Graphical Abstract

Tandem intramolecular Diels-Alder/retro-Diels-Alder cycloaddition of 2*H*-chromen-2-one as dienes with the expulsion of CO₂

Jian Zhang, Jin-Long Wu

Laboratory of Asymmetry and Catalysis, Department of Chemistry, Zhejiang University, Hangzhou 310027, China

A series of chiral *N*-benzyl-*N*-allyl-amides that contain a 2*H*-chromen-2-one moiety were designed for the synthesis of benzof[isoindol]-1-ones *via* an intramolecular Diels-Alder and a subsequent retro-Diels-Alder reaction with the expulsion of CO₂. Both the yield (80%–89%) and absolute stereocontrol of the tandem reaction were high when an electron-withdrawing group was attached to the dienophile.

Tandem intramolecular Diels-Alder/retro-Diels-Alder cycloaddition of 2*H*-chromen-2-one as dienes with the expulsion of CO₂

Jian Zhang, Jin-Long Wu *

Laboratory of Asymmetry and Catalysis, Department of Chemistry, Zhejiang University, Hangzhou 310027, China

ARTICLE INFO

ABSTRACT

Article history:

Received 15 February 2016

Received in revised form 2 March 2016

Accepted 7 March 2016

Available online

Keywords:

2*H*-chromen-2-one

intramolecular Diels-Alder

retro-Diels-Alder

benzo[*f*]isoindol-1-one

dihydroxylation

To study the intramolecular Diels-Alder cycloaddition of 2*H*-chromen-2-one as a diene, a series of chiral *N*-benzyl-*N*-allyl-amides that contain a 2*H*-chromen-2-one moiety were designed for the synthesis of benzo[*f*]isoindol-1-ones via an intramolecular Diels-Alder and a subsequent retro-Diels-Alder cycloaddition with the expulsion of CO₂. Both the yield (80%–89%) and absolute stereocontrol of the tandem reaction were high when an electron-withdrawing group was attached to the dienophile. The double bond in the styrene substructure remained in the products could be further derivatized by dihydroxylation.

1. Introduction

Because of the stability of an aromatic ring, the exocyclic double bond in styrene commonly reacts as a dienophile in [4+2] cycloaddition reactions [1] and it is quite difficult for styrene to participate as a diene in thermal Diels-Alder cycloaddition unless extremely reactive dienophiles are employed [2]. 2*H*-pyran-2-one and its derivatives are a class of important electron-rich diene in the Diels-Alder reaction [3] and are widely used in organic synthesis [4]. There is a feature of this type of dienes in the Diels-Alder reaction: Retro-Diels-Alder reaction will happen under certain conditions by eliminating one molecule of CO₂, which introduces a carbon-carbon double bond in the ring [5]. Several reports claimed that 2*H*-chromen-2-one, a kind of 2*H*-pyran-2-one fused with a benzene ring, can be used in the Diels-Alder cycloaddition as a dienophile [6]. However, only one case where it was used as a diene was reported in the tandem intramolecular Diels-Alder (IMDA) and retro-Diels-Alder cycloaddition with acetylene as shown in Scheme 1 [7]. The reaction must be carried out in a sealed tube placed in a 300 °C bath, and surprisingly, the acetylenic hydrogen replaced by an electron-withdrawing group (EWG), carboethoxy, **1e** failed to cyclize to form **2e**. In our continuous works on synthesis of polycyclic compounds using IMDA reaction [8], herein, we report the tandem IMDA and retro-Diels-Alder reaction of chiral *N*-(4-methoxybenzyl)-2-oxo-*N*-(1-phenylbut-3-en-2-yl)-2*H*-chromene-3-carboxamides for stereo-controlled synthesis of 3-benzyl-2-(4-methoxybenzyl)-2,3,3a,4-tetrahydro-1*H*-benzo-*f*]isoindol-1-ones under relatively mild conditions.

