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Aza-Diels–Alder reaction of Danishefsky's diene with immines catalyzed by porous α-zirconium hydrogen phosphate and SDS under solvent-free conditions

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ABSTRACT

The aza-Diels–Alder reaction between benzaldimines **1** and Danishefsky's diene in solvent-free conditions is reported for the first time. The reaction occurs rapidly at 30 °C and is catalyzed by porous α-zirconium hydrogen phosphate (p-αZrP) in the presence of sodium dodecyl sulfate (SDS). The yields were excellent. The recycling of the catalyst has also been investigated.

1. Introduction

Solid Brønsted-acid catalysts have received attention in organic synthesis because they (i) are easily available, even in large amounts, (ii) avoid the problem of the metal leaching, often toxic, into the products, and (iii) can be easily recovered by simple filtration or centrifugation if insoluble in the reaction medium [1].

Zirconium phosphates and phosphonates are chemically and thermally stable compounds that are insoluble in water and organic solvents; they have a layered structure onto which organic functionalities may be attached and lodged [2,3]. The loading and catalytic efficiency of these compounds strongly depend on their porosity and surface area. As the porosity and surface area increase, the beneficial effects increase with respect to the reaction rate and selectivity (chemo-, regio-, diastereo-) of the process and smaller amounts of catalyst are required.

The α-zirconium hydrogen phosphate α-$Zr(HPO_4)_2{\cdot}H_2O$ (αZrP) is a layered weakly acidic solid (pKa = 2.0–3.0) with regularly spaced P–OH groups [3]. We have shown that at room temperature it effectively catalyzes (yields 70–84%) the direct aza-Diels–Alder reaction between 2-cyclohexen-1-one and benzaldimines in water in the presence of 0.4 equiv. of sodium dodecyl sulfate (SDS) [4]. Microcrystalline αZrP has a relatively small surface area of 2–10 m^2/g and is not considered to be porous [3]. Recently, a porous α-zirconium hydrogen phosphate (p-αZrP) with a larger surface area (83 m^2/g) and a mesoporosity (mesopore volume 0.17 cm^3/g) was prepared by template method [5] in order to compare its catalytic effectiveness with that of αZrP.

Owning to our experience in the Diels–Alder reaction [6], and chemistry in water [7] and under solvent-free conditions (SolFC) [8] we have chosen the aza-Diels–Alder cycloaddition as reaction-probe because it is known to be a powerful method for the preparation of nitrogen-containing six-membered ring compounds. These are important units in medicinal chemistry and are useful building blocks and intermediates in organic synthesis [9]. Specifically, we chose the reaction of benzaldimines **1** with Danishefsky's diene **2** that allows, by acidic hydrolysis of the adduct **3**, the synthesis of 2,3-dihydro-4-pyridones **4** (Scheme 1) [9,10]. This type of reaction, because of its importance in organic synthesis, has been investigated in organic solvent [10–13] and in aqueous medium [14–16] but never under solvent-free conditions. In water both the two- and three-component version have been studied under (i) neutral conditions catalyzed by organic and inorganic alkaline salts [14] and (ii) under acidic conditions catalyzed by *p*-dodecylbenzensulfonic acid (DBSA) [15], and HBF_4-SDS [16]. AgOTf and HBF_4 have also been used as catalysts in water–organic solvent mixtures [16,17]. Nafion-H has also been used as solid acid catalyst [18]. When the cycloaddition is performed in organic solvent the Diels–Alder adduct **3** is then converted into dihydro-4-pyridones **4** by aqueous acidic treatment, while when the reaction is performed in aqueous medium catalyzed by a Brønsted acid, the intermediate **3** is not detected since it is rapidly hydrolyzed into heterocyclic α,β-unsaturated carbonyl compounds **4**.

