Unusual regioselectivity in nucleophilic addition to η^3-p-allylpalladium complex in conventional heating and under microwave irradiation

Alok Kumar Mitra*[a], Nilay Karchaudhuri[b], Aparna De[c], Jayati Mitra[a], and Tanusri Mahapatra[a]

[a]*Department of Chemistry, University of Calcutta, 92, Acharya Prafulla Chandra Road, Calcutta – 700 009, India*
E-mail: a_k_mitra@hotmail.com / akmitra@cucc.ernet.in
[b]*Barrackpore Rastraguru Surendranath College, 85, Middle Road and 6, Riverside Road, Barrackpore, PIN – 700 120, India*
E-mail: n_karchaudhuri@rediffmail.com
[c]*Deshabandhu Mahavidyalaya, Chittaranjan, Burdwan, PIN – 713 331, India*
E-mail: deparna@rediffmail.com

(received 27 Nov 03; accepted 29 Feb 04; published on the web 11 March 04)

Abstract

Nucleophilic attack of 3-hydroxycoumarin on η^3-p-allylpalladium complex formed from substituted cinnamyl alcohols and acetates in the presence of palladium acetylacetonate and triphenylphosphine resulted normal addition product like 4-(3′-phenylallyl)-3-hydroxycoumarin, except for cinnamyl acetate, which provided an unusual product 4-(1′-phenylallyl)-3-hydroxycoumarin by conventional and microwave heating.

Keywords: Nucleophilic addition, η^3-p-allylpalladium complex, 3-hydroxycoumarin, cinnamyl alcohols and acetates, microwave activation

Introduction

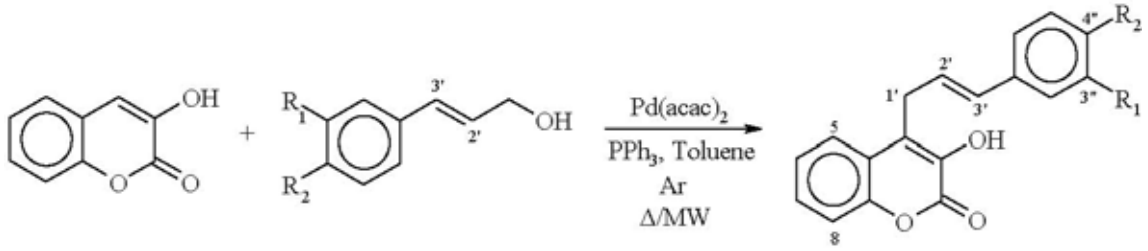
Palladium-catalyzed allylic substitution reactions[1-5] have been receiving a great deal of attention in recent years, utilizing a wide range of nucleophiles. Since the coumarin moiety has several biological activities[6,7] and has been utilized as therapeutic agents in different diseases, 3-hydroxycoumarin has been exploited for the first time as nucleophile in η^3-p-allylpalladium complex mediated reaction by us. Several substituted cinnamyl alcohols and acetates have been chosen for this reaction. The reactions were carried out not only by conventional heating but also under microwave irradiation. MORE[8] (Microwave – induced Organic Reaction Enhancement)

chemistry is the most emerging trend in global perspective. Microwave irradiation has provided a versatile method to speed up many chemical reactions[9,10,11] delivering high yields in a few minutes. The process is not only rapid but also energy-efficient, cost-effective. So we have carried out allylic substitution reaction under microwave irradiation also.

