Tetrahedron 64 (2008) 10924–10929

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Intramolecular hetero-Diels–Alder reaction of 1-oxa-1,3-butadienes with terminal acetylenes in aqueous media using CuI

Malihe Javan Khoshkholgh [a], Saeed Balalaie [a,*], Rolf Gleiter [b], Frank Rominger [b]

[a] Department of Chemistry, K. N. Toosi University of Technology, P.O. Box 15875-4416, Tehran, Iran
[b] Organisch-Chemisches Institut der Universität Heidelberg, Im Neuenheimer Feld 270, D-69120, Heidelberg, Germany

ARTICLE INFO

Article history:
Received 12 May 2008
Received in revised form 5 August 2008
Accepted 21 August 2008
Available online 27 August 2008

Keywords:
Intramolecular hetero-Diels–Alder reaction
Cuprous iodide
1,3-Oxa-butadienes
Aqueous media
Unactivated acetylene
Oxa-helicene

ABSTRACT

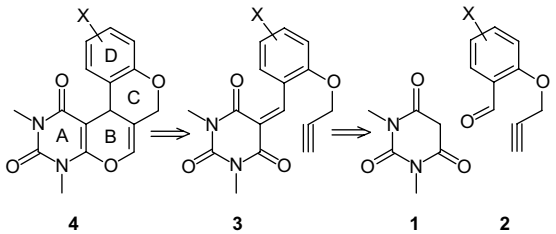
A new method for the preparation of tetracyclic uracils (oxa-helicene) **4** was developed. The intramolecular hetero-Diels–Alder reaction of 1-oxa-1,3-butadiene **3** and an unactivated alkyne in the presence of CuI led to tetracyclic uracils **4** in aqueous media with good yields. The 1-oxa-1,3-butadiene **3** was prepared through Knoevenagel reaction of *O*-propargylated salicylaldehyde derivatives and barbituric acid or 1,3-dimethylbarbituric acid.

1. Introduction

One of the important objectives in organic synthesis is the development of highly efficient synthetic procedures toward complex molecules. The hetero-Diels–Alder reaction represents one of the most effective methods for the synthesis of heterocyclic compounds, especially for natural products synthesis.[1,2] In recent years, intramolecular hetero-Diels–Alder (IMHDA) reactions have been used widely in numerous reactions of prominence in organic synthesis, because of their economical and stereocontrolled nature.[3] These reactions allow the formation of two or more rings at once, avoiding sequential chemical transformations. Among these reactions, the 1-oxa-1,3-butadiene Diels–Alder reaction provides a means for the synthesis of pyran moieties. The 1-oxa-1,3-butadiene cycloaddition with dienophiles, usually an alkene, has been described in the literature.[1b,4]

Due to the lower reactivity of unactivated alkynes in comparison to the corresponding alkenes, only a few examples of hetero-Diels–Alder reactions with unactivated acetylenes have been reported. The examples given in the literature are restricted to 1-aza-1,3-butadienes,[5] no hetero-Diels–Alder reaction of 1-oxa-1,3-butadienes with unactivated alkynes has been reported; only cycloadditions of alkynes with donor–acceptor substituents were described so far.[6] Recently, different Lewis acids[7] provide new opportunities for various catalytic alkyne reactions. Some of the most frequently used transition metal catalysts are copper(I) compounds. These are useful catalysts for a wide variety of organic transformations such as intramolecular cyclizations,[8] halogen exchange,[9] [3+2] cycloadditions,[10]and coupling reactions.[11] The significant catalytic effect of specific transition metal complexes for activating the triple bond, made the utilization of alkynes in the hetero-Diels–Alder reaction possible.

In this paper, a new and efficient strategy for the preparation of the cyclic compounds **4** via the catalytic intramolecular hetero-Diels–Alder cycloaddition of 1-oxa-1,3-butadiene derivatives **3** is reported (Scheme 1). Reactions were carried out in the presence of CuI (40%), and water as the solvent. The use of water as solvent has been an active area of research in Green Chemistry and has been usually applied for HAD reactions.[12]



Scheme 1. Retrosynthetic analysis of the synthesis.

* Corresponding author. Fax: +98 21 2285 3650.
E-mail address: balalaie@kntu.ac.ir (S. Balalaie).

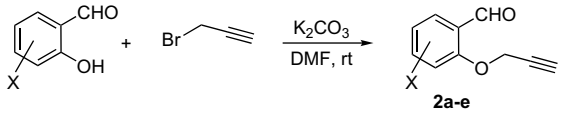
0040-4020/$ – see front matter © 2008 Published by Elsevier Ltd.
doi:10.1016/j.tet.2008.08.056

Our goal was to design an efficient way to prepare the tetracyclic systems **4**, which consist of a uracil ring (A) annulated to a dihydropyran ring (B) (Scheme 1). System **3** seemed to be very suitable for a ring closure using the Diels–Alder reaction as the key step. It could be readily available from barbituric acid or its 1,3-dimethyl derivatives, and *O*-propargylated salicylaldehyde compounds **2a–e**.

2. Results and discussion

2.1. Preparation of substrates for the hetero-Diels–Alder reaction

The *O*-propargylated salicylaldehydes **2a–e** were prepared[13] from the corresponding substituted salicylaldehydes with good to excellent yields by applying Williamsons ether synthesis (Scheme 2). A Knoevenagel condensation between barbituric acid or 1,3-dimethylbarbituric acid and the aldehydes **2a–e** afforded compounds **3a–i** (Scheme 3, Table 2) in yields between 75 and 94%. X-ray crystallography data confirm the structure of **3a**. In Figure 1, the molecular structure of **3a** is shown.



Scheme 2. Synthesis of *O*-propargylated aldehydes at room temperature.

2.2. Intramolecular hetero-Diels–Alder reaction of 1-oxa-1,3-butadienes with terminal acetylene

The intramolecular hetero-Diels–Alder reaction of several 1-oxa-1,3-butadienes with terminal acetylenes was investigated. At first, compound **3a** was used as the model system to achieve and optimize the desired Diels–Alder reaction. Heating **3a** in toluene under reflux for 72 h did not provide our goal. After this failure, we tried various Lewis acids; we only got satisfactory results with CuI. By variation of CuI ratios and the solvent type, we obtained good yields with 30 and 40% CuI and boiling water as reaction medium. The results are summarized in Table 1.

Using these optimized conditions, we investigated the intramolecular hetero-Diels–Alder reaction of compounds **3a–i** (Scheme 3, Table 2). Compounds **4a–i** have been prepared in 70–84% yields. The results are summarized in Table 2. The structures of the products were deduced from their elemental analysis and spectroscopic data.