Scheme 1. Tandem IMDA and retro-Diels-Alder reaction of 2*H*-chromen-2-one with acetylene.

2. Experimental

2.1. General procedure for the synthesis of **4a–g**

* Corresponding author.

E-mail address: wjz@zju.edu.cn (J.-L. Wu).

A solution of **3** (0.1 mmol) in CH₃CN (2 mL) in a sealed vial was heated in an oil bath at 160 °C. After the reaction completed (monitored by TLC analysis), the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (ethyl acetate / petroleum ether = 1 / 3) to give **4** (Scheme 2).

(3*S*,3*aS*,4*R*)-ethyl-3-benzyl-2-(4-methoxybenzyl)-4-methyl-1-oxo-2,3,3*a*,4-tetrahydro-1*H*-benzo[*f*]isoindole-4-carboxylate **4a**: White crystalline solid, yield 82%, mp 204–205 °C (EtOAc–hexane); [α]_D²⁵ +13.9 (*c* 1.0, CHCl₃); *R*_f = 0.20 (20% EtOAc in hexane); IR (film, cm⁻¹): 3061, 3028, 2979, 2933, 2836, 1721, 1685, 1611, 1512, 1447, 1409, 1298, 1247, 1174, 1093, 1031, 909, 755, 731, 700; ¹H NMR (400 MHz, CDCl₃): δ 7.29–7.21 (m, 6H), 7.19 (d, 1H, *J* = 3.2 Hz), 7.11–7.09 (m, 2H), 6.94–6.90 (m, 3H), 6.78 (d, 2H, *J* = 8.8 Hz), 5.34 and 3.91 (ABq, 2H, *J* = 14.8 Hz), 4.32 (dq, 1H, *J* = 10.8, 7.2 Hz), 4.19 (dq, 1H, *J* = 10.8, 7.2 Hz), 3.79 (s, 3H), 3.76 (dt, 1H, *J* = 5.2, 3.6 Hz), 3.65 (dd, 1H, *J* = 4.8, 3.2 Hz), 3.12 (dd, 1H, *J* = 15.2, 3.2 Hz), 2.66 (dd, 1H, *J* = 15.2, 5.6 Hz), 1.31 (t, 3H, *J* = 7.2 Hz), 1.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.8, 167.0, 159.0, 139.6, 136.4, 132.2, 131.6, 129.7, 129.6 ($\times 2$), 129.2 ($\times 2$), 129.1, 128.6 ($\times 2$), 127.9, 127.7, 126.8, 126.0, 125.4, 114.0 ($\times 2$), 61.6, 55.6, 55.2, 51.2, 44.2, 42.9, 38.2, 17.2, 14.2; HRMS (+EI) calcd. for C₃₁H₃₁NO₄⁺ (*M*⁺) 481.2253; found 481.2246.

(3*S*,3*aR*)-3-benzyl-2-(4-methoxybenzyl)-4,4-dimethyl-2,3,3*a*,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-one **4e**: Colorless oil, yield 11%, [α]_D²⁵ +7.6 (*c* 1.0, CHCl₃); *R*_f = 0.19 (25% EtOAc in hexane); IR (film, cm⁻¹): 3066, 3030, 3003, 2965, 2929, 2866, 2834, 1676, 1611, 1516, 1453, 1409, 1304, 1239, 1174, 1031, 834, 811, 751, 703; ¹H NMR (400 MHz, CDCl₃): δ 7.27–7.19 (m, 8H), 7.09–7.04 (m, 4H), 6.85 (d, 2H, *J* = 8.8 Hz), 5.40 and 4.01 (ABq, 2H, *J* = 14.8 Hz), 3.81 (s, 3H), 3.67–3.63 (m, 1H), 3.02–2.92 (m, 2H), 2.78–2.75 (m, 1H), 1.03 (s, 3H), 0.74 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 167.4, 159.1, 144.8, 136.6, 133.7, 132.5, 129.8 ($\times 2$), 129.5, 129.4 ($\times 2$), 128.9, 128.7 ($\times 2$), 128.1, 126.9, 126.8, 126.7, 123.6, 114.0 ($\times 2$), 56.2, 55.3, 46.0, 44.1, 40.1, 37.5, 24.3, 21.6; HRMS (+EI) calcd. for C₂₉H₂₉NO₂⁺ (*M*⁺) 423.2198; found 423.2204.