In this paper we investigate the catalytic effectiveness of porous α-zirconium hydrogen phosphate (p-αZrP) as recyclable

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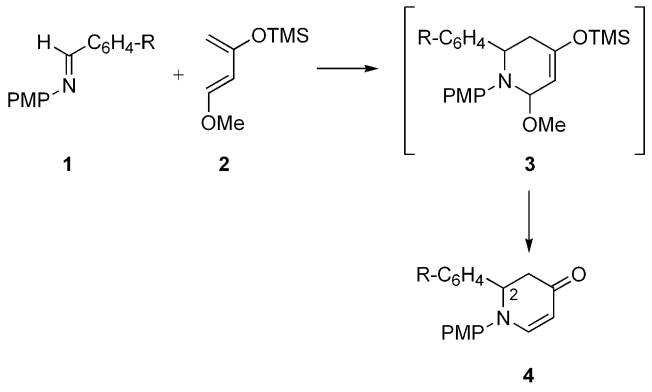


1 2 3 4

PMP = *p*OMe-C_6H_4
R = H, *p*Cl, *m*Cl, *o*Cl, *p*Br, *p*F, *p*NO_2, *p*SMe, *p*OMe, *p*Me, *p*CN

Scheme 1. Aza-Diels–Alder reaction of benzaldimines **1** with Danishefsky's diene **2**.

Brønsted-acid catalyst in the aza-Diels–Alder reaction of *N*-PMP-benzaldimines **1** with Danishefsky's diene **2** in water and under solvent-free conditions.

2. Experimental

2.1. General remarks

All chemicals were purchased and used without any further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100.6 MHz, respectively in $CDCl_3$ solution. IR spectra were recorded with a FT-IR instrument, using $CHCl_3$ as solvent. GC analyses were performed with a DB35H fused silica capillary column (30 m, 0.53 mm diameter) on an split/split-less injector and FID detector with hydrogen as the gas carrier. Centrifugation was performed at 12,000 rpm for 10 min. Thin Layered Chromatography analyses were performed on silica gel on aluminium plates. Column chromatography were performed by using silica gel 230–400 mesh eluting with petroleum ether/ethyl acetate 30:70. Recrystallization of adducts **4** was performed in *n*-hexane/ethyl acetate mixture. Melting point is uncorrected. Layered α-zirconium hydrogen phosphate (αZrP) was prepared as reported in the literature [19]. The benzaldimines **1** are known compounds and were prepared as reported in the literature [20]. The adducts **4** (R=H, *p*Cl, *o*Cl, *p*OMe, *p*Me) are known compounds [12,13,16,21]. For all adducts, complete characterization has been reported below.

2.2. Preparation of porous zirconium hydrogen phosphate (p-αZrP)

p-ZrP was prepared by the template method as described in Ref. [5]. Briefly, sodium bis(2-ethylhexyl)sulfosuccinate (AOT) (0.2 g, 0.45 mmol) was mixed with 100 mL of deionized water and stirred until all of the surfactant was dissolved. Zirconyl chloride octahydrate (1.28 mmol) and phosphoric acid (5.12 mmol) were added to the solution and stirred for 16 h ([P] = 0.05 M, [Zr] = 0.0125 M, P/Zr = 4).

The white gel product was centrifuged (8000 rpm, 15 min), and the solid obtained was washed with water (3× 100 mL) and ethanol (3× 100 mL) to remove the surfactant. The solid was dried under vacuum at 60 °C.

N_2-adsorption/desorption isotherms were measured at 77 K using a computer controlled Micromeritics ASAP2010 volumetric adsorption analyzer. For the surface area measurement, based on the B.E.T. method, a value of 83 m^2/g was found. The pore-size distribution is based on the B.J.H. method and the mesopore volume was 0.17 cm^3/g.

2.3. General procedure for aza-Diels–Alder reaction

Imine **1** (0.2 mmol), Danishefsky's diene **2** (0.4 mmol, 2 equiv.) and SDS (0.04 mmol, 0.2 equiv.) were added, in a 2 mL vial, to the dried p-ZrP (0.04 mmol, 20 mol%). The mixture was stirred at 30 °C for 1 h and then it was diluted with ethyl acetate (1 mL). The organic phase was separated from heterogeneous catalyst by centrifugation. The catalyst was washed with ethyl acetate (2× 1 mL) and the combined organic layers were concentrated under reduced pressure. The product was purified by column chromatography and recrystallized.

