

Rearrangement of Dypnones to 1,3,5-Triarylbenzenes

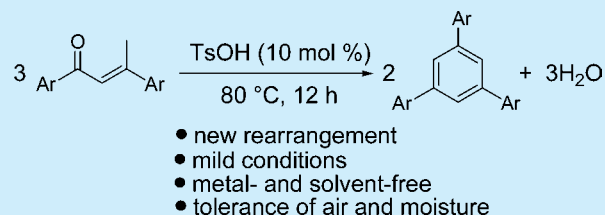
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S Supporting Information

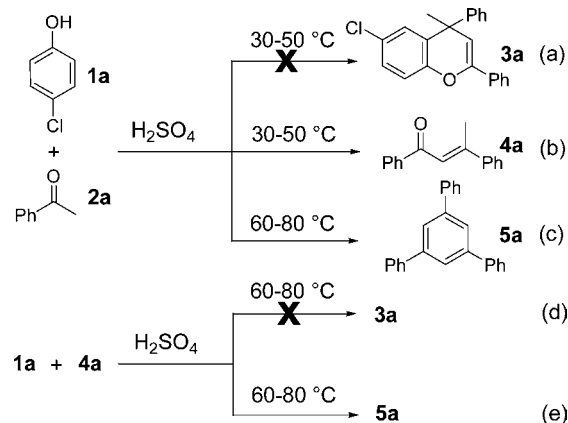
ABSTRACT: Rearrangement of dypnones to 1,3,5-triarylbenzenes is described. The reaction is proposed to involve an aldol-type self-condensation of dypnones, followed by an intramolecular [2 + 2] cycloaddition and a retro-[2 + 2] cycloaddition. The reaction goes smoothly under obviously milder conditions in comparison to the cyclotrimerization of acetophenones to 1,3,5-triarylbenzenes (10 mol % of TsOH, 80 °C versus 130–148 °C). This unexpected rearrangement would provide new possible considerations in dypnone-involved organic synthesis.



1,3,5-Triarylbenzenes have been a subject of consistent interest due to their wide range of applications in the fields of special ligands¹ and functional materials including electrode devices,² resistance materials,³ conducting polymers,⁴ organic light emitting diodes,⁵ etc. Besides, 1,3,5-triarylbenzenes are also versatile building blocks for the synthesis of polycyclic aromatic hydrocarbons (PAHs),⁶ dendrimers,⁷ and fullerene fragments.⁸ Accordingly, various synthetic methods have been developed for the construction of 1,3,5-triarylbenzenes,^{1–11} which include substitution of 1,3,5-trihalobenzenes with arylation agents,⁹ and cyclotrimerization of acetophenones¹⁰/arylethynes.¹¹ Recently, Jia has developed an elegant cyclotrimerization of acetophenones to 1,3,5-triarylbenzenes in the presence of *p*-toluenesulfonic acid (PTSA, TsOH) at 130–148 °C.¹⁰ⁱ Here, we would like to report a new access to 1,3,5-triarylbenzenes via a TsOH-catalyzed dypnone rearrangement under mild conditions (80 °C).

The discovery of dypnone-to-triarylbenzene rearrangement was somewhat serendipitous, which started with our attempts to synthesize 4*H*-chromenes from deactivated phenols and acetophenones. H₂SO₄-promoted synthesis of 4*H*-chromenes from activated phenols and acetophenones at 30–50 °C was reported.¹² Unfortunately, treatment of 4-chlorophenol (**1a**), a weak deactivated phenol, with acetophenone (**2a**) under the same conditions failed to generate the expected 4*H*-chromene **3a** (Scheme 1a), in which the annulation of dypnone **4a** with phenol **1a** did not take place (Scheme 1a–b).¹² At higher temperatures (60–80 °C), 1,3,5-triarylbenzene (**5a**) instead of 4*H*-chromene **3a** was obtained in 10–15% yields, which was thought to be formed via the annulation of dypnone **4a** with acetophenone **2a** (Scheme 1c).¹⁰ To avoid this side reaction, dypnone **4a** was used instead of acetophenone **2a** to react with phenol **1a**, which still did not afford 4*H*-chromene **3a** (Scheme 1d). Inspiringly, dypnone **4a** itself was unexpectedly rearranged to 1,3,5-triarylbenzene **5a** at 60–80 °C, even in the absence of phenol **1a** (Scheme 1d–e). Considering the potential applications of this rearrangement in dypnone-involved organic synthesis, we then turned to optimizing the reaction conditions for the synthesis of

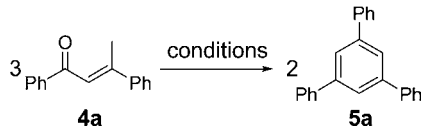
Scheme 1. Discovery of Dypnone–Triarylbenzene Rearrangement