Scheme 2. Synthesis of compounds **4a-g**.

2.2. General procedure for the synthesis of **5a-c**.

To a solution of **4** (0.1 mmol) in a mixed solvent of 2-methyl-2-propanol (1 mL) and water (1 mL) were added methanesulfonamide (0.1 mmol) and AD-mix α (145 mg). After stirring at 0 °C for 10–24 h, the reaction mixture was quenched with saturated aqueous Na₂S₂O₃ (5 mL) and stirred at room temperature for another 20 min, then the mixture was extracted with ethyl acetate (10 mL $\times$ 3). The combined organic phase was dried over anhydrous Na₂SO₄, filtrated and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (EtOAc / PE = 1 / 1) to give **5** (Scheme 3).

(1*S*,3*aS*,4*R*,9*R*,9*aS*)-1-benzyl-3*a*-hydroxy-2-(4-methoxybenzyl)-9-methyl-3*a*,4,9,9*a*-tetrahydro-1*H*-4,9-(epoxymethano)benzo[*f*]isoindole-3,10(2*H*)-dione **5a**: White crystalline solid, yield 90%; mp 102–107 °C (EtOAc–hexane); [α]_D²⁵ –4.2 (*c* 1.0, CHCl₃); *R*_f = 0.22 (50% EtOAc in hexane); IR (film, cm⁻¹): 3387, 3063, 3033, 2980, 2938, 2840, 1757, 1676, 1513, 1453, 1373, 1245, 1043, 1004, 843, 778, 745, 701; ¹H NMR (400 MHz, CDCl₃): δ 7.48–7.46 (m, 1H), 7.41–7.34 (m, 2H), 7.33–7.25 (m, 3H), 6.99–6.94 (m, 3H), 6.67 (d, 2H, *J* = 8.8 Hz), 6.23 (d, 2H, *J* = 8.8 Hz), 5.64 (s, 1H), 4.78 and 3.72 (ABq, 2H, *J* = 14.8 Hz), 3.83 (s, 3H), 3.15 (dd, 1H, *J* = 13.2, 3.6 Hz), 2.73 (ddd, 1H, *J* = 9.6, 3.6, 2.4 Hz), 2.55 (dd, 1H, *J* = 13.2, 9.6 Hz), 2.34 (d, 1H, *J* = 2.4 Hz), 0.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 173.3, 170.7, 159.0, 135.5, 135.3, 134.3, 129.8, 129.7 ($\times 2$), 129.4 ($\times 2$), 129.0 ($\times 2$), 128.1, 127.4, 125.4, 125.3, 123.9, 114.1 ($\times 2$), 82.1, 81.5, 58.1, 55.3, 47.8, 47.6, 43.8, 39.8, 12.6; HRMS (+EI) calcd. for C₂₉H₂₇NO₅⁺ (*M*⁺) 469.1889; found 469.1881.

Scheme 3. Synthesis of compounds **5a-c**

2.3. Synthesis of **6c** [9]

Some biological studies on the approved and developing γ -lactam drugs showed that the N-H type lactams are more active than the corresponding *N*-substituted one [11], therefore we completed the transformation of **4c** to **6c** as an example using ceric (IV) ammonium nitrate (CAN). To a solution of **4c** (72 mg, 0.137 mmol) in a mixed solvent of CH₃CN (3 mL) and H₂O (1 mL) was added ceric ammonium nitrate (298 mg, 0.544 mmol) in one portion. After stirring for 30 min at room temperature, H₂O (3 mL) was added and

then the mixture was extracted with ethyl acetate (10 mL $\times$ 3) (Scheme 4). The combined organic layer was washed with saturated aqueous NaHCO₃ (1.5 mL $\times$ 3) and brine (1.5 mL). The organic phase was dried over anhydrous Na₂SO₄, filtrated and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (ethyl acetate / petroleum = 1 / 1) to give **6c** (46 mg, 83%) as a colorless oil.