The characteristic peaks for **4a–i** in the ^{1}H NMR spectra are an AB quartet for the –OCH_2 group between 4.6 and 4.9 ppm followed closely by a singlet for the OCH═ group. The diastereotopicity of the two protons of the OCH_2– groups is due to the helical shape of rings A–D in **4a–i**. The corresponding signals of the OCH_2 and

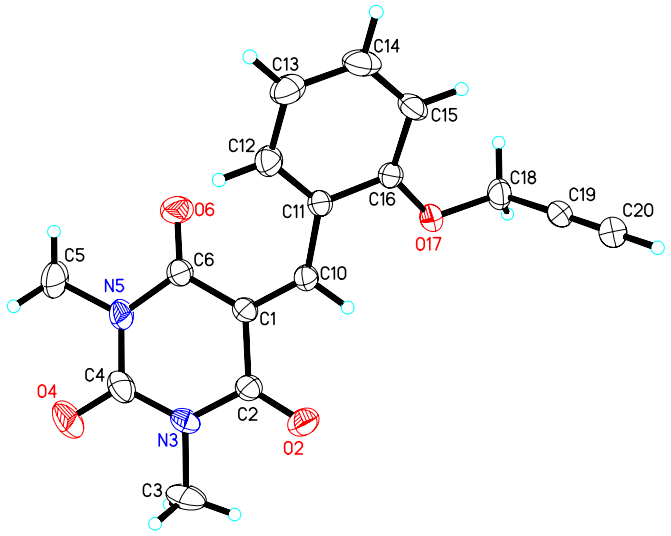


Figure 1. ORTEP representation of the structure of **3a**.

Table 1
Effect of solvent and catalyst in the hetero-Diels–Alder reaction of **3a**

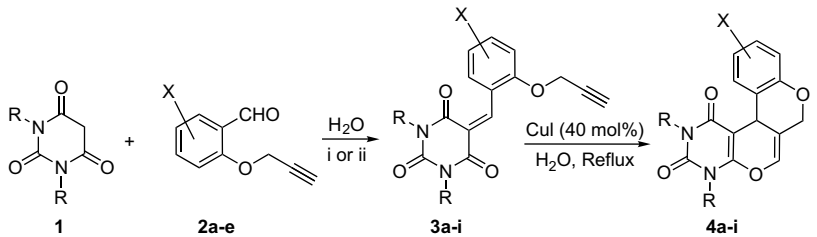
Lewis acid	Lewis acid (%)	Solvent	Time (h)	Yield (%)
—	—	Toluene	72	—
Ag(OTf)	20	Acetonitrile	24	—
$AuCl_3$	20	Acetonitrile	24	—
Cu(OTf)	20	Acetonitrile	24	—
CuI	20	Toluene	6	40
CuI	20	Acetonitrile	24	45
CuI	20	Water	20	53
CuI	25	Water	20	68
CuI	30	Water	20	76
CuI	40	Water	20	84

OCH═ groups in the ^{13}C NMR spectra appear at 67 ppm and 85 ppm, respectively.

The helical shape of **4a** was confirmed by X-ray crystallography (Fig. 2). The angle between two planes is 66.3° (the angle between the two planes C (1) N (2) C (3) C (4) C (17) N (18) and C (6) C (7) C (8) C (9) C (10) C (11)).

It seems that the initial step is probably the formation of a π-complex with CuI. Research has shown that copper(I) salts can be coordinated to the triple bond and act as a π-electrophilic Lewis acid.[14] This complexation likely increases alkyne activity toward cyclization.

In conclusion, we have developed a general method for the synthesis of tetracyclic uracil derivatives via the intramolecular hetero-Diels–Alder cyclization in water. The investigation proceeds using unactivated alkynes as dienophiles and 1-oxa-1,3-butadienes as dienes in the presence of CuI. The research for finding novel hetero-Diels–Alder reaction with unactivated alkynes using different Lewis acids is still in progress in our laboratory.



i: R= H, 10% HCl
ii: R= Me, 20% $(NH_4)_2HPO_4$

Scheme 3.

Table 2
Synthesis of annulated uracil derivatives using CuI

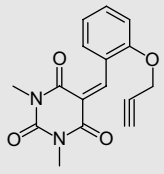
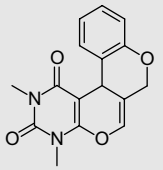
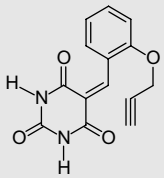
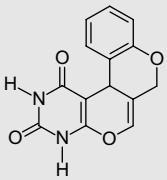
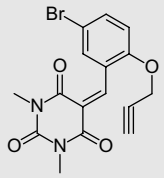
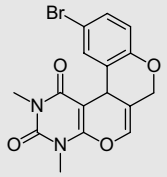
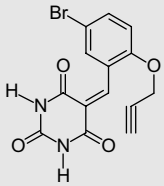
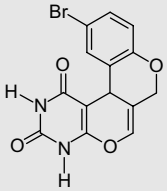
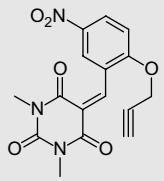
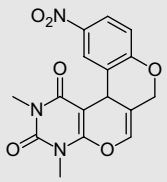
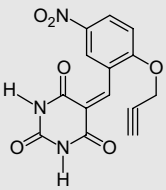
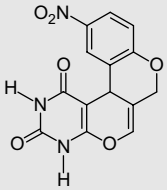
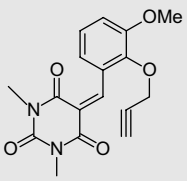
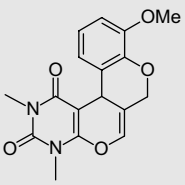
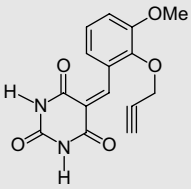
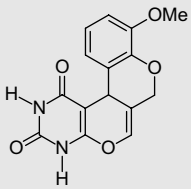
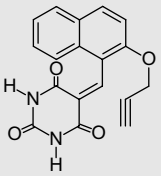
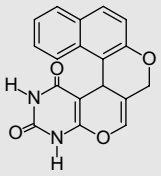
Entry	Alkene	Yield (%)	Product	Time (h)	Yield[a] (%)
1	 **3a**	84	 **4a**	20	84
2	 **3b**	90	 **4b**	28	73
3	 **3c**	88	 **4c**	25	70
4	 **3d**	86	 **4d**	30	76
5	 **3e**	80	 **4e**	6	81
6	 **3f**	91	 **4f**	10	75
7	 **3g**	75	 **4g**	10	80

Table 2 (*continued*)

Entry	Alkene	Yield (%)	Product	Time (h)	Yield[a] (%)
8	 **3h**	94	 **4h**	13	82[b]
9	 **3i**	93	 **4i**	15	72[b]

Reactions were performed with alkenes **3a–i** (1 mmol) and CuI (40 mol %) in water at reflux.
[a] Yields of isolated product.
[b] The solvent was toluene.

