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Solvent-free heterogeneous organocatalysis: stereoselective isomerization of α,β-ynones to (*E*,*E*)-α,β-γ,δ-dienones catalyzed by polymer-supported tertiaryphosphines

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Abstract—Stereoselective isomerization of α,β-ynones was catalyzed by polymer-supported tertiaryphosphines under solvent-free conditions. (*E*,*E*)-α,β-γ,δ-Dienones were obtained with up to 93% isolated yields when ***JJ*-TPP** was employed.

In order to protect human health and the environment, the emerging area of green chemistry envisages minimum hazard as a performance criterion for the design of new chemical processes.[1] One of the approaches for achieving this target is to explore alternative reaction conditions, catalyst and media to accomplish the desired reactions.[2] Thus, the use of catalytic processes with high atom efficiency, simple work-up procedures, immobilized catalysts, as well as organic solvent-free conditions, is highly desirable to minimize hazard.

Conjugated dienes are important intermediates in organic synthesis[3] and biologically active natural compounds.[4] Among a variety of approaches for their preparation, the triphenylphosphine-catalyzed isomerization of electron-deficient alkynes to conjugated dienes, one of the useful methods with atom economy, has been studied in detail by many famous groups such as Trost's group,[5] Lu's group,[6] Rychnovsky's group[7] and Kazmaier's group.[8] Furthermore, the immobilized triphenylphosphine such as polystyrene-supported triphenylphosphine (**PS–TPP**) could make the isomerization undergo with simple work-up procedures.[9] The separation of products and the recovery of catalysts become easier than before. However, the utilization of toxic and volatile toluene or benzene as solvent is still a serious challenge to the protection of human health and the environment. Toward the target of green chemical processes, herein we continue our ongoing research and report a solvent-free heterogeneous organocatalysis for the stereoselective isomerization of α,β-ynones to (*E*,*E*)-α,β-γ,δ-dienones.

The immobilized catalyst screening protocol employed the isomerization reaction of 1-phenyl-non-2-yn-1-one (**1a**) to 1-phenyl-nona-2,4-dien-1-one (**2a**). At first, we examined the relationship between catalyst efficiency and polymer backbone. As depicted in Table 1, the polarity of resin backbone affected the isomerization of **1a** (Table 1, entries 1–6). Using poly(ethylene glycol)-supported phosphine **3a** (**PEG–TPP**) and polymer-supported diphosphinoamine **3c** (**PS–PNP**),[10] no isomerization product was detected (Table 1, entries 1 and 3). Amphilic resins **3b** (**PS–PEG–DPP**)[11] afforded the corresponding product in only 17% yield (Table 1, entry 2). These facts promoted us to test weak polar immobilized phosphines. Just as expected, catalyst **3d** (**PS–DPP**), **3e** (**PS–TPP**) and **3f** (***JJ*-TPP**) could give the desired product **2a** in 38–95% GC yields (Table 1, entries 4–6). Excitingly, triphenylphosphine supported on *JandaJel* resin (***JJ*-TPP**), previously used as the catalyst for the Aza-Baylis–Hillman reaction,[12] was found for the first time to efficiently catalyze the isomerization of **1a** under solvent-free conditions (Table 1, entry 6). Even if reaction scale was increased to 5 mmol (1.07 g), the reaction could proceed smoothly with 96% GC yield and 93% GC purity.

Keywords: Heterogeneous catalysis; Isomerization; Stereoselective; Polymer-supported terephosphines; α,β-Ynones; (*E*,*E*)-α,β-γ,δ-Dienones.
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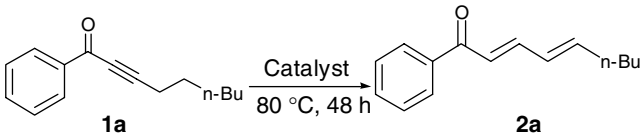
Table 1. Isomerization reaction of **1a** under different immobilized catalysts[a]