Results and Discussion

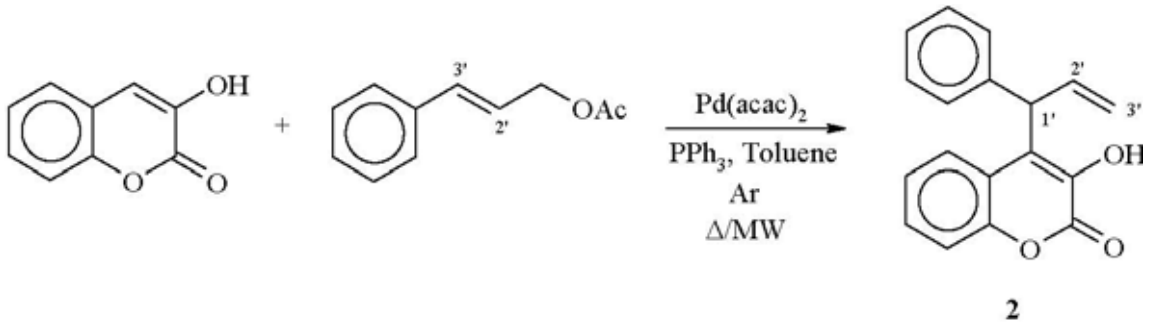
Treatment of cinnamyl alcohol with 3-hydroxycoumarin in toluene (at 80°C for 8 hours / 10 min., MW) in the presence of palladium acetylacetonate and triphenylphosphine under argon atmosphere resulted in 4-(3′-phenylallyl)-3-hydroxycoumarin (**1a**) as the only product in good yield (70% in conventional heating, 78% under microwave irradiation) (Scheme 1). The structure of the addition product (**1a**) was established by the presence of nine aromatic protons at δ 7.57-7.12 ppm, two olefinic protons at δ 6.47 and 6.23 as doublet (J = 15.8 Hz) and double triplet (J = 15.8 and 6.2 Hz) for 3′-H and 2′-H respectively in ^{1}H NMR spectrum. Two 1′-H protons appear as doublet (J = 6.2 Hz) at δ 3.69. In ^{13}C NMR besides the usual aromatic ring carbons, olefinic carbons appear at δ 132.6 and 125.0 ppm and C-1′ carbon resonates at δ 28.1.

Similar products, 4-[3′-(3′′,4′′-dimethoxyphenyl)allyl]-3-hydroxycoumarin (**1b**) and 4-[3′-(3′′-benzyloxy, 4′′-methoxyphenyl)allyl]-3-hydroxycoumarin (**1c**) were obtained when 3,4-dimethoxycinnamyl alcohol and 3-benzyloxy-4-methoxycinnamyl alcohol were used separately under identical condition, in 72% yield by conventional heating and 73%, 65% yield respectively under microwave irradiation (Scheme 1).



1a : $R_1 = R_2 = H$
1b : $R_1 = R_2 = OMe$
1c : $R_1 = OBn$, $R_2 = OMe$

Scheme 1. Reaction of 3-hydroxycoumarin with cinnamyl alcohols.

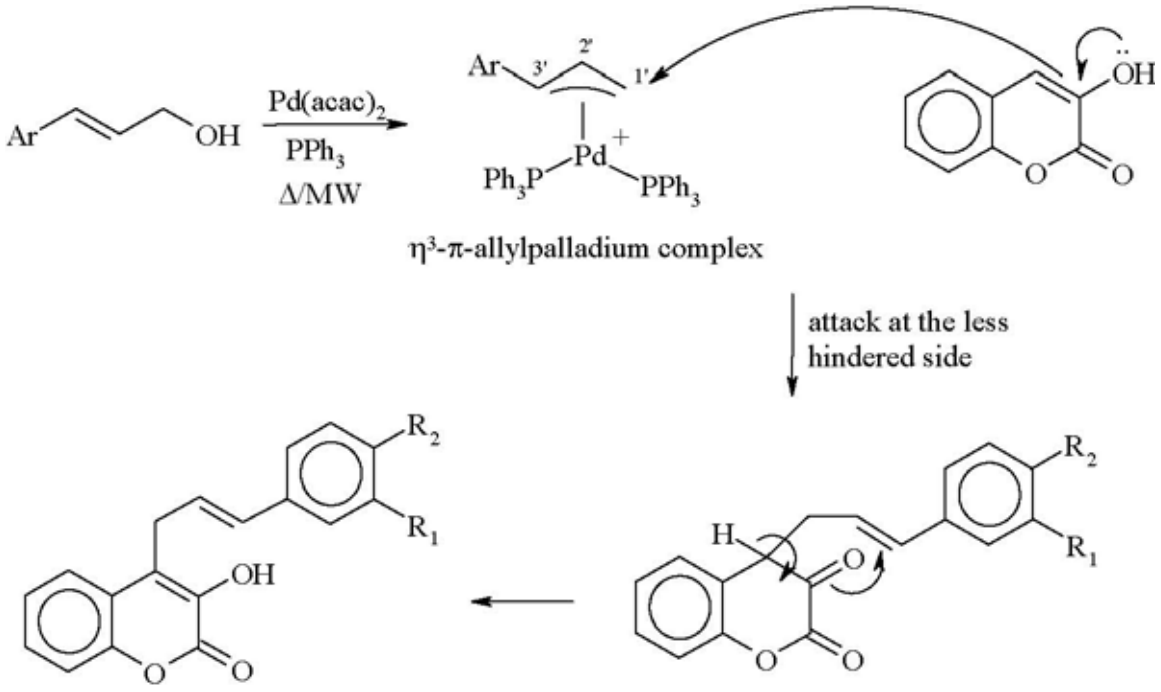


Scheme 2. Reaction of 3-hydroxycoumarin with cinnamyl acetate.