3. Experimental

3.1. General

Commercially available materials were used without further purification. Compounds **2a–e** were prepared in excellent purity.[13] Melting points were determined on an *Electrothermal 9100* apparatus and were uncorrected. IR spectra were obtained on an ABB FTIR (FTLA 2000) spectrometer. ^{1}H NMR and ^{13}C NMR spectra were run on Bruker DRX-300 and DRX-500 AVANCE spectrometers at 300 and 500 MHz for ^{1}H NMR, and 125 and 75 MHz for ^{13}C NMR. $CDCl_3$ and DMSO-d_6 were used as solvents. High resolution mass spectra were recorded on JEOL JMS-700 (HR-EI) spectrometer. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O rapid analyzer. X-ray structure determinations were carried out on Bruker Smart (**3a**) and APEX (**4a**) diffractometers. CCDC 676951 (**3a**) and 635913 (**4a**) 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.

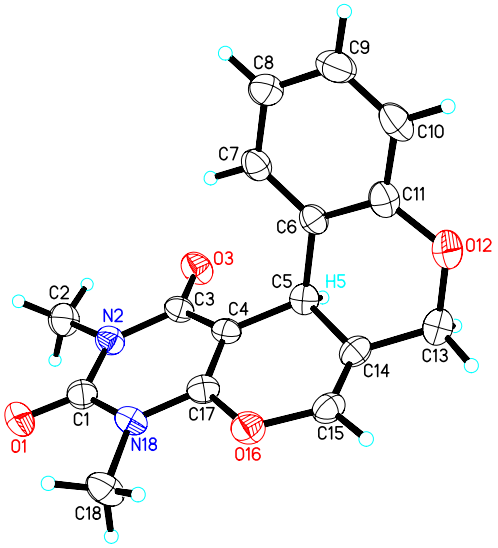


Figure 2. ORTEP representation of the structure of **4a**.

3.2. General procedure for the synthesis of starting materials for hetero-Diels–Alder reaction

*3.2.1. O-Propargylation of salicylaldehyde derivatives **2a–e***

To a stirred solution of salicylaldehyde derivative (5 mmol) and potassium carbonate (5 mmol, 0.069 g) in DMF (25 ml) was added propargyl bromide (6 mmol, 0.071 g). After stirring for 4–24 h, water was added and the precipitated solid was filtered and washed with water.

*3.2.1.1. 2-(2-Propynyloxy)benzaldehyde (**2a**).* White solid, yield=90%; mp 69–70 °C (lit.[15] 66–68 °C); ν_{max} (KBr) 3271, 2120, 1689; δ_H (300 MHz, $CDCl_3$) 2.59 (1H, t, *J* 2.4 Hz, H-acetylenic), 4.86 (2H, d, *J* 2.4 Hz, O*CH*$_2$), 7.11 (1H, t, *J* 7.7 Hz, H_{Ar}), 7.14 (1H, d, *J* 8.5 Hz, H_{Ar}), 7.60 (1H, dt, *J* 8.5, 1.5 Hz, H_{Ar}), 7.90 (1H, dd, *J* 7.7, 1.8 Hz, H_{Ar}), 10.50 (1H, d, *J* 0.5 Hz, H*C*=O); δ_C (75 MHz, DMSO-d_6) 56.4, 78.6, 79.0, 114.3, 121.5, 124.8, 127.8, 136.2, 159.5, 188.9; HRMS (EI): $[M]^+$, found 160.0501. $C_{10}H_8O_2$ requires 160.0524.

*3.2.1.2. 5-Bromo-2-(2-propynyloxy)benzaldehyde (**2b**).* White solid, yield=94%; mp 94–96 °C (lit.[15] 89–91 °C); ν_{max} (KBr) 3281, 2120, 1684; δ_H (300 MHz, $CDCl_3$) 2.60 (t, 1H, *J* 2.4 Hz, H-acetylenic), 4.84 (2H, d, *J* 2.4 Hz, O*CH*$_2$), 7.05 (1H, d, *J* 8.9 Hz, H_{Ar}), 7.66 (1H, dd, *J* 8.9, 2.6 Hz, H_{Ar}), 7.97 (1H, d, *J* 2.6 Hz, H_{Ar}), 10.41 (1H, s, *H*C=O); δ_C (75 MHz, DMSO-d_6) 56.8, 78.2, 79.4, 113.4, 117.0, 126.3, 130.0, 138.2, 158.5, 187.8; HRMS (EI): $[M]^+$, found 237.9602. $C_{10}H_7O_2^{79}Br$ requires 237.9625; $[M+2]^+$, found 239.9606. $C_{10}H_7O_2^{81}Br$ requires 239.9609.

*3.2.1.3. 5-Nitro-2-(2-propynyloxy)benzaldehyde (**2c**).* White solid, yield=92%; mp 91.5–93 °C; ν_{max} (KBr) 3245, 2125, 1684; δ_H (300 MHz, $CDCl_3$) 2.68 (1H, t, *J* 2.4 Hz, H-acetylenic), 4.99 (2H, d, *J* 2.4 Hz, O*CH*$_2$), 7.30 (1H, d, *J* 9.2 Hz, H_{Ar}), 8.47 (1H, dd, *J* 9.2, 2.9 Hz, H_{Ar}), 8.47 (1H, d, *J* 2.9 Hz, H_{Ar}), 10.48 (1H, s, *H*C=O); δ_C (75 MHz, DMSO-d_6) 57.4, 77.6, 80.0, 115.2, 123.6, 124.4, 130.6, 141.3, 163.3, 187.6; HRMS (EI): $[M]^+$, found 205.0356. $C_{10}H_7NO_4$ requires 205.0375.

*3.2.1.4. 3-Methoxy-2-(2-propynyloxy)benzaldehyde (**2d**).* White solid, yield=80%; mp 51–52.5 °C (lit.[16] oil); ν_{max} (KBr) 3271, 2125, 1684; δ_H (500 MHz, $CDCl_3$) 2.52 (1H, t, *J* 2.4 Hz, H-acetylenic), 3.96 (3H, s, O*Me*), 4.93 (2H, d, *J* 2.4 Hz, O*CH*$_2$), 7.22 (2H, m, H_{Ar}), 7.51 (1H, dd, *J* 1.9, 7.4 Hz, H_{Ar}), 10.54 (1H, s, *H*C=O); δ_C (75 MHz, DMSO-d_6) 56.1, 60.5, 78.8, 79.6, 117.9, 118.6, 125.1, 130.5, 148.9, 152.8, 189.9; HRMS (EI): $[M]^+$, found 190.0645. $C_{14}H_{10}O_3$ requires 190.0630.