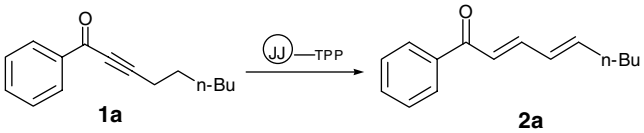


1a **2a**

Entry	Catalyst[d]	Cat. (mol %)	Yield[b] (%)
1	**PEG–TPP 3a**[c]	0.02 g	0
2	**PS–PEG–DPP 3b**	20	17
3	**PS–PNP 3c**	20	0
4	**PS–DPP 3d**	20	38
5	**PS–TPP 3e**	20	76
6	***JJ*-TPP 3f**	20	95

[a] Reaction conditions: 1-Phenyl-non-2-yn-1-one (0.25 mmol) and catalyst (20 mol %) at 80 °C for 48 h under solvent free conditions.
[b] Determined by GC.
[c] Loading amount of phosphorous is unknown.
[d] **PEG–TPP**, **PS–DPP** and ***JJ*-TPP** were purchased from Fluka or Aldrich.

Table 2. ***JJ*-TPP**-catalyzed isomerization reaction of ynone **1a** under different reaction time and temperature[a]



1a **2a**

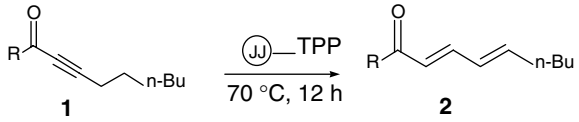
Entry	Cat. (mol %)	Time (h)	Temperature (°C)	Conv.[b] (%)	Yield[b] (%)
1	20	48	80	100	95
2	10	24	80	100	92
3	5	24	80	31	25
4	10	12	80	100	94
5	10	6	80	86	82
6	10	12	70	100	99
7	10	12	60	100	95
8	10	18	50	97	86
9	10	24	40	92	84
10	10	24	30	0	0

[a] Reaction conditions: 1-Phenyl-non-2-yn-1-one (0.25 mmol) and ***JJ*-TPP** (10 mol %) under solvent free conditions.
[b] Determined by GC.

We next optimized reaction conditions including a comparative study of the amount of catalyst ***JJ*-TPP**, reaction time and temperature (Table 2). When the amount of the catalyst was reduced from 20 mol % to 5 mol %, the yields of **2a** were sharply dropped from 95% to 25% (Table 2, entries 1–3). The reaction time and temperature could affect the isomerization to some extent. The proper time is beyond 12 h. Decreasing the temperature to 30 °C resulted in no reaction. Thus, the optimized reaction conditions are 10 mol % of ***JJ*-TPP** at 70 °C for 12 h, which yield (*E*,*E*)-α,β-γ,δ-dienone **2a** in 100% conversion and 99% GC yield under solvent-free conditions (Table 2, entry 6).

Under these optimized reaction conditions, a variety of ynones were applied for the isomerization reaction by using ***JJ*-TPP** as a catalyst to the desired products with isolated yields of 31–93% (Table 3).[13,14] Investigation of representative ynones demonstrates that the transformation is feasible for aromatic and aliphatic ynones. The aromatic ynones with different substituents on the aryl

Table 3. Scope of the ***JJ*-TPP**- catalyzed isomerization synthesis of (*E*,*E*)-α,β-γ,δ-dienones[a]



1 **2**

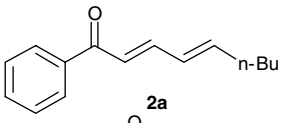
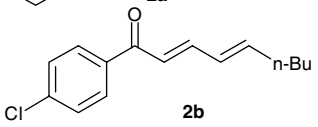
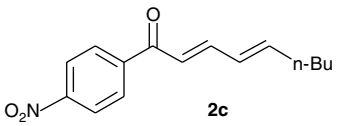
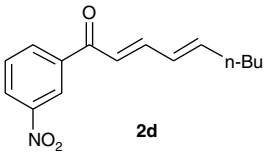
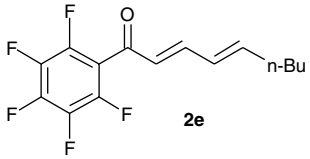
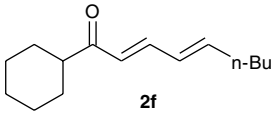
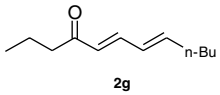
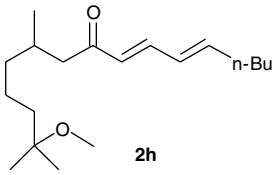
Entry	Products	Conv.[b] (%)	Yield[c] (%)	Selectivity for **2**[b]
1	 **2a**	100	93[d]	100
2	 **2b**	98	72	94
3	 **2c**	97	68	90
4	 **2d**	95	65	95

