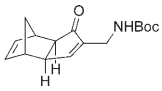
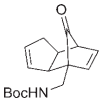
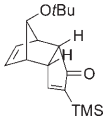
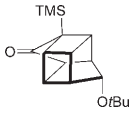
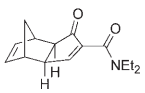
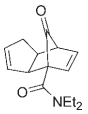
a triplet sensitizer. Thus, after 3 h of irradiation, **3a** was isolated from the crude product mixture in 70% yield. The molecular structure of rearranged product **3a** was confirmed by X-ray diffraction on a monocrystal grown from dichloromethane[9] (Figure 1).

The substrate scope of the rearrangement was next studied. A set of alkynes with a wide variety of functional groups was selected. Norbornadiene PKR adducts **1b–g**, with the usual *exo* configuration, were prepared from a series of terminal alkynes by using standard catalytic or stoichiometric PKR methods. Irradiation at 350 or 365 nm[10] of these adducts afforded the expected rearranged products **3b–g** in good yields. Unsubstituted adduct **1b** derived from acetylene cleanly gave the rearranged product **3b**, albeit in moderate yield due to the volatility of the compound (Table 1, entry 2). The photochemical transformation tolerates most functional groups:. Aromatic (phenyl, **1c**), bulky aliphatic (*tert*-butyl, **1d**), alcohol (1-hydroxy-1-methylethyl, **1e**), nitrogenated

Table 1: Photochemical rearrangement of PKR adducts **1**.

Entry	Starting adduct	Conditions[a]	Product	Yield[b] [%]	Entry	Starting adduct	Conditions[a]	Product	Yield[b] [%]
1	 **1a**	MeOH 15 °C, 3 h	 **3a**	70	8	 **1h**	MeOH 15 °C, 4 h	 **3h**	64[e]
2	 **1b**	pentane 15 °C, 3 h	 **3b**	33[c]	9	 **1i**	hexane 15 °C, 4 h	 **3i**	86[e]
3	 **1c**	MeOH 15 °C, 5 h	 **3c**	70	10	 **1j**	MeOH 15 °C, 6 h	 **3j**	69[f]
4	 **1d**	MeOH 15 °C, 5 h	 **3d**	80	11	 **1k**	MeOH 15 °C, 3.5 h	 **4**	52
5	 **1e**	MeOH 15 °C, 4 h	 **3e**	78	12	 *endo*-**1a**	MeOH 15 °C, 4.5 h	 **5a**	83
6	 **1f**	MeOH 15 °C, 4 h	 **3f**	67[d]	13	 *endo*-**1l**	MeOH 15 °C, 4.5 h	 **5l**	87
7	 **1g**	MeOH 15 °C, 3.5 h	 **3g**	53					

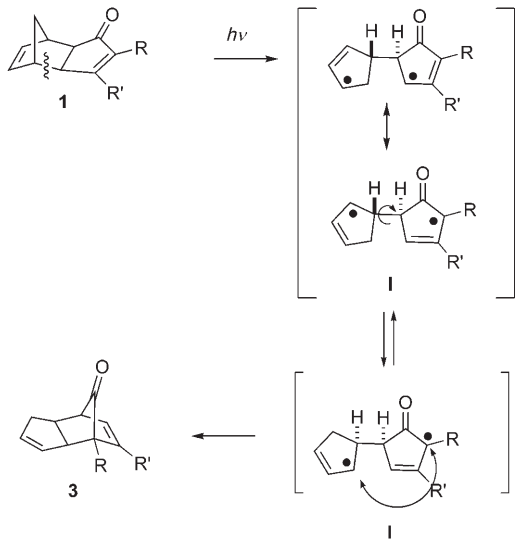
[a] The reactions were carried out in a Rayonet apparatus equipped with 16 lamps (8 W, 350 nm).[10] [b] Yield of isolated product. [c] The low yield is mainly due to the volatility of the product. [d] 9% of starting material was recovered after chromatography. [e] 5% of starting material was recovered after chromatography. [f] 10% of starting material was recovered after chromatography.

(butoxycarbonylamino (BocNH), **1f**) and carboxamide (diethylamido, **1g**) derivatives also gave good yields of rearranged products **3c–g** (Table 1, entries 3–7).

We then focused on substrates derived from internal alkynes. The corresponding 2,3-disubstituted cycloadducts **1h** (from 4-octyne), **1i** (from dimethylacetylene dicarboxylate), **1j** (from 3-trimethylsilylpropyn-1-ol), and **1k** (from diphenylacetylene) were prepared by conventional PKR. These compounds were also irradiated. As anticipated, good yields of the rearranged products were obtained from **1h** and **1i**, which have two alkyl or methoxycarbonyl substituents, respectively. Cycloadduct **1j** arising from an unsymmetrical disubstituted alkyne also gave the expected product **3j** as a single stereoisomer in good yield. However, the cycloadduct derived from diphenylacetylene (**1k**) gave the unexpected compound **4** containing a phenanthryl group (Table 1, entry 11). The structure of **4** was confirmed by X-ray diffraction (see the Supporting Information). This compound was most likely formed by photochemical electrocyclic ring closure followed by aromatization. This transformation is known for stilbenes,[11] although it usually occurs in the presence of an oxidant such as oxygen or iodine.[12]