*3.2.1.5. 2-(2-Propynyloxy)-1-naphthaldehyde (**2e**).* Red-brown solid, yield=72%; mp 109.5–110.5 °C (lit.[16] 116 °C); ν_{max} (KBr, cm^{-1}) 3248, 2119, 1656; δ_H (500 MHz, $CDCl_3$) 2.63 (1H, t, *J* 2.4 Hz, H-acetylenic), 5.0 (2H, d, *J* 2.4 Hz, O*CH*$_2$), 7.43 (1H, d, *J* 9.1 Hz, H_{Ar}), 7.50 (1H, dt, *J* 1.0, 7.6 Hz, H_{Ar}), 7.68 (1H, dt, *J* 1.3, 7.6 Hz, H_{Ar}), 7.84 (1H, d, *J* 8.1 Hz, H_{Ar}), 8.12 (1H, d, *J* 9.1 Hz, H_{Ar}), 9.32 (1H, d, J 8.1 Hz, H_{Ar}), 10.95 (1H, s, *H*C=O); δ_C (75 MHz, DMSO-d_6) 57.4, 78.6, 79.3, 115.2, 116.8, 124.0, 125.0, 128.6, 129.8, 130.5, 137.6, 162.0, 191.2; HRMS (EI): $[M]^+$, found 210.0692. $C_{14}H_{10}O_2$ requires 210.0681.

3.2.2. The synthesis of the uracil derivatives

*3.2.2.1. Procedure A: preparation of the uracil derivatives at room temperature (**3a**, **c**, **e**, **g**).* To a stirred solution of *N*,*N*′-dimethylbarbituric acid (187 mg, 1.2 mmol) in water (20 ml) containing $(NH_4)_2HPO_4$ (20 mol %, 0.014 g) were added propargylated aldehydes **2a–c** (1 mmol) at room temperature. After stirring for 4–15 h, the yellow precipitated was filtered and washed with water and ethanol.

*3.2.2.2. Procedure B: preparation of the uracil derivatives at room temperature (**3b**, **d**, **f**, **h**, **i**).* To a stirred solution of barbituric acid (153 mg, 1.2 mmol) in aqueous HCl (25 ml, 10%) were added propargylated aldehydes **2a–e** (1 mmol) at room temperature. After stirring for 2–10 h, the precipitated material was filtered and washed with water and ethanol.

*3.2.2.2.1. 1,3-Dimethyl-5-{[2-(2-propynyloxy)phenyl]methylene}-2,4,6(1H,3H,5H)-pyrimidinetrione(**3a**).* Yellow solid, yield=84%; mp 142.5–143.5 °C; ν_{max} (KBr) 3245, 2115, 1684; δ_H (300 MHz, $CDCl_3$) 2.49 (1H, t, *J* 2.3 Hz, H-acetylenic), 3.3 (3H, s, N*Me*), 3.37 (3H, s, N*Me*), 4.73 (2H, d, *J* 2.3 Hz, O*CH*$_2$), 7.00 (2H, m, H_{Ar}), 7.45 (1H, dt, *J* 8.2, 1.4 Hz, H_{Ar}), 7.93 (1H, d, *J* 7.6 Hz, H_{Ar}), 8.79 (1H, s, =C*H*); δ_C (75 MHz, $CDCl_3$) 28.3, 28.9, 56.3, 76.3, 77.8, 1141.4, 117.9, 120.6, 122.8, 132.6, 134.0, 151.4, 154.8, 157.3, 160.3, 162.4; HRMS (EI): $[M]^+$, found 298.0938. $C_{16}H_{14}N_2O_4$ requires 298.0953.

*3.2.2.2.2. 5-{[2-(2-Propynyloxy)phenyl]methylene}-2,4,6(1H,3H,5H)-pyrimidinetrione (**3b**).* Yellow solid, yield=90%; mp 296–298 °C; ν_{max} (KBr) 3281, 3203, 3060, 1742, 1663; δ_H (300 MHz, DMSO-d_6) 3.64 (1H, d, *J* 1.8 Hz, H-acetylenic), 4.95 (2H, br s, O*CH*$_2$), 7.01 (1H, t, *J* 7.6 Hz, H_{Ar}), 7.17 (1H, d, *J* 8.1 Hz, H_{Ar}), 7.52 (1H, t, *J* 8.1 Hz, H_{Ar}), 7.97 (1H, d, *J* 7.6 Hz, H_{Ar}), 8.45 (1H, s, =C*H*), 11.18 (1H, s, N*H*), 11.37 (1H, s, N*H*); δ_C (75 MHz, DMSO-d_6) 56.2, 78.8, 112.3, 119.0, 120.2, 122.1, 132.5, 133.6, 149.6, 150.2, 156.8, 161.4, 163.3; HRMS (EI): $[M]^+$, found 270.0636. $C_{14}H_{10}N_2O_4$ requires 270.0641.

*3.2.2.2.3. 5-{[5-Bromo-2-(2-propynyloxy)phenyl]methylene}-1,3-dimethyl-2,4,6(1H,3H,5H)-pyrimidinetrione (**3c**).* Yellow solid, yield=88%; mp 156–156.5 °C (decomp.); ν_{max} (KBr) 3260, 2115, 1679; δ_H (300 MHz, $CDCl_3$) 2.56 (1H, br s, H-acetylenic), 3.36 (3H, s, N*Me*), 3.43 (3H, s, N*Me*), 4.77 (2H, d, *J* 2.1 Hz, O*CH*$_2$), 6.97 (1H, d, *J* 8.9 Hz, H_{Ar}), 7.58 (1H, dd, *J* 8.9, 2.3 Hz, H_{Ar}), 8.08 (1H, d, *J* 2.3 Hz, H_{Ar}), 8.69 (1H, s, =C*H*); δ_C (75 MHz, DMSO-d_6) 28.0, 28.5, 56.6, 78.4, 79.1, 111.7, 114.7, 120.2, 124.4, 133.9, 135.2, 148.4, 151.1, 155.6, 160.1, 161.8; HRMS (EI): $[M]^+$, found 376.0058. $C_{16}H_{13}N_2O_4^{79}Br$ requires 376.0059; $[M+H]^+$, found 378.0027. $C_{16}H_{13}N_2O_4^{81}Br$ requires 378.0038.

*3.2.2.2.4. 5-{[5-Bromo-2-(2-propynyloxy)phenyl]methylene}-2,4,6(1H,3H,5H)-pyrimidinetrione (**3d**).* Yellow solid, yield=86%; mp 226–228 °C; ν_{max} (KBr) 3291, 3204, 3091, 2115, 1740, 1684; δ_H (300 MHz, DMSO-d_6) 3.67 (1H, s, H-acetylenic), 4.96 (2H, s, O*CH*$_2$), 7.15 (1H, d, *J* 8.9 Hz, H_{Ar}), 7.68 (1H, d, *J* 8.9 Hz, H_{Ar}), 8.09 (1H, s, H_{Ar}), 8.28 (1H, s, =C*H*), 11.24 (1H, s, N*H*), 11.42 (1H, s, N*H*); δ_C (75 MHz, DMSO-d_6) 56.5, 78.4, 79.1, 11.7, 114.7, 120.4, 124.2, 134.2, 135.2, 147.3, 150.2, 155.7, 161.4, 163.0; HRMS (EI): $[M]^+$, found 347.9742. $C_{14}H_9N_2O_4^{79}Br$ requires 347.9746; $[M+2]^+$, found 349.9717. $C_{14}H_9N_2O_4^{81}Br$ requires 349.9725.

