

Synthesis of spirobiindanes via bis-cyclization reaction of the 1,5-diaryl-3-pentanones catalyzed by heteropoly acids

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Abstract—Bis-cyclization reaction of the 1,5-diaryl-3-pentanones catalyzed by heteropoly acids (HPAs) was examined for the first time, and a series of spirobiindanes were synthesized. 1,5-Diaryl-3-pentanones were refluxed and dehydrated in toluene in the presence of 0.15 equiv of a heteropoly acid to furnish spirobiindanes in moderate to high yield. For the known 4,4'-dibromo-7,7'-dimethoxy-1,1'-spirobiindane, the yield was upgraded from 66% to 80%.
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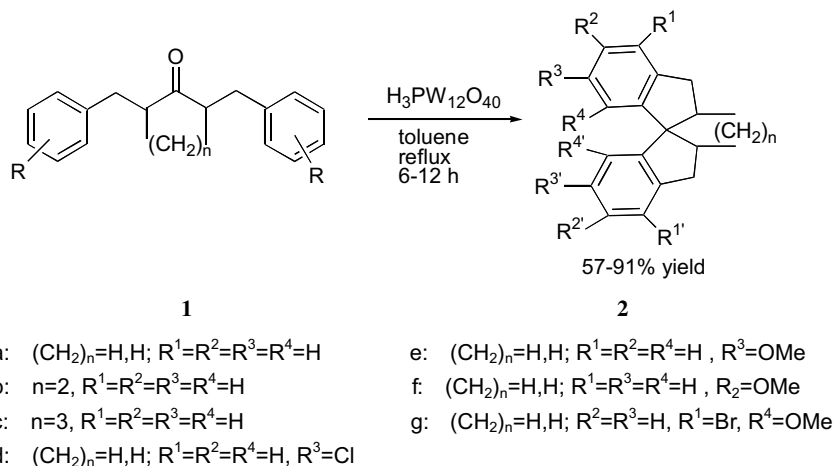
C₂ symmetric chiral compounds, such as BINOL (1, 1'-binaphthalene-2,2'-diol),^{1a,b} BINAP [2,2'-bis(diphenylphosphino)-1,1'-binaphthyl],² TADDOL ($\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanols)³, etc., have been widely used in catalytic and stoichiometric asymmetric synthesis. Recent reports demonstrated that spirobiindanes, another class of molecules with axial symmetry, could also be used in the field of catalytic chemistry with interesting results^{4a} due to their better rigidity and stability than those of BINOL. For example, a new spirobiindane derivative, 1,1'-spirobiindane-7,7'-diol (SPINOL) has showed good chiral induction when applied to asymmetry catalytic reactions.^{4b-f} However, the synthesis of SPINOL is not very easy and convenient in the literature.⁵ And the key step for their preparation is cyclization via intramolecular dehydration of 1,5-bis-(2-bromo-5-methoxyphenyl)-3-pentanone using POCl₃ or poly-phosphoric acid (PPA) as catalyst. It is well known that the reaction mediated by POCl₃ should be performed under anhydrous conditions, and a great amount of hydrochloric acid (HCl) would be generated. Thus, it is inevitable to produce a mass of acidic wasted water. Alternatively, using PPA as catalyst in the reaction, large volume of solvent is needed for extraction of the product.

In recent years, using solid acid as heterogeneous catalysts has received much attention in organic synthesis.⁶

In comparison with the liquid mineral acids, solid acids could be easily separated from the reaction mixture by simple filtration with high recovery. This advantage directly leads to a decrease in of equipment cauterization and environment pollution. Among various solid acids, heteropoly acids (HPAs) are with unique physical-chemical properties. Their acidity is significantly higher than that of traditional mineral acids. Furthermore, HPAs are capable of protonating and activating the substrate; and in some cases, HPAs are more effective than usual inorganic acid and the traditional acid catalyst. Therefore, they are widely used as homogeneous and heterogeneous acid catalyst for the synthesis reaction.⁷ However, the intramolecular cyclodehydration reaction of aromatic compound catalyzed by HPAs has hardly been reported. In order to simplify the preparation of the spirobiindane derivatives, we recently examined the intramolecular cyclocondensation of 1,5-biaryl-3-pentanones in the presence of a heteropoly acid, and as a result a series of spirobiindanes were obtained in good yield (Scheme 1). Herein, we would like to report the results on this investigation.

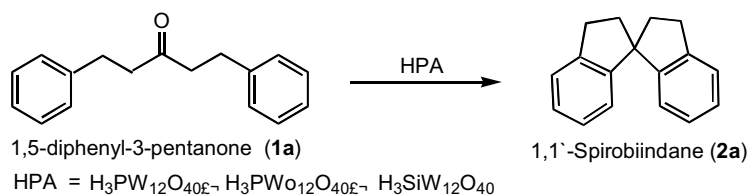
As a reaction model, cyclocondensation of 1,5-biphenyl-3-pentanone catalyzed by HPAs was investigated under different reaction conditions, the result was summarized in Table 1. It can be seen that the three kinds of HPAs (H₃PW₁₂O₄₀, H₃PMo₁₂O₄₀ and H₄SiW₁₂O₄₀) used in the experiments show high catalytic activity toward the bis-cyclization (entries 2, 7, and 8), and it was found that H₃PW₁₂O₄₀ is the best catalyst for the reaction (entry 2). This may be due to H₃PW₁₂O₄₀ which has the highest

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Scheme 1. Bis-cyclization of 1,5-diaryl-3-pentanones catalyzed by H₃PW₁₂O₄₀.