But surprisingly, when cinnamyl acetate was treated under identical condition, only a regioselective unexpected product was obtained in appreciable amount (62% by conventional heating and 60% under microwave irradiation) with the structure 4-(1′-phenylallyl)-3-hydroxycoumarin (**2**). Its structure was evidenced by the appearance of nine aromatic protons at δ 7.44-7.01 ppm, three olefinic protons, one at δ 6.46 (2′-H) as multiplet and two at δ 5.24 (3′-H) as double doublet (J = 13.5, 6.5 Hz) and one methine proton at δ 5.39 (1′-H) as doublet (J = 7.8 Hz) in ^{1}H NMR spectrum. In ^{13}C NMR spectrum, carbons of coumarin moiety and aromatic carbons of cinnamyl residue appear at usual range. Two olefinic carbons, C-2′ and C-3′ appear at δ 136.2 and 118.6 ppm respectively and C-1′ carbon shows signal at δ 46.0 ppm which evidences the structure **2**[2].

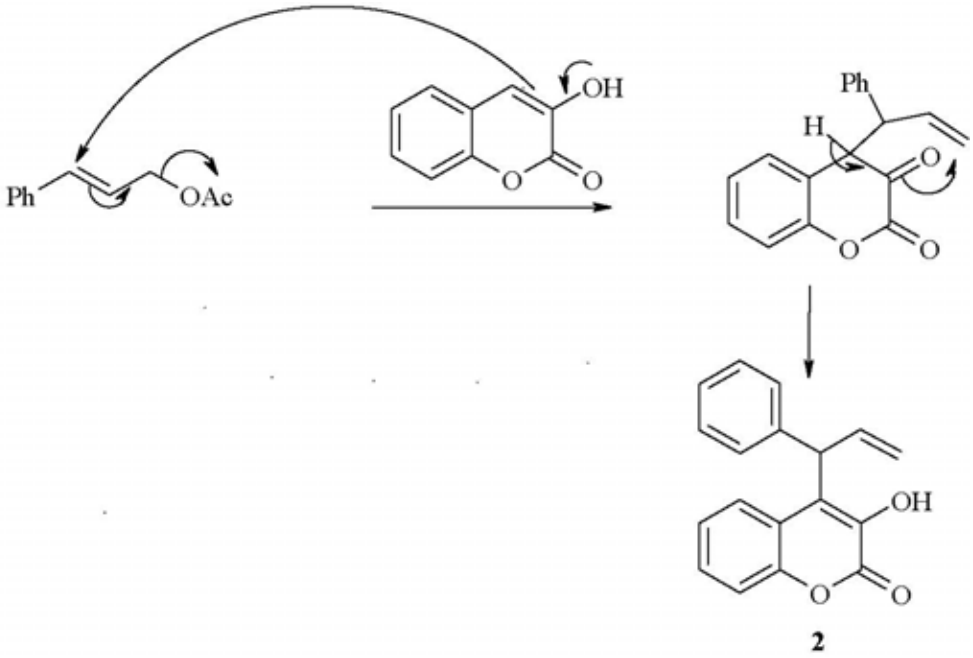
To generalize the formation of this unusual product, under similar condition with the aid of Pd(0), other substituted cinnamyl acetates e.g. 3,4-dimethoxycinnamyl acetate and 3-benzyloxy-4-methoxycinnamyl acetate were treated with 3-hydroxycoumarin separately, providing the products **1b** and **1c** respectively in 64% (conventional heating) / 69% (microwave irradiation) and 67% (conventional heating) / 71% (microwave irradiation) yields. So, the formation of 4-(1′-phenylallyl)-3-hydroxycoumarin (**2**) is unique.

For cinnamyl alcohols, attack of the nucleophile, 3-hydroxycoumarin occurs via C-4 at the less hindered side of the electon deficient η^3-p-allylpalladium complex formed from cinnamyl alcohol, palladium acetylacetonate and triphenylphosphine resulting the products **1a**, **1b** & **1c** (Scheme 3).