(3*S*)-Ethyl 3-benzyl-4-methyl-7-nitro-1-oxo-2,3,3a,4-tetrahydro-1*H*-benzo[*f*] isoindole-4-carboxylate **6c**: Yield 83%; [α]_D¹⁵ +2.1 (*c* 1.0, CHCl₃); *R*_f = 0.29 (50% EtOAc in hexane); IR (film, cm⁻¹): 3405, 3214, 3066, 3024, 2979, 2935, 2873, 1730, 1697, 1608, 1584, 1519, 1456, 1346, 1292, 1239, 1090, 1050, 1016, 909, 825, 736, 698; ¹H NMR (400 MHz, CDCl₃): δ 8.14–8.12 (m, 2H), 7.35 (t, 2H, *J* = 7.2 Hz), 7.29 (d, 1H, *J* = 7.2 Hz), 7.25 (d, 1H, *J* = 3.2 Hz), 7.21 (d, 1H, *J* = 7.2 Hz), 7.19 (d, 2H, *J* = 8.0 Hz), 6.18 (br s, 1H), 4.47–4.34 (m, 2H), 3.98–3.93 (m, 1H), 3.70 (dd, 1H, *J* = 6.0, 3.6 Hz), 2.98 (dd, 1H, *J* = 13.6, 2.8 Hz), 2.60 (dd, 1H, *J* = 13.6, 10.0 Hz), 1.39 (t, 3H, *J* = 7.2 Hz), 1.38 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.7, 167.1, 147.3, 146.1, 136.4, 135.3, 132.8, 129.1 ($\times$ 2), 129.0 ($\times$ 2), 127.3, 126.7, 124.32, 124.29, 123.4, 62.3, 54.6, 51.0, 46.4, 42.0, 17.8, 14.2; HRMS (+EI) calcd. for C₂₃H₂₂N₂O₅⁺ (*M*⁺) 406.1529; found 406.1538.

Scheme 4. Transformation from **4c** to **6c** by removing PMB with CAN.

3. Results and discussion

We designed and synthesized a series of chiral *N*-benzyl-*N*-allyl amides containing the moiety of 2*H*-chromen-2-one (**3a–g**) for the IMDA reaction with the expectation that the 2*H*-chromen-2-one moiety and the allyl group act as the diene and the dienophile, respectively. The optimized reaction conditions are by heating a solution of chiral amide **3** in acetonitrile in a sealed vial placed in an oil bath at 160 °C. The chiral *N*-(4-methoxybenzyl)-2-oxo-*N*-(1-phenylbut-3-en-2-yl)-2*H*-chromene-3-carboxamides **3a–g** were transformed into tricyclic compounds, 3-benzyl-2-(4-methoxy-benzyl)-2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-ones **4a–g** (entries 1–7, Table 1) *via* an IMDA followed by a retro-Diels-Alder reaction with the expulsion of CO₂. The stereochemistry of these adducts was absolutely controlled by the preexisting chiral center.

Table 1
Results of tandem IMDA and retro-Diels-Alder reaction of **3**.

Entry	Product	R ¹	R ²	X	t (h)	Yield (%) ^a
1	4a	CH ₃	CO ₂ Et	H	12	82
2	4b	CH ₃	CO ₂ Et	Cl	12	89
3	4c	CH ₃	CO ₂ Et	NO ₂	12	80
4	4d	H	CO ₂ Et	H	12	80
5	4e	CH ₃	CH ₃	H	5 days	11 ^b
6	4f	CH ₃	CH ₃	Cl	5 days	28
7	4g	CH ₃	CH ₃	NO ₂	5 days	15

^aIsolated yield.