2.3.1. 1-(4′-Methoxyphenyl)-2-phenyl-2,3-dihydropyridin-4(1H)-one (4 R=H)[12]

Yellow crystals; m.p. 116–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.75 (dd, *J* = 16.4, 3.9 Hz, 1H, H-3), 3.25 (dd, *J* = 16.4, 7.1 Hz, 1H, H-3), 3.73 (s, 3H, OMe), 5.18 (dd, *J* = 7.1, 3.9 Hz, 1H, H-2), 5.22 (d, *J* = 7.7 Hz, 1H, H-5), 6.79 (m, 2H, H-2′ and H-6′), 6.94 (m, 2H, H-3′ and H-5′), 7.21–7.33 (m, 5H, Ph), 7.54 (d, *J* = 7.7 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.3, 55.4, 62.3, 101.5, 114.5 (2 C), 121.0 (2 C), 126.2 (2 C), 127.8, 128.8 (2 C), 138.17, 138.20, 149.6, 156.8, 189.9. IR ($CHCl_3$): ν = 1640.0, 1592.5, 1513.4, 1282.6, 1249.3, 1098.9, 1040.4, 830.4, 698.5, 653.9 cm^{-1}.

2.3.2. 2-(4″-Chlorophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pCl) [21]

Yellow crystals; m.p. 143–144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74 (dd, *J* = 16.4, 4.0 Hz, 1 H, H-3), 3.26 (dd, *J* = 16.4, 7.1 Hz, 1H, H-3), 3.77 (s, 3H, OMe), 5.17 (dd, *J* = 7.1, 4.0 Hz, 1H, H-2), 5.26 (d, *J* = 7.7 Hz, 1H, H-5), 6.82 (m, 2H, H-2′ and H-6′), 6.95 (m, 2H, H-3′ and H-5′), 7.21 (m, 2H, H-3″ and H-5″), 7.29 (m, 2H, H-2″ and H-6″), 7.53 (d, *J* = 7.7 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.5, 55.5, 61.9, 101.6, 114.7 (2 C), 121.3 (2 C), 127.8 (2 C), 129.1 (2 C), 133.8, 136.8, 138.0, 149.7, 157.1, 189.6. IR($CHCl_3$): ν = 1643.5, 1584.1, 1511.6, 1283.2, 1251.4, 1095.9, 831.4, 710.1, 651.2 cm^{-1}.

2.3.3. 2-(3″-Chlorophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=mCl)

Yellow-orange crystals; m.p. 90–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71 (dd, *J* = 16.4, 3.6 Hz, 1H, H-3), 3.25 (dd, *J* = 16.4, 7.2 Hz, 1H, H-3), 3.74 (s, 3H, OMe), 5.14 (dd, *J* = 7.2, 3.6 Hz, 1H, H-2), 5.23 (d, *J* = 7.7 Hz, 1H, H-5), 6.81 (m, 2H, H-2′ and H-6′), 6.93 (m, 2H, H-3′ and H-5′), 7.12–7.18 (m, 1H, H-5″), 7.20–7.26 (m, 3H, H-2″, H-4″, H-6″), 7.53 (d, *J* = 7.8 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 40.8, 55.5, 61.8, 101.8, 114.7 (2 C), 120.9 (2 C), 124.5, 126.4, 128.1, 130.2, 134.7, 138.0, 140.4, 149.4, 157.0, 189.5. IR ($CHCl_3$): ν = 1642.6, 1584.0, 1511.4, 1282.5, 1250.4, 1097.6, 1040.4, 828.7, 710.2, 651.1 cm^{-1}. Anal. Calcd for $C_{18}H_{16}ClNO_2$ (313.78): C, 68.90; H, 5.14; N, 4.46. Found: C, 68.85; H, 5.23; N, 4.39.