*3.2.2.2.5. 1,3-Dimethyl-5-{[5-nitro-2-(2-propynyloxy)phenyl]-methylene}2,4,6(1H,3H,5H)-pyrimidinetrione (**3e**).* Yellow solid, yield=80%; mp 177–178.6 °C; ν_{max} (KBr) 3286, 2125, 1689, 1519, 1350; δ_H (300 MHz, $CDCl_3$) 2.63 (1H, t, *J* 2.3 Hz, H-acetylenic), 3.36 (3H, s, N*Me*), 3.44 (3H, s, N*Me*), 4.90 (2H, d, *J* 2.3 Hz, O*CH*$_2$), 7.19 (1H, d, *J* 9.2 Hz, H_{Ar}), 8.37 (1H, dd, *J* 9.2, 2.8 Hz, H_{Ar}), 8.67 (1H, s, =CH), 8.81 (1H, d, *J* 2.8 Hz, H_{Ar}); δ_C (75 MHz, $CDCl_3$) 28.5, 29.0, 57.0, 76.4, 77.5, 11.9, 120.3, 123.2, 128.0, 128.0, 128.2, 141.1, 151.0, 151.4, 159.8, 160.7, 161.5; HRMS (EI): $[M]^{+\bullet}$ found 343.0784. $C_{16}H_{13}N_3O_6$ requires 343.0804.

*3.2.2.2.6. 5-{[5-Nitro-2-(2-propynyloxy)phenyl]methylene}2,4,6(1H,3H,5H)-pyrimidinetrione (**3f**).* Yellow solid, yield=91%; mp 236–238 °C; ν_{max} (KBr) 3286, 3209, 3082, 2115, 1745, 1684, 1537, 1355; δ_H (300 MHz, DMSO-d_6) 3.46 (1H, s, H-acetylenic), 5.12 (2H, s, O*CH*$_2$), 7.38 (1H, d, *J* 9.3 Hz, H_{Ar}), 8.26 (1H, s, =C*H*), 8.40 (1H, d, *J* 9.3 Hz, H_{Ar}), 8.81 (1H, s, =C*H*), 11.30 (1H, s, N*H*), 11.46 (1H, s, N*H*); δ_C (75 MHz, DMSO-d_6) 57.3, 77.9, 79.7, 113.0, 121.7, 122.6, 127.8, 128.0, 140.3, 146.2, 150.2, 160.9, 161.4, 162.8; HRMS (EI): $[M]^+$, found 315.0453. $C_{14}H_9N_3O_6$ requires 315.0492.

*3.2.2.2.7. 1,3-Dimethyl-5-{[3-methoxy-2-(2-propynyloxy)phenyl]-methylene}-2,4,6(1H,3H,5H)-pyrimidinetrione (**3g**).* Yellow solid, yield=75%; mp 131–132 °C, ν_{max} (KBr) 3258, 2116, 1684; δ_H (500 MHz, DMSO-d_6) 3.14 (3H, s, N*Me*), 3.22 (3H, s, N*Me*), 3.48 (1H, t, *J* 4 Hz, H-acetylenic), 3.84 (3H, s, O*Me*), 4.77 (2H, d, J 4 Hz, O*CH*$_2$),

7.11 (1H, t, *J* 8.3 Hz, H_{Ar}), 7.20 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.41 (1H, d, *J* 8.3 Hz, H_{Ar}), 8.59 (1H, s, =C*H*); δ_C (75 MHz, DMSO-d_6) 28.2, 28.7, 56.2, 59.8, 78.9, 79.2, 116.5, 120.7, 123.5, 123.6, 128.5, 145.9, 150.5, 151.0, 152.1, 151.2, 163.5; HRMS (EI): $[M]^+$, found 328.1058. $C_{17}H_{16}N_2O_5$ requires 328.1059.

*3.2.2.2.8. 5-{[3-Methoxy-2-(2-propynyloxy)phenyl]methylene}-2,4,6(1H,3H,5H)-pyrimidinetrione (**3h**).* Yellow solid, yield=94%; mp 197–199 °C; ν_{max} (KBr) 3271, 3122, 3060, 2120, 1745, 1684; δ_H (500 MHz, DMSO-d_6) 3.51 (1H, t, *J* 2.3 Hz, H-acetylenic), 3.86 (3H, s, O*Me*), 4.79 (2H, d, *J* 2.3 Hz, OCH_2), 7.12 (1H, t, *J* 7.7 Hz, H_{Ar}), 7.22 (1H, d, *J* 7.7 Hz, H_{Ar}), 7.49 (1H, d, *J* 7.7 Hz, H_{Ar}), 8.52 (1H, s, =C*H*), 11.18 (1H, s, N*H*), 11.38 (1H, s, N*H*); δ_C (75 MHz, DMSO-d_6) 55.9, 59.8, 78.8, 79.1, 116.0, 120.2, 123.3, 123.5, 128.1, 145.7, 150.2, 150.8, 151.8, 161.1, 163.0; HRMS (EI): $[M]^+$, found 300.0746. $C_{15}H_{16}N_2O_5$ requires 300.0732.

*3.2.2.2.9. 5-{[2-(2-Propynyloxy)-1-naphthyl]methylene}-2,4,6-(1H,3H,5H)-pyrimidinetrione (**3i**).* Red solid, yield=93%; mp 157–159 °C; ν_{max} (KBr) 3510, 3502, 3271, 2118, 1679; δ_H (300 MHz, DMSO-d_6) 3.60 (1H, t, *J* 2.2 Hz, H-acetylenic), 4.94 (1H, d, *J* 16.2 Hz, C*H*O), 5.02 (1H, d, J 16.2 Hz, C*H*O), 7.41 (1H, dt, *J* 7.5, 1.0 Hz, H_{Ar}), 7.46 (1H, dt, *J* 1.0, 7.5 Hz, H_{Ar}), 7.53 (1H, d, *J* 9 Hz, H_{Ar}), 7.68 (1H, d, *J* 7.5 Hz, H_{Ar}), 7.91 (1H, d, *J* 7.5 Hz, H_{Ar}), 8.05 (1H, d, *J* 9 Hz, H_{Ar}), 8.52 (1H, s, =C*H*), 11.11 (1H, s, N*H*), 11.44 (1H, s, N*H*); δ_C (75 MHz, DMSO-d_6) 56.9, 78.6, 79.2, 114.3, 118.4, 123.1, 124.1, 127.1, 128.3, 128.4, 130.7, 131.6, 148.5, 150.3, 153.0, 160.6, 162.6; HRMS (EI): $[M]^+$, found 320.0797. $C_{18}H_{12}N_2O_4$ requires 320.0797.