^b53% substrate recovered.

The reactivity of amides varied depending on the substitution pattern at the terminal of the allyl double bond. As shown in Table 1, those amides attached to a *trans* electron-withdrawing group, carboethoxy, at the terminal of the allyl double bond **3a–d** reacted to furnish **4a–d** within 12 h in high yields (80%–89%) (Table 1, entries 1–4). However, amides attached to two methyl groups at the terminal allyl double bond **3e–g** were transformed into **4e–g** in low yields (11%–28%) and much longer time (5 days) was needed (Table 1, entries 5–7). These results show that an electron-withdrawing group on the dienophiles facilitates the reaction but an electron-donating group is unfavorable. Interestingly, these results are completely different from that of the IMDA reaction of 2*H*-chromen-2-one with acetylenic groups. That reaction required higher temperature (300 °C) and was retarded by an electron-withdrawing group, carboethoxy, attached to the terminal acetylene (Scheme 1). The substituents on the benzene ring of 2*H*-chromen-2-one do not apparently affect the reactivity (entries 1–3 and 5–7, Table 1), but weak electron-withdrawing groups on the benzene ring of 2*H*-chromen-2-one facilitate the reaction (entries 2 and 6, Table 1).

The structure of the product **4a**, depicted in Fig. 1, was determined by X-ray diffraction analysis. The crystallographic data of **4a** have been deposited in the Cambridge Crystallographic Data Centre (No. CCDC 1451810). The structures of **4b–g** were deduced from **4a** by comparing the ¹H NMR data. The coupling constants between H3 and H3a of **4b–g** are in a range of 3.6–5.6 Hz and similar to that of **4a** (4.8 Hz).

Fig. 1 X-ray structure for **4a**.

Paddon-Row and Sherburn [10] performed computational studies on the stereoselectivity in IMDA reactions of penta-1,3-dienyl acrylates and found that *trans* adducts were generally favored. Accordingly, we hypothesized a possible pathway of cycloaddition of **3a** as shown in Scheme 5. The chiral *N*-benzyl-*N*-allyl amide transforms into IMDA adduct **B** via transition state **A**, and the subsequent elimination of carbon dioxide from **B** generates the 2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-one derivative **4a**.

Scheme 5. An assumed possible pathway from **3a** to **4a**.

Due to the C9–C9a double bond, these 2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-ones can be subjected to further modifications. Stereo-controlled dihydroxylation of **4a–c** by AD-mix α followed by esterification afforded **5a–c** in high yields (83%–90%) (Scheme 3). It is surprising to us that the formed products had a δ -lactone structure. These results show that the two introduced hydroxyl groups were kept in the same face of the carbon ring with carboethoxy, which led to the formation of the δ -lactone with the hydroxyl at the C9 position under basic conditions.

4. Conclusion

The tandem IMDA/retro-Diels-Alder reaction of chiral *N*-benzyl-*N*-allyl-amides containing 2*H*-chromen-2-one constitutes an absolute stereo-controlled entry to 2,3,3a,4-tetrahydro-1*H*-benzo[*f*]isoindol-1-ones. The reactivity was affected by groups attached in the dienophile, and an electron-withdrawing group facilitates the reaction. Adducts can be further modified by removing the PMB group or dihydroxylation of the double bond. Further studies on the scope and application of this tandem IMDA/retro-Diels-Alder reaction of *N*-benzyl-*N*-allyl-amides containing 2*H*-chromen-2-ones are in progress.

Acknowledgment

This work was supported by the research grant from the National Science Foundation of China (No. 21172191). Mr. Jiyong Liu of the X-ray crystallography facility of Zhejiang University is acknowledged for his assistance in the crystal structure analysis.