Table 3 (*continued*)

Entry	Products	Conv.[b] (%)	Yield[c] (%)	Selectivity for **2**[b]
5	 **2e**	93	75	100
6	 **2f**	51	40	100
7	 **2g**	78	42	94
8	 **2h**	49	31	100

[a] Reaction conditions: Ynone (0.25 mmol) and ***JJ*-TPP** (10 mol %) at 70 °C for 12 h under solvent free conditions.
[b] Determined by GC.
[c] Isolated yields.
[d] Without further purification.

ring could be isomerized to the corresponding products with high conversions and selectivities (Table 3, entries 1–5), but the aliphatic substitutional ynones showed relatively lower conversions and yields (Table 3, entries 6–8). The increased steric hindrance of the substrates may be responsible for the decreased yields especially for sterically encumbered 2-methoxy-2,6-dimethyl-hexadec-9-yn-8-one (**1h**). These experimental results showed that ***JJ*-TPP** could be employed as an efficient organocatalyst under solvent-free conditions.

To verify that the optimized conditions can be applied to other types of ynone, the symmetrical bis-ynone **1i** was treated with 10 mol % of ***JJ*-TPP** to generate **2i** in 55% isolated yield (Scheme 1).

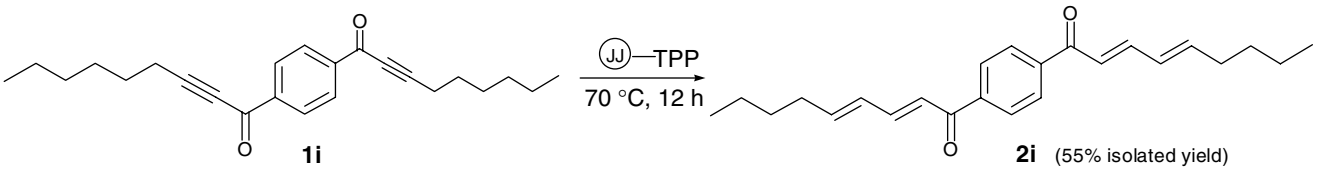
We finally investigated the reusability of ***JJ*-TPP** under solvent-free conditions. Catalyst **3f** could be recovered easily by simple filtration and reused in the isomerization of **1a**. It was found that the ***JJ*-TPP**, reused twice, gave **2a** in 67% and 35% GC yields, respectively.

To examine whether some leaching of the active species of catalyst occurred during the reaction, the phosphine content of crude product was analyzed using elemental analysis, which showed $P<0.5\%$. Compared to heterogeneous catalyst, the isomerization of **1a** was performed with 3 mol % of homogeneous catalyst PPh_3 in toluene at 70 °C for 12 h and the product was obtained in only 20% GC yield.

The solid state ^{31}P NMR spectrum of the *JandaJel* resin-supported triphenylphosphine (CPMAS spectrum) after the first recycling was also examined, which showed a 26.4 ppm signal corresponding to *JandaJel* resin-supported triphenylphosphine oxide.

Therefore, the oxidation of tertiaryphosphine[15] and the leaching of catalyst amount might be responsible for the sharp decrease in yield. It remains a problem as to how to keep the catalytic activity of ***JJ*-TPP** in its recycles.

In summary, we have developed a simple and effective solvent-free heterogeneous organocatalytic process. In this process, polymer-supported triphenylphosphine (***JJ*-TPP**) is the best catalyst for the stereoselective isomerization of α,β-ynones to (*E*,*E*)-α,β-γ,δ-dienones. The protocol offers several advantages such as solvent-free



1i **2i** (55% isolated yield)

Scheme 1.

conditions, easy isolation, the high stereoselectivity, compatibility to various substrates and simple work-up procedures making it an appealing alternative to currently available methods.