3.3. General procedure C for the intramolecular hetero-Diels–Alder reaction

A solution of compound **4a–i** (1 mmol), CuI (0.4 equiv, 76 mg) in water (25 ml) or toluene was heated to reflux for 6–30 h. The progress of reaction was monitored by TLC. The precipitated dark yellow solid was filtered and recrystallized in ethyl acetate.

*3.3.1. 2,4-Dimethyl-4,12b-dihydro-1H,7H-chromeno[4′,3′:4,5]-pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4a**)*

Following general procedure C in water, compound **4a** was produced (250.4 mg, 84%) as a dark primrose solid; mp 222.5–224 °C; [Found: C, 64.25; H, 4.60; N, 9.28. $C_{16}H_{14}N_2O_4$ requires C, 64.42; H, 4.73; N, 9.39%.] ν_{max} (KBr) 1704, 1632; δ_H (300 MHz, $CDCl_3$) 3.40 (3H, s, N*Me*), 3.47 (3H, s, N*Me*), 4.63 (1H, d, *J* 11.8 Hz, C*H*), 4.74 (1H, s, C*H*), 4.81 (1H, d, *J* 11.8 Hz, C*H*), 6.65 (1H, s, =C*H*), 6.80 (1H, d, *J* 8.1 Hz, H_{Ar}), 6.87 (1H, t, *J* 7.5 Hz, H_{Ar}), 7.10 (2H, m, H_{Ar}); δ_C (75 MHz, $CDCl_3$) 27.7, 28.3, 29.4, 65.8, 85.7, 113.0, 116.1, 120.1, 125.6, 126.1, 127.3, 132.8, 149.7, 152.5, 152.8, 162.6; HRMS (EI): $[M]^+$, found 298.0926. $C_{16}H_{14}N_2O_4$ requires 298.0953.

*3.3.2. 4,12b-Dihydro-1H,7H-chromeno[4′,3′:4,5]pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4b**)*

Following general procedure C in water, compound **4b** was produced (197.2 mg, 73%) as a dark yellow solid; mp 265–267 °C; [Found: C, 62.13; H, 3.70; N, 10.26. $C_{14}H_{10}N_2O_4$ requires C, 62.23; H, 3.73; N, 10.37%.] ν_{max} (KBr) 1735, 1699; δ_H (500 MHz, DMSO-d_6) 4.50 (1H, s, CH), 4.64 (1H, d, *J* 10.7 Hz, –C*H*), 4.77 (1H, d, *J* 10.7 Hz, –C*H*), 6.71 (1H, d, *J* 7.2 Hz, H_{Ar}), 6.78 (1H, s, =C*H*), 7.05 (3H, m, H_{Ar}), 11.24 (1H, s, N*H*), 11.83 (1H, s, N*H*); HRMS (EI): $[M]^+$, found 270.0628. $C_{14}H_{10}N_2O_4$ requires 270.0641.

*3.3.3. 11-Bromo-2,4-dimethyl-4,12b-dihydro-1H,7H-chromeno-[4′,3′:4,5]pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4c**)*

Following general procedure C in water, compound **4c** was produced (263.2 mg, 70%) as a dark yellow solid; mp 240.5–242 °C; [Found: C, 50.75; H, 3.38; N, 7.18. $C_{16}H_{13}N_2O_4Br$ requires C, 50.95; H, 3.47; N, 7.43%.] ν_{max} (KBr) 1709, 1642; δ_H (300 MHz, DMSO-d_6) 3.26 (3H, s, N*Me*), 3.27 (3H, s, N*Me*), 4.63 (1H, s, C*H*), 4.71 (1H, d, *J* 11.6 Hz, C*H*), 4.84 (1H, d, 1H, *J* 11.6 Hz, –C*H*), 6.72 (1H, d, *J* 8.5 Hz, H_{Ar}), 7.12 (2H, s, H_{Ar} and =C*H*), 7.25 (1H, d, *J* 8.5 Hz, H_{Ar}); δ_C (75 MHz, $CDCl_3$) 29.0, 29.8, 30.4, 67.1, 85.7, 112.3, 112.8, 119.7, 130.1, 130.4, 131.4, 136.0, 150.9, 153.6, 154.7, 163.9; HRMS (EI): $[M]^+$, found 376.0064. $C_{16}H_{13}N_2O_4^{79}Br$ requires 376.0059; $[M+2]^+$, found 376.0030. $C_{16}H_{13}N_2O_4^{81}Br$ requires 376.0039.

*3.3.4. 11-Bromo-4,12b-dihydro-1H,7H-chromeno[4′,3′:4,5]pyrano-[2,3-d]pyrimidine-1,3(2H)-dione(**4d**)*

Following general procedure C in water, compound **4d** was produced (264.5 mg, 76%) as a dark yellow solid; mp 295–297 °C; [Found: C, 48.07; H, 2.53; N, 7.96. $C_{14}H_9N_2O_4Br$ requires C, 48.16; H, 2.60; N, 8.02%.] ν_{max} (KBr) 3115, 3004, 1699, 1627; δ_H (500 MHz, DMSO-d_6) 4.56 (1H, s, –C*H*), 4.67 (1H, d, *J* 11.5 Hz, C*H*), 4.78 (1H, d, *J* 11.5 Hz, C*H*), 6.71 (1H, d, *J* 8.7 Hz, H_{Ar}), 7.04 (1H, s, =C*H*), 7.23 (1H, s, H_{Ar}), 7.25 (1H, d, *J* 8.7 Hz, H_{Ar}), 11.28 (1H, s, N*H*), 11.90 (1H, s, N*H*); HRMS (EI): $[M]^+$, found 347.9710. $C_{14}H_9N_2O_4^{79}Br$ requires 347.9746; $[M+2]^+$, found 349.9692. $C_{14}H_9N_2O_4^{81}Br$ requires 347.9725.

*3.3.5. 2,4-Dimethyl-11-nitro-4,12b-dihydro-1H,7H-chromeno-[4′,3′:4,5]pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4e**)*

Following general procedure C in water, compound **4e** was produced (302.2 mg, 81%) as a dark yellow solid; mp 254–255 °C; [Found: C, 55.75; H, 3.69; N, 12.08. $C_{16}H_{13}N_3O_6$ requires C, 55.98; H, 3.79; N, 12.24%.] ν_{max} (KBr) 1704, 1638, 1521, 1340; δ_H (300 MHz, DMSO-d_6) 3.27 (3H, s, N*Me*), 3.30 (3H, s, N*Me*), 4.77 (1H, s, C*H*), 4.86 (1H, d, *J* 11.6 Hz, C*H*), 4.98 (1H, d, *J* 11.6 Hz, C*H*), 6.95 (1H, d, *J* 9.0 Hz, H_{Ar}), 7.18 (1H, s, =C*H*), 7.97 (1H, s, H_{Ar}), 8.02 (1H, d, *J* 8.0, H_{Ar}); δ_C (75 MHz, DMSO-d_6) 28.6, 29.5, 30.0, 67.6, 85.2, 111.0, 118.0, 124.0, 124.5, 128.0, 136.4, 140.8, 150.5, 154.4, 159.8, 163.6; HRMS (EI): $[M]^+$, found 343.0805. $C_{16}H_{13}N_3O_6$ requires 373.0804.