1,3,5-triarylbenzene **5a** via the rearrangement of dypnone **4a**. Table 1 lists the representative results. Treatment of **4a** in the presence of concentrated H₂SO₄ (10 mol %) in toluene (PhMe) at 80 °C afforded **5a** in 63% yield within 12 h (entry 1). Trifluoroacetic acid (CF₃CO₂H), trichloroacetic acid (CCl₃CO₂H), acetic acid (CH₃CO₂H), and formic acid (HCO₂H) were not effective catalysts for this reaction. Treatment of **4a** in toluene at 80 °C for 12 h in the presence of these Brønsted acids (10 mol %) afforded **5a** in only 6–13% yields, and most of the starting material was recovered (entries 2–5). Instead, trifluoromethanesulfonic acid (TfOH), benzenesulfonic acid (PhSO₃H), 2,4-dinitrobenzenesulfonic acid (DNBSA), and TsOH displayed good efficiency for this reaction, which afforded **5a** in 71–88% yields under otherwise the same conditions (entries 6–9). Unsurprisingly, the reaction did not work in the absence of a

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Table 1. Survey of Conditions for the Rearrangement of Dypnone (4a) to 1,3,5-Triarylbenzene (5a)^a


entry	catalyst	solvent	temp	yield
1	H ₂ SO ₄	PhMe	80 °C	63%
2	CF ₃ CO ₂ H	PhMe	80 °C	13%
3	CCl ₃ CO ₂ H	PhMe	80 °C	12%
4	CH ₃ CO ₂ H	PhMe	80 °C	6%
5	HCO ₂ H	PhMe	80 °C	11%
6	TfOH	PhMe	80 °C	71%
7	PhSO ₃ H	PhMe	80 °C	81%
8	DNBSA	PhMe	80 °C	83%
9	TsOH	PhMe	80 °C	88%
10	–	PhMe	80 °C	0
11	Fe(OTf) ₃	PhMe	80 °C	73%
12	FeCl ₃	PhMe	80 °C	5%
13	Fe ₂ (SO ₄) ₃	PhMe	80 °C	3%
14	Bi(OTf) ₃	PhMe	80 °C	76%
15	TsOH	DMF	80 °C	trace
16	TsOH	H ₂ O	80 °C	trace
17	TsOH	EtOH	80 °C	53%
18	TsOH	CH ₃ NO ₂	80 °C	73%
19	TsOH	<i>n</i> -hexane	80 °C	83%
20	TsOH	1,4-dioxane	80 °C	85%
21	TsOH	DCE	80 °C	90%
22	TsOH	–	80 °C	93%
23 ^b	TsOH	–	80 °C	18%
24 ^b	TsOH	–	130 °C	91%
25	TsOH	–	60 °C	67%
26	TsOH	–	70 °C	88%
27	TsOH	–	90 °C	91%
28 ^c	TsOH	–	80 °C	82%
29 ^d	TsOH	–	80 °C	92%

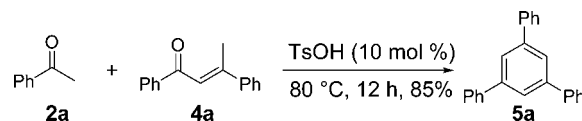
^aGeneral conditions: **4a** (1.0 mmol) and catalyst (0.1 mmol) in solvent (0.2 mL) for 12 h. DNBSA: 2,4-dinitrobenzenesulfonic acid. ^bAcetophenone (**2a**, 2.0 mmol) was used instead of dypnone (**4a**). ^c5 mol % of TsOH was used. ^dReaction was carried out at 2.22 g scale of **4a** (10.0 mmol) under an air atmosphere.

catalyst (entry 10). TsOH is the most efficient catalyst for this reaction in all screened Brønsted acids and Lewis acids (entries 1–9, 11–14). With the use of *N,N*-dimethylformamide (DMF), water (H₂O), ethanol (EtOH), nitromethane (CH₃NO₂), *n*-hexane, and 1,4-dioxane in comparison to toluene, relatively lower yields were observed (entries 9 and 15–20). Fortuitously, **5a** was obtained in excellent yields when the reaction was performed in 1,2-dichloroethane (DCE) or under solvent-free conditions (entries 21–22). When acetophenone (**2a**, 2.0 mmol) was used instead of dypnone (**4a**, 1.0 mmol), an obviously higher reaction temperature was required (entries 22–24).¹⁰ⁱ Further parameter optimization identified 80 °C as the most effective reaction temperature (entries 22, 25–27). The reaction went well when the loading of TsOH was not less than 10 mol % (entries 22, 28). Furthermore, by scaling up **4a** to 2.22 g the reaction provided the yield at an excellent level, which was easy to perform under an air atmosphere (entry 29).