Table 1. Preparation of spirobiindane (**2a**) via bis-cyclization of 1,5-diphenyl-3-pentanone (**1a**) catalyzed by heteropoly acids^a



Entry	Substrate (mmol)	Catalyst (mmol)	Solvent	Yield (%)
1	1a (10)	H ₃ PW ₁₂ O ₄₀ (2.0)	Toluene	87
2	1a (10)	H ₃ PW ₁₂ O ₄₀ (1.5)	Toluene	91
3	1a (10)	H ₃ PW ₁₂ O ₄₀ (1.0)	Toluene	65
4	1a (10)	H ₃ PW ₁₂ O ₄₀ (1.5)	Xylene	61
5	1a (10)	H ₃ PW ₁₂ O ₄₀ (1.5)	Benzene	35
6	1a (10)	H ₃ PW ₁₂ O ₄₀ (1.5)	Cyclohexane	0
7	1a (10)	H ₃ PMo ₁₂ O ₄₀ (1.5)	Toluene	83
8	1a (10)	H ₄ SiW ₁₂ O ₄₀ (1.5)	Toluene	70

^a All the experiments were carried out for 6 h under reflux condition.

acidity,⁷ and is favorable for cyclocondensation. As far as the amount of the catalyst used is concerned, using 0.15 equiv of the catalyst offers the desired product in the highest yield; more catalyst cannot improve the yield further (entry 1). It is also observed that the reaction medium influences considerably the yield of the cyclization product; toluene is the most appropriate solvent for the cyclocondensation, and the reactions in xylene and benzene give the product in lower yields, while the cyclocondensation does not occur in cyclohexane (entries 2, 4–6). The above result indicates that HPAs are better

to excellent catalyst for bis-cyclization of 1,5-diphenyl-3-pentanone under the optimized condition, and 1,5-biphenyl-3-pentanone was refluxed in toluene in the presence of 0.15 equiv of H₃PW₁₂O₄₀ to offer 1,1'-spirobiindane in up to 91% yield.

The above optimized condition was applied to bis-cyclization of the other 1,5-diaryl-3-pentanones (**1b–g**, Scheme 1) and the results obtained are summarized in Table 2. It can be seen that in most of cases, the reactions offer the desired 1,1'-spirobiindanes in better to

Table 2. Preparation of spirobiindanes (**2a–f**) via bis-cyclization of 1,5-diaryl-3-pentanones (**1a–g**) catalyzed by H₃PW₁₂O₄₀

Substrates (1a–g)	Time (h)	Products (2a–f) ^a	Mp (°C)	Yield ^b (%)
1,5-Diphenyl-3-pentanone	6	1,1'-Spirobiindane (2a)	Oil	91(82 ^{8a})
2,5-Dibenzylcyclopentanone	10	2,2'-Ethylene-1,1'-spirobiindane (2b)	100–102	77(79 ^{8b})
2,6-Dibenzylcyclohexanone	10	2,2'-Propylene-1,1'-spirobiindane (2c)	Oil	57
1,5-Bis(3-methoxyphenyl)-3-pentanone	12	5,5'-Dimethoxy-1,1'-spirobiindane (2d)	72–74	68(56.8 ^{8c})
1,5-Bis(4-methoxyphenyl)-3-pentanone	12	6,6'-Dimethoxy-1,1'-spirobiindane (2e)	128–130	78(20 ^{8d})
1,5-Bis(4-chlorophenyl)-3-pentanone	10	6,6'-Dichloro-1,1'-spirobiindane (2f)	120–122	72
1,5-Bis(2-bromo-5-methoxy-phenyl)-3-pentanone	10	4,4'-Dibromo-7,7'-dimethoxy-1,1'-spirobiindane (2g)	160–162	80(66 ⁵)

^a All the experiments were performed in toluene under reflux condition (Ref. 9) and the characteristic data were showed in Ref. 10.

^b The yield reported in the literature.

good yield except that of 2,6-dibenzylcyclohexanone (**1c**) derived from cyclohexanone, and the yields are considerably higher than those in the literature. It should be specially pointed out that in the case of $H_3PW_{12}O_{40}$ catalyzed biscyclization of 1,5-bis(2-bromo-5-methoxyphenyl)-3-pentanone (**1g**), the yield of 4,4'-dibromo-7,7'-dimethoxy-1,1'-spirobiindane (**2g**) was upgraded from 66%⁵ to 80%, which is significantly important for the preparation of 1,1'-spirobiindane-7,7'-diol.