The tricyclo[5.2.1.$0^{2,6}$]deca-3,8-dien-10-one skeleton is relatively rare in the literature. Access to this organic scaffold is of great interest, as the broad scope of the PKR would provide a route to interesting new compounds. Some derivatives of 1,8-dioxodicyclopentadiene have been prepared by Diels–Alder reactions and therefore have *endo* configuration.[13] Consequently, *exo* derivatives are almost unknown.[14] It is well known that intermolecular PKR is highly stereoselective and generally yields *exo* adducts. In the preparation of **1a** by catalytic PKR with [$Co_2(CO)_8$] as a catalyst, only 13% of the product corresponds to the *endo* isomer. However, this isomer (*endo*-**1a**) was isolated by chromatography, and its irradiation at 350 nm in methanol led to a [2+2] cycloaddition between the enone and the alkene, instead of the aforementioned arrangement, to yield cage compound **5a** (Table 1, entry 12). This is a known transformation in the photochemistry of compounds derived from Diels–Alder adducts.[15] Contrary to Diels–Alder chemistry, the PK cycloaddition usually gives *exo* isomers with high selectivity. During the preparation of a large set of intermolecular PKR adducts we found that the only example in which the main product of a PKR had *endo* configuration was the reaction between *tert*-butoxynorbornadiene and trimethylsilylacetylene. Irradiation of *endo*-**1l** under our standard conditions led to the corresponding 1,3-bis-homocubanone **5l** (Table 1, entry 13). This result indicated that the preferred reaction pathway for *endo* isomers is [2+2] cycloaddition between the enone and the double bond to afford a cage compound. The scope of the present rearrangement is therefore limited to *exo* isomers.

A simple connectivity analysis revealed that a plausible mechanism for the transformation of a PKR adduct **1** into the rearranged product **3** would involve γ-bond breaking of the enone to give a bis-allyl diradical intermediate **I** (Scheme 3). This reaction has a direct precedent in the photochemistry of PKR adducts derived from cyclopropene.[5–6] In the case at hand, however, both fragments of the diradical intermediate **I** are allylic, and thus the type of hydrogen shift that occurs in the intermediate derived from cyclopropene adducts is prevented. A new bond between the opposite sides of the two allyl radicals must therefore be formed after a requisite conformational change by rotation about the single bond linking both fragments. Although some bis-allyl diradicals have been reported,[16] to the best of our knowledge this rearrangement is unprecedented.[17] A complete theoretical study to find the electronic states of the species involved in the reaction pathway and how radiationless decay to the singlet ground state occurs is now being performed and will be reported in due course.



Scheme 3. Proposed reaction pathway for the photochemical formation of **3**.

In summary, we have studied the photochemical transformations of 4-substituted and 4,5-disubstituted tricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-ones **1**. These compounds are easily obtained by Pauson–Khand cycloaddition between norbornadiene and the corresponding alkyne. Whereas irradiation at 350 nm of the *endo* cycloadducts—usually the minor stereoisomers—gave the expected cage compounds by [2+2] cycloaddition, the major isomers lead to tricyclo[5.2.1.$0^{2,6}$]deca-3,8-dien-10-ones **3**. This new photorearrangement tolerates a wide variety of functional groups and affords the rearranged products in good yields.

Received: April 15, 2007
Published online: July 3, 2007

Keywords: cycloaddition · photochemistry · radical reactions · rearrangement · synthetic methods

[1] Selected reviews: a) J. Blanco-Urgoiti, L. Anorbe, L. Perez-Serrano, G. Dominguez, J. Perez-Castells, *Chem. Soc. Rev.* **2004**, *33*, 32; b) S. E. Gibson (née Thomas), A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800; c) K. M. Brummond, J. L. Kent, *Tetrahedron* **2000**, *56*, 3263; d) Y. Keun Chung, *Coord. Chem. Rev.* **1999**, *188*, 297; e) S. L. Buchwald, F. A. Hicks in *Comprehensive Asymmetric Catalysis*