References

- [1] (a) J.S. Meek, R.T. Merrow, S.J. Cristol, The Diels-Alder reaction of isoprene with styrene and 2-vinylpyridine, *J. Am. Chem. Soc.* 74 (1952) 2667–2668; (b) T.G. Corbett, W. Davies, Q.N. Porter, Reactions of *o*-quinones with 1-vinylnaphthalene, *Aust. J. Chem.* 18 (1965) 1775–1779;

- (c) D.R. Arnold, L.B. Gillis, E.B. Whipple, Photocycloaddition of 2-acetylnaphthalene to methyl cinnamate. A 2 + 4 electron photocycloaddition, *J. Chem. Soc. D*, (1969) 918-919;
- (d) N.N. Podgornova, E.S. Lipina, T.Y. Paperno, V.V. Perekalin, 1,4-dinitrodienes in a "reversed" Diels-Alder condensation reaction, *Zh. Org. Khim.* 12 (1976) 25-32;
- (e) V.M. Berestovitskaya, M.V. Titova, V.V. Perekalin, Dinitro-3-sulfolenes as sources of dinitro-1,3-butadienes in the Diels-Alder reaction with "inverse" electron properties, *Zh. Org. Khim.* 16 (1980) 891-892;
- (f) D. Hartsough, G.B. Schuster, The triplex Diels-Alder reaction: Stereospecific addition of methylstyrenes to 1,3-cyclohexadiene, *J. Org. Chem.*, 54 (1989) 3-4;
- (g) V. Nair, D. Maliakal, P.M. Treasa, N.P. Rath, G. K. Eigendorf, [4+2] cycloaddition reactions of o-benzoquinones with styrenes: A facile synthesis of bicyclo[2.2.2]octenediones, *Synthesis*, (2000) 850-856;
- (h) Y.S. Lin, S.Y. Chang, M.S. Yang, et al., Diels-Alder reactions of 4-triflyloxy-2,6,6-trimethyl-2,4-cyclohexadienone. An expedient methodology for the synthesis of bicyclo[2.2.2]oct-5-en-2-ones and bicyclo[2.2.2]octa-5,7-dien-2-ones, *J. Org. Chem.* 69 (2004) 447-458.
- [2] W. J. Theodor, Thermische und photochemische additionen von dienophilen an arene sowie deren vinyloge und hetero-analoga; ii, *Synthesis* 1980 (1980) 769-798.
- [3] (a) J.A. Reed, C.L. Schilling Jr, R. Tarvin, T.A. Rettig, J. K. Stille, Diels-Alder reactions of 2-pyrones. Direction of the addition reaction with acetylenes, *J. Org. Chem.*, 34 (1969) 2188-2192;
- (b) K.H. Posner, B.D. Nelson, C.M. Kinter, K. Afarinkia, 3-Bromo-2-pyrone: An easily prepared chameleon diene and a synthetic equivalent of 2-pyrone in thermal Diels-Alder cycloadditions, *Tetrahedron Lett.* 32 (1991) 5295-5298;
- (c) K. Afarinkia, G.H. Posner, 5-Bromo-2-pyrone: An easily prepared ambiphilic diene and a synthetic equivalent of 2-pyrone in mild, thermal, Diels-Alder cycloadditions, *Tetrahedron Lett.* 33 (1992) 7839-7842;
- (d) K. Afarinkia, B. C. Jose, Diels-Alder cycloaddition of 5-aryl-2-pyrones, *Tetrahedron Lett.* 41 (2000) 4955-4958;
- (e) C.G. Cho, Y.W. Kim, Y.K. Lim, et al., Diels-Alder cycloadditions of 3,5-dibromo-2-pyrone: A new ambident diene, *J. Org. Chem.* 67 (2002) 290-293;
- (f) K. Afarinkia, M.J. Bearpark, A. Ndibwami, An experimental and computational investigation of the Diels-Alder cycloadditions of halogen-substituted 2(H)-pyran-2-ones, *J. Org. Chem.* 70 (2005) 1122-1133.