In conclusion, HPAs are more appropriate catalysts than PPA and $POCl_3$ for the preparation of 1,1'-spirobiindanes via biscyclization of 1,5-diaryl-3-pentanone. In the experimental condition, seven spirobiindanes were obtained, and two are reported for the first time. 1,5-Diaryl-3-pentanones were catalytically biscyclized by 0.15 equiv of a heteropoly acid in toluene to furnish the spirobiindanes in 57–91% yield.

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- General procedure: 1,5-Diaryl-3-pentanone (10 mmol), $H_3PW_{12}O_{40}$ (1.5 mmol) and 30 mL toluene were charged in a 50 mL flask with water segregator and reflux condenser, followed by reflux and dehydration until no water was separated for about 6–12 h, cooled, filtered, and washed with $CHCl_3$. The organic phase was combined. The product was purified by recrystallization or column chromatography on SiO_2 gel.
- The characteristic data of the products. *1,1'-Spirobiindane (2a)* a colorless oil, 1H NMR (300 MHz, $CHCl_3$): δ 2.14–2.35 (m, 4H) 3.02 (t, $J = 13$ Hz, 4H) 6.92 (d, $J = 7$ Hz, 2H) 7.11–7.29 (m, 6H); IR (KBr, in film): ν 1602, 1455, 751 (cm^{-1}). *2,2'-Ethylene-1,1'-spirobiindane (2b)*: a colorless solid: mp 373–375 K. 1H NMR (300 MHz, $CHCl_3$): δ 1.48–1.51 (m, 2H), 2.00–2.08 (m, 2H), 2.72–2.82 (m, 4H), 3.33–3.41 (m, 2H), 6.83 (d, $J = 7$ Hz, 2H), 7.09–7.22 (m, 6H). ^{13}C NMR (75 MHz, $CHCl_3$): δ 29.1, 34.3, 38.6, 53.0, 124.5, 124.6, 126.8, 127.2, 143.0, 150.9. IR (KBr, in film): ν 1636, 1478, 752 (cm^{-1}). *2,2'-Propylene-1,1'-spirobiindane (2c)*: a colorless oil, 1H NMR (300 MHz, $CHCl_3$): δ 1.42–1.49 (m, 2H), 1.55–1.66 (m, 4H), 2.58–2.66 (m, 2H), 2.77–2.84 (m, 2H), 3.12–3.19 (m, 2H), 6.81 (d, $J = 7$ Hz, 2H), 7.11–7.36 (m, 6H). ^{13}C NMR (75 MHz, $CHCl_3$): δ 19.9, 27.7, 36.4, 43.9, 61.3, 123.4, 125.2, 126.7, 126.8, 143.0, 149.3. IR (KBr, in film): ν 1587, 1476, 1263, 1082, 776 cm^{-1} . Anal. Calcd for $C_{20}H_{20}$: C 92.22, H 7.78. Found C 91.94, H 7.66. *5,5'-Dimethoxy-1,1'-spirobiindane (2d)*: a colorless solid, mp 345–347 K. 1H NMR (300 MHz, $CHCl_3$): δ 2.08–2.32 (m, 4H), 2.96 (t, $J = 16$ Hz, 4H), 3.78 (s, 6H), 6.67 (d, $J = 9$ Hz, 2H), 6.75–6.87 (m, 4H). IR (KBr, in film): ν 1606, 1489, 1243, 805 cm^{-1} . *6,6'-Dimethoxy-1,1'-spirobiindane (2e)*: a colorless solid: mp 401–403 K. 1H NMR (300 MHz, $CHCl_3$): δ 2.11–2.33 (m, 4H), 2.93 (t, $J = 15$ Hz, 4H), 3.70 (s, 6H), 6.46 (s, 2H), 6.72 (d, $J = 8$ Hz, 2H), 7.15 (d, $J = 8$ Hz, 2H). ^{13}C NMR (75 MHz, $CHCl_3$): δ 30.9, 41.7, 56.1, 61.9, 108.9, 113.0, 124.9, 135.8, 151.6, 158.9. IR (KBr): ν 1609, 1497, 1246, 1034, 813 cm^{-1} . *6,6'-Dichloro-1,1'-spirobiindane (2f)*: a colorless solid: mp 393–395 K. 1H NMR (300 MHz, $CHCl_3$): δ 2.14–2.35 (m, 4H), 2.97 (t, $J = 14$ Hz, 4H), 6.87 (s, 2H), 7.14–7.2 (m, 4H). ^{13}C NMR (75 MHz, $CHCl_3$): δ 30.6, 41.0, 61.2, 123.8, 125.8, 127.3, 132.7, 142.2, 151.9. IR (KBr): ν 1476, 1095, 816 cm^{-1} . Anal. Calcd for $C_{17}H_{14}Cl_2$: C 70.60, H 4.88; Found C 70.34, H 4.66. *4,4'-Dibromo-7,7'-dimethoxy-1,1'-spirobiindane (2g)*: a colorless solid: mp 433–436 K. 1H NMR (300 MHz, $CHCl_3$): δ 2.11–2.39 (m, 4H), 2.90–3.10 (m, 4H), 3.51 (s, 2H), 6.50 (d, $J = 9$ Hz, 2H) 7.23 (d, $J = 9$ Hz, 2H). IR (KBr): ν 1595, 1471, 1267, 737 cm^{-1} .