*3.3.6. 11-Nitro-4,12b-dihydro-1H,7H-chromeno[4′,3′:4,5]pyrano-[2,3-d]pyrimidine-1,3(2H)-dione (**4f**)*

Following general procedure C in water, compound **4f** was produced (236.2 mg, 75%) as a dark yellow solid; mp >350 °C (decomp.); [Found: C, 53.28; H, 2.69; N, 13.21. $C_{14}H_9N_3O_6$ requires C, 53.34; H, 2.88; N, 13.33%.] ν_{max} (KBr) 1699, 1632, 1530, 1350; δ_H (500 MHz, DMSO-d_6) 4.69 (1H, s, C*H*), 4.82 (1H, d, *J* 11.6 Hz, C*H*), 4.93 (1H, d, *J* 11.6 Hz, C*H*), 6.94 (1H, d, *J* 8.7 Hz, H_{Ar}), 7.12 (1H, s, =C*H*), 8.01 (1H, d, *J* 8.7 Hz, H_{Ar}), 8.11 (1H, s, H_{Ar}), 11.39 (1H, s, N*H*), 11.96 (1H, s, N*H*); HRMS (EI): $[M]^+$, found 315.0488. $C_{14}H_9N_3O_6$ requires 315.0491.

*3.3.7. 2,4-Dimethyl-9-methoxy-4,12b-dihydro-1H,7H-chromeno-[4′,3′:4,5]pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4g**)*

Following general procedure C in water, compound **4g** was produced (262.5 mg, 80%) as a poor red solid; yield=80%; mp 228.5–229.5 °C; [Found: C, 62.10; H, 4.86; N, 8.48. $C_{17}H_{16}N_2O_5$ requires C, 62.23; H, 4.90; N, 8.57%.] ν_{max} (KBr) 1707, 1639; δ_H (500 MHz, DMSO-d_6) 3.25 (3H, s, N*Me*), 3.26 (3H, s, N*Me*), 3.70 (3H, s, O*Me*), 4.55 (1H, s, C*H*), 4.69 (1H, d, *J* 11.7 Hz, C*H*), 4.81 (1H, d, *J* 11.7 Hz, C*H*), 6.54 (1H, d, *J* 7.9 Hz, H_{Ar}), 6.70 (1H, t, *J* 7.9 Hz, H_{Ar}), 6.79 (1H, d, *J* 7.9 Hz, H_{Ar}), 7.03 (1H, s, =C*H*); δ_C (125 MHz, DMSO-d_6) 27.3, 28.1, 28.7, 54.9, 65.3, 84.5, 110.0, 112.4, 117.4, 118.9, 127.4, 133.4, 141.9, 147.4, 149.3, 152.8, 162.0; HRMS (EI): $[M]^+$, found 328.1057. $C_{17}H_{16}N_2O_5$ requires 328.1059.

*3.3.8. 9-Methoxy-4,12b-dihydro-1H,7H-chromeno[4′,3′:4,5]pyrano-[2,3-d]pyrimidine-1,3(2H)-dione(**4h**)*

Following general procedure C in toluene, compound **4b** was produced (264.0 mg, 82%) as a dark yellow solid; mp 266.5–268 °C; [Found: C, 59.78; H, 4.00; N, 9.16. $C_{15}H_{12}N_2O_5$ requires C, 60.00; H, 4.03; N, 9.33%.] ν_{max} (KBr) 3276, 3194, 1751, 1640; δ_H (500 MHz, DMSO-d_6) 3.71 (3H, s, O*Me*), 4.47 (1H, s, C*H*), 4.66 (1H, d, *J* 11.7 Hz, C*H*), 4.77 (1H, d, *J* 11.7 Hz, C*H*), 6.63 (1H, d, *J* 7.8 Hz, H_{Ar}), 6.74 (1H, t, *J*

7.8 Hz, H_{Ar}), 6.81 (1H, d, *J* 7.8 Hz, H_{Ar}), 6.97 (1H, s, =CH), 11.23 (1H, s, N*H*), 11.83 (1H, s, N*H*); δ_C (125 MHz, DMSO-d_6) 29.45, 56.4, 67.0, 86.0, 111.4, 113.6, 119.1, 120.6, 129.0., 135.1, 143.5, 148.9, 150.4, 155.6, 165.8; HRMS (EI): $[M]^+$, found 300.0702. $C_{15}H_{12}N_2O_5$ requires 300.0747.

*3.3.9. 7,8-Naphtyl-4,12b-dihydro-1H,7H-chromeno[4′,3′:4,5] pyrano[2,3-d]pyrimidine-1,3(2H)-dione (**4i**)*

Following general procedure C in toluene, compound **4i** was produced (230.4 mg, 72%) as a dark red solid; mp 243–244.5 °C; [Found: C, 67.04; H, 3.56; N, 8.55. $C_{18}H_{12}N_2O_4$ requires C, 67.54; H, 3.78; N, 8.75%.] ν_{max} (KBr) 3178, 3019, 1720, 1617; δ_H (500 MHz, DMSO-d_6) 4.66 (1H, s, C*H*), 4.73 (1H, d, 1H, *J* 12.7 Hz, C*H*), 4.93 (1H, d, *J* 12.7 Hz, C*H*), 6.94 (1H, s, =C*H*), 7.25 (1H, t, *J* 7.4 Hz, H_{Ar}), 7.3 (1H, t, *J* 7.4 Hz, H_{Ar}), 7.35 (1H, d, *J* 7.7 Hz, H_{Ar}), 7.75 (1H, d, *J* 8.1 Hz, H_{Ar}), 7.81 (d, 1H, *J* 7.7 Hz, H_{Ar}), 7.98 (1H, d, *J* 8.1 Hz, H_{Ar}), 11.30 (1H, s, N*H*), 11.98 (1H, s, N*H*); δ_C (125 MHz, DMSO-d_6) 28.3, 66.7, 85.6, 116.5, 119.1, 121.9, 125.0, 125.6, 128.3, 129.1, 131.2, 133.3, 149.2, 153.1, 155.2, 164.1; HRMS (EI): $[M]^+$, found 320.0781. $C_{18}H_{12}N_2O_4$ requires 320.0797.

3.4. Crystal structure

*3.4.1. Crystal data of the **3a***

Compound **3a**: (CCDC 676951) $C_{16}H_{14}N_2O_4$, yellow crystals, triclinic, $P\bar{1}$, Z=2, a=3.9693(1) Å, b=11.4451(1) Å, c=15.3766(3) Å, α=81.049(1)°, β=88.767(1)°, γ=87.394(1)°, V=689.25(2) Å^3, D_{cal}=1.44 g/cm^3, μ=0.10 m m^{-1}, 6929 reflections collected, 3108 independent (R_{int}=0.0360), 2195 observed, R_1=0.048, wR_2=0.105($I>2\sigma(I)$).