With the optimized reaction conditions in hand, the scope of the reaction was subsequently investigated, and the representative results are summarized in Table 2. With the aromatic rings of

dypnones bearing hydrogen atoms (entry 1), electron-withdrawing groups (entries 2–5), and electron-donating groups (entries 6–9), rearrangement of dypnones **4a–i** went smoothly in the presence of TsOH (10 mol %) at 80 °C to afford 1,3,5-triarylbenzenes **5a–i** in excellent yields within 12 h. Rearrangement of dypnone **4j** went uneventfully to afford 1,3,5-triarylbenzenes **5j** in 62% yield under the standard conditions, albeit at 60 °C within 24 h (entry 10). No reaction took place when 4'-benzyloxyacetophenone was used instead of dypnone **4j** under otherwise the same conditions, and debenzoylation was observed when the temperature exceeded 80 °C. The result indicated that, in contrast to the cyclotrimerization of acetophenones, the present protocol is milder and thus could tolerate more functional and protecting groups. 3,3'-Dichlorodypnone (**4k**) and 3,3'-dimethyldypnone (**4l**) underwent rearrangement under the standard conditions to afford 1,3,5-triarylbenzenes **5k** and **5l** in 68% and 81% yields, respectively (entries 11–12). 2,2'-Dimethyldypnone (**4m**), a relatively sterically hindered dypnone, underwent rearrangement uneventfully under the standard conditions to generate 1,3,5-triarylbenzene **5m** in a moderate yield (entry 13). 3,3',4,4'-Tetramethyldypnone (**4n**) has also been investigated, which underwent rearrangement under the standard conditions to afford 1,3,5-triarylbenzene **5n** in 61% yield (entry 14). These reactions are very easy to perform without the need to use anhydrous solvent and an inert atmosphere.

Acetophenone **2a** could be detected in the TsOH-catalyzed rearrangement of dypnone **4a** to 1,3,5-triarylbenzene **5a**. Treatment of acetophenone **2a** with an equal equivalent of dypnone **4a** in the presence of TsOH at 80 °C afforded 1,3,5-triarylbenzene **5a** in 85% yield within 12 h (Scheme 2), in which

Scheme 2. Reaction of Acetophenone 2a with Dypnone 4a

dypnone **4a** was completely converted to 1,3,5-triarylbenzene **5a** whereas nearly 20% of acetophenone **2a** remained. As mentioned in Table 1 (entry 23), the cyclotrimerization of acetophenone **2a** went slowly at 80 °C. Therefore, the reaction of acetophenone **2a** with dypnone **4a** in the presence of TsOH at 80 °C should include processes of dypnone rearrangement and acetophenone–dypnone annulation.

Based on the above results, a possible reaction mechanism for the rearrangement of dypnones **4** to 1,3,5-triarylbenzenes **5** is illustrated (Scheme 3). Dypnones **4** undergo an enolization followed by an aldol-type addition with dypnones **4** and a subsequent dehydration to form the intermediates **8**, which are converted to 1,3,5-triarylbenzenes **5** and acetophenones **2** via an intramolecular [2 + 2] cycloaddition and a subsequent retro-[2 + 2] cycloaddition. On the other hand, an aldol-type condensation of acetophenones **2** with compounds **6** followed by subsequent dehydration and an enolization generates the intermediates **11**, which undergo a 6 π -electrocyclization and a dehydration to afford 1,3,5-triarylbenzenes **5**.¹⁰

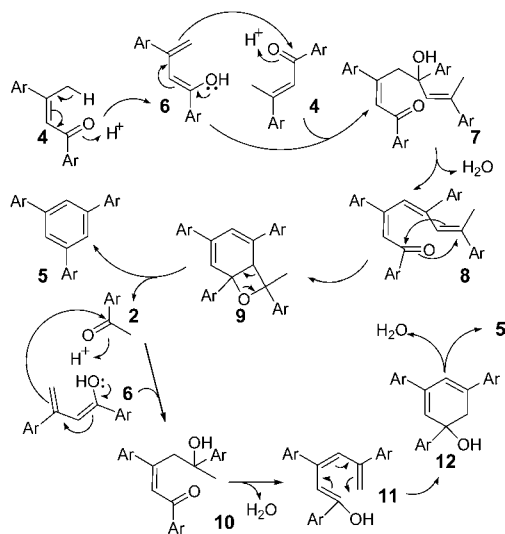
In summary, we have developed an unprecedented dypnone-to-triarylbenzene rearrangement under metal- and solvent-free conditions, which provided a mild, facile, and environmentally benign approach for the synthesis of 1,3,5-triarylbenzenes, a

Table 2. Rearrangement of Dypnones 4 to 1,3,5-Triarylbenzenes 5^a

entry	dypnones 4	1,3,5-triarylbenzenes 5	entry	dypnones 4	1,3,5-triarylbenzenes 5
1			9		
2			10 ^b		
3			11		
4			12		
5			13		
6			14		
7					
8					

^aGeneral conditions: 4 (1.0 mmol) and TsOH (0.1 mmol) at 80 °C for 12 h. ^bThe reaction was performed at 60 °C for 24 h.

Scheme 3. Proposed Mechanism



privileged motif found in a large number of special ligands and functional materials. Synthetic applications of this reaction are under investigation.

■ ASSOCIATED CONTENT

S Supporting Information

General experimental procedure and characterization data of the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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