Acknowledgements

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13. Ynones **1a**–**i** were prepared according to the reported methods. (a) Browden, K.; Hellbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39–45; (b) Wang, Y.-G.; M.S. Thesis, Guangzhou Institute of Chemistry, Chinese Academy of Sciences at Guangzhou, **2005**.
14. A typical procedure for the isomerization. To a pear-shaped flask ***JJ*-TPP** (10 mol %, 10 mg) and ynones (0.25 mmol) were added and reacted at 70 °C for 12 h. After the catalyst was separated by filtration, the residue was isolated by preparative TLC to obtain pure product **2**. (*E,E*)-*1-Phenyl-nona-2,4-dien-1-one* (**2a**). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91–7.94 (m, 2H), 7.53 (dd, $J_1 = 14.8$ Hz, $J_2 = 11.2$ Hz, 1H), 7.36–7.45 (m, 3H), 6.85 (d, $J = 15.2$ Hz, 1H), 6.22–6.30 (m, 2H), 2.17–2.23 (m, 2H), 1.26–1.46 (m, 4H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 190.9, 146.6, 145.5, 138.2, 132.4, 129.1, 128.4, 128.3, 123.5, 32.8, 30.7, 22.2, 13.8; IR (film) v: 1666, 1589, 1008 cm^{-1}; MS (70 eV) m/z (%): 214 (M^+), 199, 185, 171, 157, 144, 128, 115, 105, 77, 51, 27. (*E,E*)-*1-(4-Chlorophenyl)-nona-2,4-dien-1-one* (**2b**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.85–7.87 (m, 2H), 7.36–7.43 (m, 3H), 6.80 (d, $J = 14.8$ Hz, 1H), 6.22–6.29 (m, 2H), 2.18–2.23 (m, 2H), 1.25–1.44 (m, 4H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 189.6, 138.9, 136.6, 130.2, 130.1, 129.7, 129.4, 129.0, 129.2, 128.8, 122.9, 32.9, 29.7, 22.2, 13.8; IR (film) v: 1661, 1592, 1008 cm^{-1}; MS (70 eV) m/z (%): 248 (M^+), 205, 191, 157, 139, 128, 111, 94, 41. (*E,E*)-*1-(4-Nitro-phenyl)-nona-2,4-dien-1-one* (**2c**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.28–8.31 (m, 2H), 8.02–8.05 (m, 2H), 7.38–7.45 (m, 1H), 6.80 (d, $J = 14.8$ Hz, 1H), 6.31–6.33 (m, 2H), 2.20–2.23 (m, 2H), 1.31–1.43 (m, 4H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 189.3, 149.8, 148.7, 147.3, 143.1, 129.2, 128.8, 123.7, 122.7, 33.0, 30.6, 22.2, 13.8; IR (film) v: 1665, 1626, 1584, 1525, 1006 cm^{-1}; MS (70 eV) m/z (%): 259 (M^+), 242, 216, 202, 186, 156, 128, 104, 78, 41. (*E,E*)-*1-(3-Nitro-phenyl)-nona-2,4-dien-1-one* (**2d**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.73 (t, $J = 2.0$ Hz, 1H), 8.37–8.40 (m, 1H), 8.23–8.26 (m, 1H), 7.66 (t, $J = 8.0$ Hz, 1H), 7.45 (dd, $J_1 = 14.8$ Hz, $J_2 = 10.0$ Hz, 1H), 6.86 (d, $J = 14.8$ Hz, 1H), 6.32–6.35 (m, 2H), 2.20–2.25 (m, 2H), 1.31–1.43 (m, 4H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 188.3, 148.6, 148.4, 147.4, 139.6, 133.9, 129.8, 128.9, 126.8, 123.1, 122.1, 33.0, 30.7, 22.3, 13.9; IR (film) v: 1666, 1620, 1590, 1532, 1348, 1254,1001 cm^{-1}; MS (70 eV) m/z (%): 259 (M^+), 230, 203, 202, 186, 156, 150, 115, 104, 81, 67, 41, 32. (*E,E*)-*1-Phentafluorophenyl-nona-2,4-dien-1-one* (**2e**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.03–7.09 (m, 1H), 6.35 (d, $J = 15.2$ Hz, 1H), 6.27–6.29 (m, 2H), 2.18–2.21 (m, 2H), 1.31–1.43 (m, 4H), 0.89 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ: 149.8, 149.0, 128.5, 127.7, 33.1, 30.6, 22.2, 13.8; IR (film) v: 1663, 1634, 1588, 1495, 1323, 1224, 996 cm^{-1}; MS (70 eV) m/z (%): 304 (M^+), 261, 247, 219, 195, 181, 167, 151, 117, 81, 67, 41. (*E,E*)-*1-Cyclohexyl-nona-2,4-dien-1-one* (**2f**). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.17 (dd, $J_1 = 15.6$ Hz, $J_2 = 10.0$ Hz, 1H), 6.13–6.16 (m, 2H), 6.10 (d, $J = 15.2$ Hz, 1H), 2.48–2.57 (m, 1H), 2.35 (t, $J = 7.2$ Hz, 2H), 1.52–1.68 (m, 4H), 1.20–1.45 (m, 10H), 0.89 (t, 3H); ^{13}C NMR ($CDCl_3$) δ: 203.7,145.7,142.9, 129.1, 126.5, 52.6, 31.5, 31.2, 29.1, 26.2, 22.8, 19.3, 14.3; IR (film) v: 1635, 1595, 1002 cm^{-1}; MS (70 eV) m/z (%): 220 (M^+), 163, 137, 109, 95, 81, 67, 55, 41. (*E,E*)-*Dodeca-5,7-dien-4-one* (**2g**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.12 (dd, $J_1 = 15.6$ Hz, $J_2 = 10.0$ Hz, 1H), 6.14–6.16 (m, 2H), 6.05 (d, $J = 15.2$ Hz, 1H), 2.50 (t, $J = 7.2$ Hz, 2H), 2.17–