2.3.4. 2-(2″-Chlorophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=oCl) [13]

Yellow crystals; m.p. 115–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.80 (dd, *J* = 16.7, 3.6 Hz, 1H, H-3), 3.24 (dd, *J* = 16.7, 7.8 Hz, 1H, H-3), 3.74 (s, 3H, OMe), 5.27 (d, *J* = 7.8 Hz., 1 H, H-5), 5.60 (dd, *J* = 7.8, 3.6 Hz, 1H, H-2), 6.79 (m, 2H, H-2′ and H-6′), 6.90 (m, 2H, H-3′ and H-5′), 7.19 (m, 2H, H-3″ and H-5″), 7.40 (m, 2H, H-4″ and H-6″), 7.63 (d, *J* = 7.8, Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 41.0, 55.5, 59.2, 101.2, 114.7 (2 C), 120.6 (2 C), 127.2, 127.6, 129.3, 130.5, 131.8, 135.3, 137.9, 150.2, 156.9, 189.7. IR ($CHCl_3$): ν = 1640.7, 1590.7, 1511.4, 1284.2, 1250.5, 1098.4, 1040.8, 830.7, 714.1, 651.0 cm^{-1}.

2.3.5. 2-(4″-Bromophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pBr)

Orange crystals; m.p. 154–156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71 (dd, *J* = 16.4, 4.0 Hz, 1H, H-3), 3.24 (dd, *J* = 16.4, 7.1 Hz, 1H,

H-3), 3.76 (s, 3H, OMe), 5.14 (dd, J = 7.1, 4.0 Hz, 1H, H-2), 5.23 (d, J = 7.7 Hz, 1H, H-5), 6.81 (m, 2H, H-2′ and H-6′), 6.93 (m, 2H, H-3′ and H-5′), 7.13 (m, 2H, H-2″ and H-6″), 7.42 (m, 2H, H-3″ and H-5″), 7.51 (d, J = 7.7 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.1, 55.5, 61.9, 101.7, 114.7 (2 C), 121.2 (2 C), 121.8, 128.1 (2 C), 132.1 (2 C), 137.3, 138.0, 149.7, 157.1, 189.6. IR ($CHCl_3$): ν = 1642.9, 1582.4, 1511.5, 1283.1, 1250.6, 1097.7, 831.5, 710.3, 651.3 cm^{-1}. Anal. Calcd for $C_{18}H_{16}BrNO_2$ (358.23): C, 60.35; H, 4.50; N, 3.91. Found: C, 60.42; H, 4.57; N, 3.94.

2.3.6. 2-(4″-Fluorophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pF)

Yellow crystals; m.p. 111–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.72 (dd, J = 16.4, 4.0 Hz, 1H, H-3), 3.23 (dd, J = 16.4, 7.1 Hz, 1H, H-3), 3.75 (s, 3H, OMe), 5.16 (dd, J = 7.1, 4.0 Hz, 1H, H-2), 5.23 (d, J = 7.7 Hz, 1H, H-5), 6.80 (m, 2H, H-2′ and H-6′), 6.93 (m, 2H, H-3′ and H-5′), 6.97 (m, 2H, H-3″ and H-5″), 7.22 (m, 2H, H-2″ and H-6″), 7.51 (d, J = 7.7 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.3, 55.4, 61.8, 101.4, 114.6 (2 C), 115.8 (d, J = 21.6 Hz, 2 C), 121.3 (2 C), 128.1 (d, J = 8.1 Hz, 2 C), 134.0 (d, J = 3.0 Hz), 138.0, 149.8, 157.0, 162.2 (d, J = 246.8 Hz), 189.8. IR ($CHCl_3$): ν = 1641.3, 1581.6, 1510.7, 1284.4, 1249.7, 1099.0, 1040.0, 832.3, 713.8, 651.3 cm^{-1}. Anal. Calcd for $C_{18}H_{16}FNO_2$ (2.97.32): C, 72.71; H, 5.42; N, 4.71. Found: C, 72.83; H, 5.33; N, 4.59.