*3.4.2. Crystal data of the **4a***

Compound **4a**: (CCDC 635913) $C_{16}H_{14}N_2O_4$, colorless crystals, monoclinic, $P2_1/n$, Z=4, a=4.2581(9) Å, b=21.678(5) Å, c=14.571(3) Å, α=90°, β=92.391(6)°, γ=90°. V=1343.8(5) Å^3, D_{cal}=1.47 g/cm^3, μ=0.11 m m^{-1}, 6280 reflections collected, 2810 independent (R_{int}=0.0361), 1871 observed, R_1=0.064, $wR2$=0.149($I>2\sigma(I)$).

Acknowledgements

S.B. is grateful to the Alexander von Humboldt foundation for the research fellowship and equipment donation. Partial support of this work by the K. N. Toosi University of Technology Research Council is appreciatively acknowledged.

References and notes

1. (a) Nicolaou, K. C.; Snyder, S. A.; Vassilikogiannakis, G.; Montagnon, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668–1698 and references cited therein; (b) Tietze, L. F.; Kettschau, G. *Top. Curr. Chem.* **1997**, *189*, 1–120; (c) Jφrgensen, K. A. *Eur. J. Org. Chem.* **2004**, 2093–2102; (d) Palacios, F.; Herran, E.; Rubiales, G.; Ezpeleta, J. M. *J. Org. Chem.* **2002**, *67*, 2131–2135; (e) Behforouz, M.; Ahmadian, M. *Tetrahedron* **2000**, *56*, 5259–5288.
2. (a) Osborn, H. M. I.; Coisson, D. *Mini Rev. Org. Chem.* **2004**, *1*, 41–45; (b) Schmidt, R. R. *Acc. Chem. Res.* **1986**, *19*, 250–259; (c) Kende, A. S.; Fan, J.; Chen, Z. *Org. Lett.* **2003**, *5*, 3205–3208; (d) Crimmins, M. T.; Smith, A. C. *Org. Lett.* **2006**, *8* 1003–1006; (e) Hughes, R. A.; Thompson, S. P.; Alcaraz, L.; Moody, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 15644–15651; (f) Chao, W.; Mahajan, Y. R.; Weinreb, S. M. *Tetrahedron Lett.* **2006**, *47*, 3815–3818.
3. (a) Amos, D. T.; Renslo, A. R.; Danheiser, R. L. *J. Am. Chem. Soc.* **2003**, *125*, 4970–4971; (b) Bland, D. C.; Raudenbush, B. C.; Weinreb, S. M. *Org. Lett.* **2000**, *2*, 4007–4009; (c) Ho, T.-L.; Kung, L.-R.; Chein, R.-J. *J. Org. Chem.* **2000**, *65*, 5774–5779; (d) Snyder, S. A.; Vosburg, D. A.; Jarvis, M. G.; Markgral, J. H. *Tetrahedron* **2000**, *56*, 5329–5335; (e) Thomas, E. J. *Acc. Chem. Res.* **1991**, *24*, 229–235; (f) Tanaka, N.; Suzuki, T.; Hosoya, Y.; Nakada, M. *Tetrahedron Lett.* **2007**, *48*, 6488–6492.
4. Tietze, L. F.; Rackelman, N. In *Multicomponent Reactions*; Zhu, J., Bienayme, H., Eds.; Wiley-VCH: Weinheim, Germany, 2005; pp 121–167.
5. (a) Palacios, F.; Alonso, C.; Ameezua, P.; Rubiales, G. *J. Org. Chem.* **2002**, *67*, 1941–1946; (b) Zhou, H.-B.; Liu, G.-S.; Yao, Z.-J. *Org. Lett.* **2007**, *9*, 2003–2006; (c) Twin, H.; Batey, R. A. *Org. Lett.* **2004**, *6*, 4913–4916; (d) Boger, D. L.; Corbett, W. L. *J. Org. Chem.* **1993**, *58*, 2068–2074; (e) Lu, J.-Y.; Arndt, H.-D. *J. Org. Chem.* **2007**, *72*, 4205–4212.
6. (a) Dell, C. P. *Tetrahedron Lett.* **1992**, *33*, 699–700; (b) Mantani, T.; Konno, T.; Ishihara, T.; Yamanaka, H. *Chem. Lett.* **2000**, 666–667; (c) Back, T. G.; Bethell, R. J.; Parvez, M.; Taylor, J. A.; Wehrli, D. *J. Org. Chem.* **1999**, *64*, 7426–7432.
7. (a) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180–3211; (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348* 2271–2296; (c) Asao, N.; Sato, K.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682–3685; (d) Asao, N.; Yudha, S.; Nogami, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 5526–5528; (e) Ermolat, D. S.; Mehta, V. P.; Eycken, E. V. V. *Synlett* **2007**, 3117–3122; (f) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104* 3079–3159.
8. (a) Chen, Ch.; Dormer, P. G. *J. Org. Chem.* **2005**, *70*, 6964–6967; (b) Evindar, G.; Batey, R. *J. Org. Chem.* **2006**, *71*, 1802–1808; (c) Patil, N. T.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 5139–5142; (d) Zhu, W.; Ma, D. *Chem. Commun.* **2004**, 888–889.
9. Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844–14845.
10. (a) Sreedhar, B.; Reddy, P. S.; Kumar, N. S. *Tetrahedron Lett.* **2006**, *47*, 3055–3058; (b) Jin, T.; Kamijo, S.; Yamamoto, Y. *Eur. J. Org. Chem.* **2004**, 3789–3791; (c) Bock, V. D.; Hiemstra, H.; Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68.
11. (a) Black, D. A.; Arndtsen, B. A. *Org. Lett.* **2004**, *6*, 1107–1110; (b) Rao, H.; Jin, Y.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem.—Eur. J.* **2006**, *12*, 3636–3646; (c) Cho, S. H.; Yoo, E. J.; Bae, I.; Chang, S. *J. Am. Chem. Soc.* **2005**, *127*, 16046–16047; (d) Zhu, W.; Ma, D. *Org. Lett.* **2006**, *8*, 261–263.
12. (a) Grieco, P. A. *Organic Synthesis in Water*; Blacky academic & professional: London, 1998; pp 82–141; (b) Li, C. J.; Chan, T. H. *Organic Reaction in Aqueous Media*; Wiley: New York, NY, 1997; (c) Li, C. J. *Chem. Rev.* **2005**, *105*, 3095–3165.
13. Bashiardes, G.; Safir, I.; Barbot, F.; Laduranty, J. *Tetrahedron Lett.* **2004**, *45*, 1567–1570.
14. (a) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68; (b) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817–7831.
15. Janietz, D.; Rudorf, W. D. *Tetrahedron* **1989**, *45*, 1661–1666.
16. Mathur, S. S.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2479–2483.