- [4] (a) D.A. Bleasdale, D.W. Jones, Regioselective Diels-Alder addition to 2-benzopyran-3-ones: A route to aromatic steroids, *J. Chem. Soc., Chem. Commun.* (1985) 1027-1028;
- (b) E.J. Bush, D.W. Jones, Asymmetric total synthesis of (-)-podophyllotoxin, *J. Chem. Soc., Chem. Commun.* (1993) 1200-1201;
- (c) I.J. Shin, E.S. Choi, C.G. Cho, Total synthesis of (±)-trans-dihydronarciclasine through a highly endo-selective Diels-Alder cycloaddition of 3, 5-dibromo-2-pyrone, *Angew. Chem.* 119 (2007) 2353-2355;
- (d) N.T. Tam, C.G. Cho, Total synthesis of (±)-joubertinamine from 3-(3,4-dimethoxyphenyl)-5-bromo-2-pyrone, *Org. Lett.* 9 (2007) 3391-3392;
- (e) M.V. Kozyska, G.B. Dudley, On the intramolecular pyrone Diels-Alder approach to basilolide B, *Tetrahedron Lett.* 49 (2008) 2899-2901;
- (f) N.T. Tam, J. Chang, E.J. Jung, C.G. Cho, Total syntheses of (±)-crinine, (±)-crinamine, and (±)-6a-epi-crinamine via the regioselective synthesis and Diels-Alder reaction of 3-aryl-5-bromo-2-pyrone, *J. Org. Chem.* 73 (2008) 6258-6264;
- (g) N.T. Tam, C.G. Cho, Total synthesis of (±)-crinine via the regioselective stille coupling and Diels-Alder reaction of 3,5-dibromo-2-pyrone, *Org. Lett.* 10 (2008) 601-603;
- (h) T.T. Nguyen, E.J. Jung, C.G. Cho, Intramolecular imino Diels-Alder approach to the synthesis of the aspidosperma alkaloid from 3,5-dibromo-2-pyrone, *Org. Lett.* 12 (2010) 2012-2014;
- (i) Y.G. Jung, H.U. Kang, H.K. Cho, C.G. Cho, B-silyl styrene as a dienophile in the cycloaddition with 3,5-dibromo-2-pyrone for the total synthesis of (±)-pancratistatin, *Org. Lett.* 13 (2011) 5890-5892;
- (j) H.K. Cho, H.Y. Lim, C.G. Cho, (e)-β-Borylstyrene in the Diels-Alder reaction with 3,5-dibromo-2-pyrone for the syntheses of (±)-1-epi-pancratistatin and (±)-pancratistatin, *Org. Lett.* 15 (2013) 5806-5809;
- (k) Y.G. Jung, S.C. Lee, H.K. Cho, et al., Total syntheses of (±)-α-lycorane and (±)-1-deoxylicorane, *Org. Lett.* 15 (2013) 132-135.
- [5] (a) B. Rickborn, The retro-Diels-Alder reaction part II. Dienophiles with one or more heteroatom, in: *Organic reactions*, John Wiley & Sons, Inc., 2004, pp. 245-252;
- (b) A. Ichihara, Retro-Diels-Alder strategy in natural product synthesis, *Synthesis* (1987) 207-222.
- [6] (a) R. Adams, W. D. McPhee, R. B. Carlin, Z. W. Wicks, The addition of dienes to coumarin and to certain substituted cinnamic acids. I., *J. Am. Chem. Soc.* 65 (1943) 356-360;
- (b) D. Amantini, F. Fringuelli, O. Piermatti, F. Pizzo, L. Vaccaro, 3-Nitrocoumarins as dienophiles in the Diels-Alder reaction in water. An approaches to the synthesis of nitrotetrahydrobenzo[c]chromenones dihydrodibenzo-[b,d]furans, *J. Org. Chem.* 68 (2003) 9263-9268;