2.3.7. 1-(4′-Methoxyphenyl)-2-(4″-nitrophenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pNO$_2$)

Orange crystals; m.p. 121–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74 (dd, J = 16.4, 3.9 Hz, 1H, H-3), 3.30 (dd, J = 16.5, 7.2 Hz, 1H, H-3), 3.75 (m, 3H, OMe), 5.26 (d, J = 7.8 Hz, 1H, H-5), 5.29 (dd, J = 7.2, 3.9 Hz, 1H, H-2), 6.81 (m, 2H, H-2′ and H-6′), 6.92 (m, 2H, H-3′ and H-5′), 7.45 (m, 2H, H-2″ and H-6″), 7.57 (d, J = 7.8 Hz, 1H, H-6), 8.16 (m, 2H, H-3″ and H-5″). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 42.9, 55.5, 61.9, 102.1, 114.8 (2 C), 121.0 (2 C), 124.2 (2 C), 127.4 (2 C), 137.6, 145.7, 147.5, 149.4, 157.2, 189.0. IR ($CHCl_3$): ν = 1641.5, 1580.2, 1509.4, 1349.1, 1283.0, 1250.5, 1049.3, 830.2, 709.9, 650.9 cm^{-1}. Anal. Calcd for $C_{18}H_{16}N_2O_4$ (324.33): C, 66.66; H, 4.97; N, 8.64. Found: C, 66.78; H, 5.13; N, 8.49.

2.3.8. 1-(4′-Methoxyphenyl)-2-[4″-(methylthio)phenyl]-2,3-dihydropyridin-4(1H)-one (4 R=pSMe)

Orange crystals; m.p. 79–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3H, SMe), 2.70 (dd, J = 16.4, 3.9 Hz, 1H, H-3), 3.21 (dd, J = 16.4, 7.1 Hz, 1H, H-3), 3.72 (s, 3H, OMe), 5.12 (dd, J = 7.1, 3.9 Hz, 1H, H-2), 5.19 (d, J = 7.7 Hz, 1H, H-5), 6.78 (m, 2H, H-2′ and H-6′), 6.93 (m, 2H, H-3′ and H-5′), 7.15 (m, 4H, H-2″, H-3″, H-5″, H-6″), 7.50 (d, J = 7.7 Hz, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.6, 43.3, 55.4, 62.0, 101.5, 114.6 (2 C), 121.1 (2 C), 126.81 (2 C), 126.83 (2 C), 134.9, 138.15, 138.17, 149.6, 156.9, 189.9. IR ($CHCl_3$): ν = 1640.5, 1581.4, 1510.9, 1283.0, 1250.3, 1094.8, 1040.2, 831.0, 711.9, 650.9 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NO_2S$ (325.43): C, 70.12; H, 5.88; N, 4.30; S, 9.58. Found: C, 70.28; H, 5.93; N, 4.39; S, 9.45.

2.3.9. 1,2-Bis(4-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one(4 R=pOMe) [12]

Pale yellow crystals; m.p. 112–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71 (dd, J = 16.4, 4.0 Hz, 1H, H-3), 3.19 (dd, J = 16.4, 7.0 Hz, 1H, H-3), 3.72 (s, 3H, OMe), 3.73 (s, 3H, OMe) 5.12 (dd, J = 7.0, 4.0 Hz, 1H, H-2), 5.19 (d, J = 7.7 Hz, 1H, H-5), 6.79 (m, 4H, H-2′, H6′, H-3″, H-5″), 6.94 (m, 2H, H-3′ and H-5′), 7.14 (m, 2H, H-2″ and H6″), 7.49 (d, J = 7.7 H, 1H, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 43.4, 55.1, 55.4, 61.8, 101.1, 114.1 (2 C), 114.4 (2 C), 121.2 (2 C), 127.5 (2 C), 130.1, 138.1, 149.7, 156.8, 159.0, 190.1. IR ($CHCl_3$): ν = 1639.8, 1578.4, 1511.2, 1282.5, 1250.5, 1097.6, 1038.5, 830.5, 716.0, 651.1 cm^{-1}.