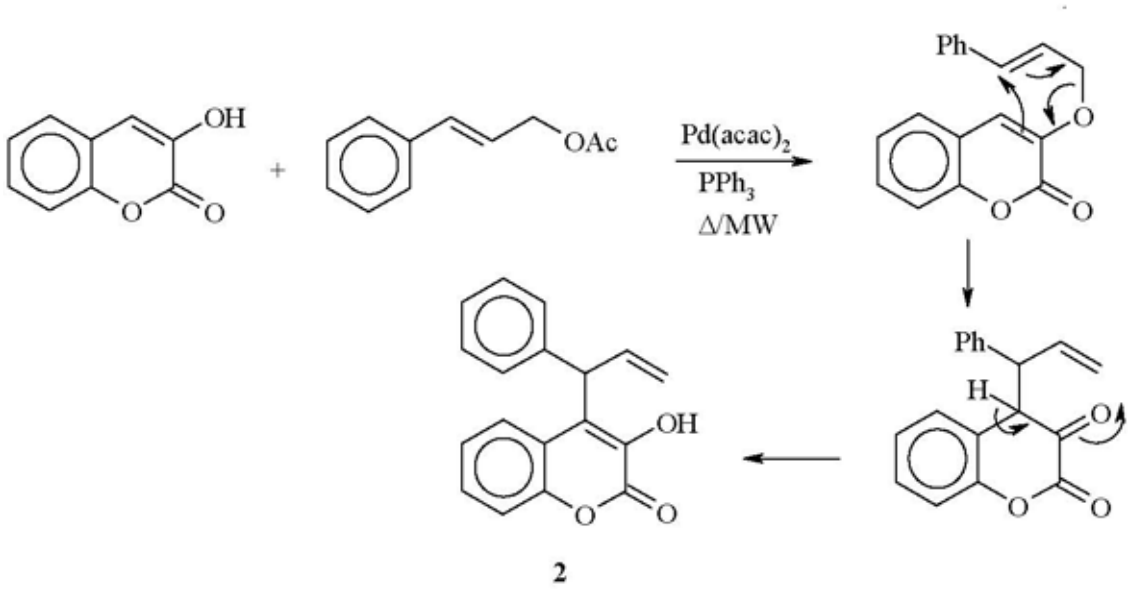
Scheme 3. Mechanism of reaction for Scheme 1.

But the formation of the unusual product **2** can be explained by a direct nucleophilic attack of the hydroxycoumarin on the internal double bond carbon followed by double bond shift and elimination of the acetoxy group (Scheme 4).



Scheme 4. Formation of 2.

This may be a reasonable possibility not involving an η3-p-allylpalladium complex intermediate.The formation of **2** can also be rationalised by Claisen type sigmatropic rearrangement (Scheme 5).



Scheme 5. Formation of **2** via Claisen type rearrangement.

Reactions of the other substituted cinnamyl acetates resulted in usual products (**1b** and **1c**) presumably due to the electron-releasing effect of these substituents. The electron-releasing effect of these substituents make the attack on the double bond more difficult, thus favouring the formation of the allyl complex.

Experimental Section

General Procedures. IR spectra were recorded on a Perkin-Elmer FTIR-RXI spectrophotometer and ^{1}H and ^{13}C NMR spectra were run on Bruker AM 300L spectrometer operating at 300 MHz and 75 MHz respectively. The chemical shifts were referenced to TMS as internal standard using *d-chloroform* as solvent. Microwave oven used was BPL, 800T / MM 261 EEP.

Experimental procedure for conventional heating method. A mixture of 3-hydroxycoumarin (0.324 g, 2 mmol), cinnamyl alcohol or acetate (2 mmol), palladium acetylacetonate (0.39 g, 1.28mmol) and triphenylphosphine (0.104 g, 0.397mmol) in toluene (5 ml) was taken in a sealed pyrex tube under argon atmosphere and heated at 80^{o}C for 8 hours. The reaction mixture was

cooled and poured into ice cold water. Then it was extracted with ethyl acetate (3x3 ml), washed with brine and dried over anhydrous sodium sulphate. Evaporation of the solvent followed by the filtration on a short silica gel column afforded the coupled product.

Experimental procedure under microwave irradiation. The same mixture (conventional heating method) was subjected to microwave irradiation for the specified time (Table 1). It was poured into ice cold water and worked up as usual.

Table 1. Reactions under microwave irradiation

Entry	Substrate	Product	Time (min.)	Yield (%)
1	Cinnamyl alcohol	1a	10	78
2	3,4-Dimethoxycinnamyl alcohol	1b	19	73
3	3-Benzyloxy-4-methoxycinnamyl alcohol	1c	16	65
4	Cinnamyl acetate	2	9	60
5	3,4-Dimethoxycinnamyl acetate	1b	15	69
6	3-Benzyloxy-4-methoxycinnamyl acetate	1c	20	71

The NMR spectroscopic data of the products are given in the Table 2 and Table 3.