I–III, **1999**, pp. 491 – 510; f) N. E. Schore in *Comprehensive Organic Synthesis*, *Vol. 5* (Ed.: B. M. Trost), Pergamon, Oxford, **1991**, pp. 1037 – 1064.
[2] V. Bernardes, N. Kann, A. Riera, A. Moyano, M. A. Pericàs, A. E. Greene, *J. Org. Chem.* **1995**, *60*, 6670.
[3] a) X. Verdaguer, A. Moyano, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahia, *J. Am. Chem. Soc.* **2000**, *122*, 10242; b) X. Verdaguer, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahia, *Organometallics* **2003**, *22*, 1868; c) X. Verdaguer, A. Lledo, C. Lopez-Mosquera, M. A. Maestro, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2004**, *69*, 8053; d) J. Solà, M. Revés, A. Riera, X. Verdaguer, *Angew. Chem.* **2007**, *119*, 5108; *Angew. Chem. Int. Ed.* **2007**, *46*, 5020.
[4] a) W. H. Horspool, *Photochemistry* **2004**, *35*, 17; b) W. M. Horspool, *Photochemistry* **2003**, *34*, 29; c) D. I. Schuster, *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd Ed., CRC Press, Boca Raton, **2004**, pp. 72/71 – 72/24.
[5] I. Marchueta, S. Olivella, L. Solà, A. Moyano, M. A. Pericàs, A. Riera, *Org. Lett.* **2001**, *3*, 3197.
[6] I. Gomez, S. Olivella, M. Reguero, A. Riera, A. Sole, *J. Am. Chem. Soc.* **2002**, *124*, 15375.
[7] a) Z. Benko, B. Fraser-Reid, P. S. Mariano, A. L. J. Beckwith, *J. Org. Chem.* **1988**, *53*, 2066; b) B. Fraser-Reid, N. L. Holder, D. R. Hicks, D. L. Walker, *Can. J. Chem.* **1977**, *55*, 3978.
[8] a) N. Mase, Y. Watanabe, T. Toru, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2957; b) D. I. Schuster, J.-M. Yang, J. Woning, T. A. Rhodes, A. W. Jensen, *Can. J. Chem.* **1995**, *73*, 2004; c) J. Wang, A. Gossauer, *Helv. Chim. Acta* **1994**, *77*, 533.
[9] CCDC-646970 and -646971 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[10] As an alternative to the standard Rayonet apparatus with 16 lamps (8 W, 350 nm), a simple home made apparatus equipped with eight lamps (Philips, TL 8W/08 FAM, 365 nm) was used.
[11] F. B. Mallory, C. S. Wood, J. T. Gordon, *J. Am. Chem. Soc.* **1964**, *86*, 3094.
[12] Some recent examples: a) S. Amin, J. Camanzo, K. Huie, S. S. Hecht, *J. Org. Chem.* **1984**, *49*, 381; b) P. H. Gore, F. S. Kamonah, *Synthesis* **1978**, 773; c) E. Martínez, J. C. Estévez, R. J. Estévez, L. Castedo, *Tetrahedron* **2001**, *57*, 1981.
[13] Selected synthetic applications of *endo*-cyclopentadien-1,8-diones: a) G. Mehta, S. S. Ramesh, *Can. J. Chem.* **2005**, *83*, 581; b) G. Mehta, R. S. Kumaran, *Tetrahedron Lett.* **2001**, *42*, 8097; c) G. Mehta, D. S. Reddy, *J. Chem. Soc. Perkin Trans. 1* **2001**, 1153; d) P. Francis Schuda, M. R. Heimann, *Tetrahedron* **1984**, *40*, 2365; e) L. A. Paquette, R. F. Daivs, D. R. James, *Tetrahedron Lett.* **1974**, *15*, 1615; f) E. Vogel, E. G. Wyes, *Chem. Ber.* **1965**, *98*, 3680; g) R. C. Cookson, N. S. Isaacs, M. Szelke, *Tetrahedron* **1964**, *20*, 717.
[14] a) P. Quadrelli, S. Romano, L. Toma, P. Caramella, *J. Org. Chem.* **2003**, *68*, 6035; b) G. Mehta, S. H. K. Reddy, *Synlett* **1993**, 75; c) G. Mehta, S. H. K. Reddy, *Tetrahedron Lett.* **1991**, *32*, 6403; d) P. E. Eaton, S. A. Cerefice, *J. Chem. Soc. Chem. Commun.* **1970**, 1494.
[15] a) C. J. Baker, G. I. Fray, G. R. Geen, K. Ryan, *J. Chem. Soc. Perkin Trans. 1* **1994**, 793; b) J. Zhu, A. J. H. Klunder, B. Zwanenburg, *Tetrahedron Lett.* **1993**, *34*, 3335; c) A. P. Marchand, P. W. Jin, J. L. Flippen-Anderson, R. Gilardi, C. George, *J. Chem. Soc. Chem. Commun.* **1987**, 1108; d) B. Fuchs, M. Pasternak, B. Pazhenchevsky, *J. Org. Chem.* **1981**, *46*, 2017; e) R. C. Cookson, J. Hudec, R. O. Williams, *Tetrahedron Lett.* **1960**, *1*, 29.
[16] a) G. Maier, S. Senger, *J. Am. Chem. Soc.* **1997**, *119*, 5857; b) P. Caramella, P. Quadrelli, L. Toma, S. Romano, K. S. Khuong, B. Nortrop, K. N. Houk, *J. Org. Chem.* **2005**, *70*, 2994.
[17] A related bond scission affording two allyl radicals was postulated in the isomerization of 5-(cyclopent-2-en-1-yl)-2,5-dihydro-1*H*-pyrrol-2-ones: M. N. Wrobel, P. Margaretha, *Chem. Commun.* **1998**, 541.