2.3.10. 1-(4′-Methoxyphenyl)-2-(4″-methylphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pMe) [16]

Yellow crystals; m.p. 108–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3H, Me), 2.75 (dd, J = 16.4, 4.0 Hz, 1H, H-3), 3.23 (dd, J = 16.4, 7.1 Hz, 1H, H-3), 3.75 (s, 3H, OMe), 5.15 (dd, J = 7.1, 4.0 Hz, 1H, H-2) 5.23 (d, J = 7.7 Hz, 1H, H-5), 6.80 (m, 2H, H-2′ and H6′), 6.96 (m, 2H, H-3′ and H-5′), 7.11 (m, 4H, H-2″, H-3″, H-5″, H6″), 7.53 (d, J = 7.7 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.0, 43.4, 55.5, 62.2, 101.4, 114.5 (2 C), 121.1 (2 C), 126.2 (2 C), 129.5 (2 C), 135.1, 137.5, 138.3, 149.7, 156.9, 190.1. IR ($CHCl_3$): ν = 1640.2, 1589.0, 1511.2, 1283.5, 1249.3, 1097.6, 1040.8, 831.4, 711.8, 650.9 cm^{-1}.

2.3.11. 2-(4″-Cyanophenyl)-1-(4′-methoxyphenyl)-2,3-dihydropyridin-4(1H)-one (4 R=pCN)

Orange crystals; m.p. = 84–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.72 (dd, J = 16.5, 3.9 Hz, 1H, H-3), 3.29 (dd, J = 16.5, 7.2 Hz, 1H, H-3), 3.75 (s, 3H, OMe), 5.24 (dd, J = 7.2, 3.9 Hz, 1H, H-2), 5.25 (d, J = 7.8 Hz, 1H, H-5), 6.81 (m, 2H, H-2′ and H6′), 6.91 (m, 2H, H-3′ and H-5′), 7.39 (m, 2H, H-2″ and H6″), 7.55 (d, J = 7.8 Hz, 1H, H-6), 7.61 (m, 2H, H-3″ and H-5″). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 42.7, 55.5, 62.0, 101.9, 111.9, 114.8 (2 C), 118.2, 121.0 (2 C), 127.2 (2 C), 132.7 (2 C), 137.7, 143.7, 149.5, 157.2, 189.0. IR ($CHCl_3$): ν = 2233.5, 1644.9, 1583.8, 1511.4, 1283.7, 1250.8, 1099.1, 1041.0, 832.0, 721.8, 665.7 cm^{-1}. Anal. Calcd for $C_{19}H_{16}N_2O_2$ (304.34): C, 74.98; H, 5.30; N, 9.20. Found: C, 75.10; H, 5.23; N, 9.36.