Table 2. ^{1}H NMR chemical shifts of the products (**1a-c, 2**)

Product	δ ppm	Nature	Proton count	Assignment
1a	7.57-7.12	m	9H	Ar-H
	6.47	d, *J* = 15.8 Hz	1H	3′-H
	6.23	dt, *J* = 15.8, 6.2 Hz	1H	2′-H
	3.69	d, *J* = 6.2 Hz	2H	1′-H
1b	7.61-6.65	m	7H	Ar-H
	6.38	d, *J* = 15.8 Hz	1H	3′-H
	6.06	dt, *J* = 15.8, 6.4 Hz	1H	2′-H
	3.79	s	6H	2xOCH_3
	3.64	d, *J* = 6.4 Hz	2H	1′-H
1c	7.61-6.71	m	12H	Ar-H
	6.36	d, *J* = 15.8 Hz	1H	3′-H
	6.02	dt, *J* = 15.8, 6.4 Hz	1H	2′-H
	5.04	s	2H	OCH_2
	3.79	s	3H	OCH_3
	3.66	d, *J* = 6.4 Hz	2H	1′-H

2	7.44-7.01	m	9H	Ar-H
	6.46	m	1H	2′-H
	5.39	d, *J* = 7.8 Hz	1H	1′-H
	5.24	dd, *J* = 13.5, 6.5 Hz	2H	3′-H

Table 3. ^{13}C NMR chemical shifts of the products (**1a-c, 2**)

Carbon	**1a**	**1b**	**1c**	**2**
C-2	160.0	160.2	160.0	160.2
C-3	137.5	137.4	137.4	137.9
C-4	124.7	126.4	—	—
C-5	124.5	124.0	124.1	125.5
C-6	124.0	122.5	122.5	124.5
C-7	128.4	128.5	128.3	128.1
C-8	116.9	116.8	116.9	117.1
C-9	149.1	149.0	149.7	149.2
C-10	120.8	120.7	120.8	119.9
C-1′	28.1	28.4	28.0	46.0
C-2′	125.0	125.0	125.0	136.2
C-3′	132.6	132.2	132.0	118.6
C-1′′	137.0	130.2	130.2	140.2
C-2′′	126.2	111.3	112.3	127.5
C-3′′	128.5	149.2	149.1	128.6
C-4′′	127.5	140.5	148.3	126.8
C-5′′	128.5	109.3	112.2	128.6
C-6′′	126.2	119.3	119.9	127.5
C-1′′′			137.2	
C-2′′′	—	—	127.4	—
C-3′′′	—	—	128.5	—
C-4′′′	—	—	127.8	—
C-5′′′	—	—	128.5	—
C-6′′′	—	—	127.4	—
OCH_2	—	—	71.4	—
OCH_3	—	55.9	56.1	—

Acknowledgements

We thank the UGC, the CSIR, New Delhi and University of Calcutta for financial support. The authors also thank the learned referees for their valuable suggestions.

References

1. Lee, P. H.; Sung, S. Y.; Lee, K.; Chang, S. *Synlett* **2002**, 146.
2. (a) Page, P. C. B.; Heaney, H.; Reignier, S.; Rassias, G. A. *Synlett* **2003**, 22. (b) Mitra, A.K.; Mukhopadhyay, A.K.; Misra, S.K.; Patra, A. *Indian J. Chem*. **1982**, *21B*, 834.
3. Sato, Y.; Yoshino, T.; Mori, M. *Org. Lett*. **2003**, *5*, 31.
4. Cδmmerer, S. S.; Viciu, M. S.; Stevens, E.D.; Nolan, S. P. *Synlett* **2003**, 1871.
5. Zablocka, M.; Koprowski, M.; Donnadieu, B.; Majoral, J-P.; Archard, M.; Buono, G. *Tetrahedron Lett*. **2003**, *44*, 2413.
6. Murray, R. D. H.; Mendez, J.; Brown, S. S. *The Natural Coumarins;* Wiley: New York, 1982.
7. Murray, R. D. H. *Prog. Chem. Org. Nat. Prod*. **1991**, *58*, 83.
8. Bose, A. K.; Banik, B. K.; Lavlinskaia, N.; Jayaraman, M.; Manhas, M. S. *CHEMTECH* **1997**, *27*, 18.
9. Loupy, A. *Microwaves in Organic Synthesis;* Wiley-VCH: Weinheim, 2002.
10. Mitra, A. K.; De, A.; Karchaudhuri, N. *Synth. Commun*. **2000**, *30*, 1651.
11. Mitra, A. K.; Banerjee, K. *Synlett* **2003**, 1509.