- (c) R. Girotti, A. Marrocchi, L. Minuti, et al., Diels-Alder reaction of 3-substituted coumarins in water and under high-pressure condition. An uncatalyzed route to tetrahydro-6H-benzo[c]chromen-6-ones, *J. Org. Chem.* 71 (2006) 70-74;
- (d) L. Minuti, A. Marrocchi, S. Landi, M. Seri, E. Gacs-Baitz, High-pressure and thermal Diels-Alder reactions of 5-nitro[2.2]paracyclophanepyrans-6-one, *Tetrahedron* 63 (2007) 5477-5481;
- (e) E. Balerini, L. Minuti, O. Piermatti, High pressure Diels-Alder approach to hydroxy substituted 6a-cyano tetrahydro-6H-benzo[c]chromen-6-ones: A route to Δ⁶-cis-cannabidiol, *J. Org. Chem.* 74 (2009) 4311-4317;
- (f) I.Y. Flores-Rarios, L. Lopez-Garrido, F.J. Martinez-Martinez, et al., Thermal [4+2] cycloaddition of 3-acetyl, 3-carbamoyl and 3-ethoxycarbonyl-coumarins with 2,3-dimethyl 1,3-butadiene under solventless conditions: a structural study, *Molecules* 15 (2010) 1513-1530;
- (g) A.G. Song, X.S. Zhang, X.X. Song, et al., Construction of chiral bridged tricyclic benzopyranes: Enantioselective catalytic Diels-Alder Reaction and a one-pot reduction/acid-catalyzed stereoselective cyclization, *Angew. Chem. Int. Ed.* 53 (2014) 4940-4944.
- [7] G. A. Kraus, J. O. Pezzanite, H. Sugimoto, Heterocyclic intraconversion, *Tetrahedron Lett.* (1979) 853-856.
- [8] (a) J. Wu, L. Sun, W.M. Dai, Microwave-assisted tandem Wittig-intramolecular Diels-Alder cycloaddition. Product distribution and stereochemical assignment, *Tetrahedron* 62 (2006) 8360-8372;
- (b) J. Wu, H. Yu, Y. Wang, X. Xing, W.M. Dai, Unexpected epimerization and stereochemistry revision of IMDA adducts from sorbate-related 1,3,8-nonatrienes, *Tetrahedron Lett.* 48 (2007) 6543-6547;
- (c) J. Wu, X. Jiang, J. Xu, W.M. Dai, Tandem Wittig-intramolecular Diels-Alder cycloaddition of ester-tethered 1,3,9-decatrienes under microwave heating, *Tetrahedron* 67 (2011) 179-192.
- [9] P. Q. Huang, T.J. Wu, Y.P. Ruan, A flexible approach to (s)-5-alkyl tetramic acid derivatives: Application to the asymmetric synthesis of (+)-preussin and protected (3s,4s)-ahppa, *Org. Lett.* 5 (2003) 4341-4344.
- [10] (a) T.N. Cayzer, M.N. Paddon-Row, D. Moran, A.D. Payne, Intramolecular Diels-Alder reaction of ester-linked 1,3,8-nonatrienes, *J. Org. Chem.* 70 (2005) 5561-5570;
- (b) M.N. Paddon-Row, D. Moran, G.A. Jones, M.S. Sherburn, On the origin of cis/trans stereoselectivity in intramolecular Diels-Alder reactions of substituted pentadienylacrylates: a comprehensive density functional study, *J. Org. Chem.* 70 (2005) 10841-10853.
- [11] D.Q. Tan, K.S. Martin, J.C. Fetting, J.T. Shaw, Ammonia synthons for the multicomponent assembly of complex gamma-lactams, *Proc. Natl. Acad. Sci.* 108 (2011) 6781-6786.