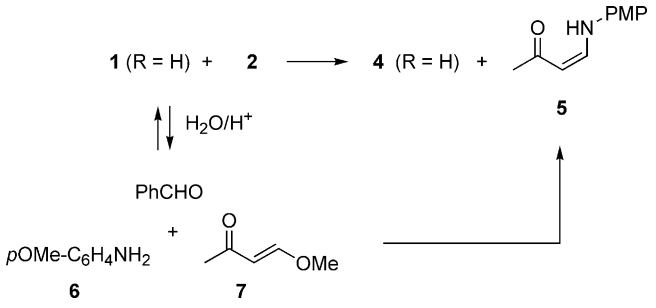
3. Results and discussion

When the cycloaddition of *N*-PMP-benzaldimine **1** (R=H) with Danishefsky's diene **2** (1.5 equiv.) was carried out at 30 °C with 20 mol% of catalyst in CH_2Cl_2, αZrP and p-αZrP did not show catalytic activity after 1 h (Table 1, entries 1 and 2) while in water p-αZrP catalyzed the reaction more efficiently than αZrP (entries 3 and 4) and allowed the reaction to be completed in 3 h (entry 5). Unexpectedly, (3*Z*)-4-[(4-methoxyphenyl)amino]but-3-en-2-one (**5**) [22] was present along with the expected dihydro-4-pyridone **4** (R=H) in ca. 1:1 ratio (Scheme 2). Both the benzaldimine **1** and the diene **2** hydrolyze partially in acidic aqueous medium producing benzaldehyde, p-methoxyaniline (**6**) and (3*E*)-4-methoxybut-3-en-2-one (**7**). The conjugative addition of **6** to the α,β-unsaturated ketone **7** generates the (*Z*)-enaminone **5** (Scheme 2)

Table 1
Aza-Diels–Alder reaction of benzaldimine **1** (R=H) with Danishefsky's diene **2**.

Entry[a]	Cat.	Reaction medium	SDS (equiv.)	Conv. (%)[b]	**4**/**5**
1	αZrP	CH_2Cl_2	–	–	–
2	p-αZrP	CH_2Cl_2	–	–	–
3	αZrP	H_2O	–	2	–
4	p-αZrP	H_2O	–	67	55/45
5	p-αZrP	H_2O	–	99[c]	53/47
6	p-αZrP	H_2O	(0.4)	99	66/34
7	αZrP	SolFC	–	–	–
8	p-αZrP	SolFC	–	21	90/10
9	p-αZrP	SolFC	–	57[d]	86/14
10	p-αZrP	SolFC	(0.4)	97	84/16
11	p-αZrP[e]	SolFC	(0.4)	99	99/1
12	p-αZrP[e]	SolFC	(0.2)	96	94/6
13	p-αZrP[e]	SolFC	(0.1)	95	86/14
14[f]	p-αZrP[e]	SolFC	(0.2)	99[g]	99/1

[a] Reaction conditions: imine **1**, Danishefsky's diene **2** (1.5 equiv.), catalyst 20 mol%, SDS (0.2 equiv.) at 30 °C under solFC for 1 h, unless specified otherwise.
[b] The complement to 100% is unreacted **1**.
[c] Reaction time 3 h.
[d] Reaction time 15 h.
[e] The catalyst was dried at 80 °C for 15 h.
[f] Danishefsky's diene **2** equiv.
[g] Yield of isolated product 89%.



Scheme 2. Formation of (3*Z*)-4-[(4-methoxyphenyl)amino]but-3-en-2-one (**5**).

Table 2
Aza-Diels–Alder reaction of benzaldimines **1** with Danishefsky's diene catalyzed by porous zirconium hydrogen phosphate (p-αZrP) and SDS under solvent-free conditions[a].

Imine **1** (R)	Conv. (%)[b]	**4**/**5**	Yield **4** (%)[c]
H	99	99/1	89
*p*Cl	97	96/4	86
*m*Cl	98	99/1	90
*o*Cl	99	98/2	87
*p*Br	94	100/0	85
*p*F	96	98/2	88
pNO_2	99	98/2	94
*p*SMe	98	100/0	88
*p*OMe	99	100/0	85
*p*Me	96	98/2	92
*p*CN	98	100/0	87

[a] Reaction conditions: imine **1**, Danishefsky's diene **2** (2 equiv.), p-αZrP dried at 80 °C for 15 h (20 mol%), SDS (0.2 equiv.) at 30 °C in SolFC for 1 h.
[b] The complement to 100% is unreacted **2**.
[c] Yield of isolated product **4**.

(footnote[1]). The amount of benzaldehyde in the reaction mixture is in keeping with this type of chemistry. The presence of SDS (0.4 equiv.) in the aqueous medium increased the catalytic activity of p-αZrP and promoted the formation of **4** (R=H) (Table 1, entry 6).