2.23 (m, 2H), 1.26–1.46 (m, 6H), 0.90 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$) δ: 201.0, 145.6, 142.9, 128.8, 127.8, 42.3, 32.7, 30.8, 28.2, 17.6, 13.8, 13.4; IR (film) v: 1637, 1597, 999 cm^{-1}; MS (70 eV) m/z (%): 180 (M^+), 162, 152, 134, 123, 108, 95, 81, 55, 43. (*E*,*E*)-*2-Methoxy-2,6-dimethyl-hexadeca-9,11-dien-8-one* (**2h**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.10 (dd, $J_1 = 15.6$ Hz, $J_2 = 10.0$ Hz, 1H), 6.14–6.16 (m, 2H), 6.05 (d, $J = 15.2$ Hz, 1H), 3.14 (s, 3H), 2.47–2.52 (m, 1H), 2.32–2.34 (m, 3H), 2.14–2.15 (m, 1H), 1.35–1.43 (m, 10H), 1.10 (s, 6H), 0.86–0.90 (m, 6H); ^{13}C NMR ($CDCl_3$) δ: 201.0, 145.8, 143.0, 128.9, 128.3, 74.6, 49.1, 48.0, 39.9, 37.5, 32.8, 30.8, 29.9, 29.7, 24.9, 22.4, 19.9, 17.9, 13.8; IR (film) v: 1660, 1608, 1588, 1262, 1002, 961 cm^{-1}; MS (70 eV) m/z (%): 137, 109, 95, 73, 67, 55, 41, 28. (*E*,*E*)-*1,4-Bis(nona-2,4-dien-1-one)benzene* (**2i**). ^{1}H NMR ($CDCl_3$,400 MHz) δ: 7.98 (s, 4H), 7.39 (dd, $J_1 = 15.2$ Hz, $J_2 = 10.0$ Hz, 2H), 6.83 (d $J = 15.2$ Hz, 2H), 6.27–6.31 (m, 4H), 2.20 (dt, $J_1 = 6.4$ Hz, $J_2 = 13.6$ Hz, 4H), 1.30–1.47 (m, 8H), 0.90 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$) δ: 190.5, 147.6, 146.4, 141.2, 129.0, 128.4, 123.4, 33.0, 30.8, 29.7, 22.3, 13.9; IR (film) v: 1657, 1625, 1583, 1005 cm^{-1}; MS (ESI) m/z (%): 351 (M+1), 350 (M^+), 327, 309, 293, 280, 257, 241, 223, 201, 185, 170, 156, 141, 128, 115, 104, 81, 57, 41.

15. Skouta, R.; Varma, R. S.; Li, C.-J. *Chem. Commun.* **2005**, 571–575.