When the cycloaddition was performed under solvent-free conditions, αZrP was ineffective, while p-αZrP showed a modest catalytic activity (entries 7–9) that increased notably by working in the presence of SDS (0.4 equiv.) (entry 10). The reaction was complete in 1 h when carefully dried p-αZrP (20 mol%) was used and only **4** (R=H) was obtained (entry 11). By using a smaller amount of SDS (0.2 or 0.1 equiv.) both the reaction conversion and percentage of **4** (R=H) decreased (entries 12 and 13). In contrast an excellent result was obtained when the amount of SDS was reduced to 0.2 equiv. accompanied by an increase of diene **2** to 0.2 equiv. (entry 14). To our knowledge this is the first example of using a surfactant under solFC. The intriguing role played by SDS under these conditions is under study. One can hypothesize that SDS favours, through Na^+/H^+ surface exchange [23], the proton transfer from the P–OH groups of solid catalyst p-αZrP to the reagents.

Surprisingly, when the reaction was performed under solFC, the Diels–Alder adduct **3** (R=H) was never observed. This could have been due to the water present in the layers of catalyst [5] and to traces of water in the reactants.

To confirm the efficiency of p-αZrP/SDS system under solFC, we considered the cycloaddition of typical *N*-PMP-benzaldimines **1**, bearing electron-withdrawing and donating substituents, with diene **2** under the best reaction conditions: dried p-αZrP (20 mol%), SDS (0.2 equiv.) at 30 °C for 1 h. The reactions were always highly chemoselective and the dihydropyrones **4** was isolated in high yields (85–94%) (Table 2).

[1] In the same reaction conditions, pure samples of *p*-methoxyaniline (**6**) and (3*E*)-4-methoxybut-3-en-2-one (**7**) produce (3*Z*)-4-[(4-methoxyphenyl)amino]but-3-en-2-one (**5**).

Table 3
Recycling of heterogeneous Brønsted acids p-αZrP in the aza-Diels–Alder reaction of *N*-PMP-benzaldimine **1** (R=H) with Danishefsky's diene (**2**).

Entry	Run[a]	Conv. (%)[b]	**4**/**5**
1	Cycle 1	99	99/1
2	Cycle 2[c]	98	97/3
3	Cycle 3[c]	95	97/3
4	Cycle 1	99	99/1
5	Cycle 2[d]	99	100/0
6	Cycle 3[d]	99	99/1
7	Cycle 4[d]	99	100/0
8	Cycle 5[d]	99	100/0

[a] Reaction conditions: imine **1**, Danishefsky's diene **2** (2 equiv.), p-αZrP (20 mol%), SDS (0.2 equiv.) at 30 °C in SolFC for 1 h.
[b] The complement to 100% is unreacted **1**.
[c] After ethyl acetate extraction, the recovered solid p-αZrP was washed with water, dried at 80 °C for 15 h and reused.
[d] The solid was washed only with acetate to recover the entire p-αZrP/SDS catalytic system that was reused without adding SDS.

Finally the recycling of the catalyst used in the reaction of **1** (R=H) with **2** was investigated by using two procedures (Table 3). (i) At the end of the reaction, the solid catalyst p-αZrP was recovered by removing the reaction product by extraction with ethyl acetate followed by centrifugation. It was washed with water to eliminate SDS, dried at 80 °C for 15 h and reused twice (Table 3, entries 1–3). (ii) The catalytic system p-αZrP/SDS was recovered totally, simply by extraction with ethyl acetate, centrifugation and drying at 80 °C for 1 h and reused, without adding SDS, four times (Table 3, entries 4–8). Both procedures gave excellent results but the second is preferred because the entire p-αZrP/SDS catalytic system was recovered and since less catalyst was lost during each cycle, it was possible to reuse the catalyst for more cycles.

4. Conclusion

In conclusion we report for the first time the aza-Diels–Alder reaction of benzaldimines **1** with Danishefsky's diene **2** in solvent-free conditions catalyzed by porous zirconium hydrogen phosphate (p-αZrP) in the presence of a catalytic amount of SDS. The reaction was fast, highly chemoselective and 2,3-dihydro-4-pyridones **4** were isolated in high yields. The recycling of p-αZrP and of the entire p-αZrP/SDS catalytic system gave very satisfactory results.

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