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# A new, fast and efficient synthesis of 3-aryl indenones: intramolecular cyclization of 1,3-diarylpropynones in superacids

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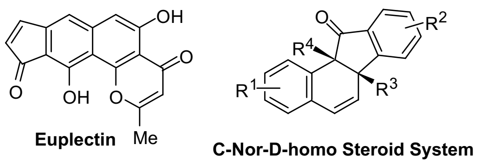
**Abstract**—1,3-Diarylpropynones were cleanly converted to the corresponding 3-arylindenones in various superacidic media. This new, simple, one-pot reaction proved to be efficient (yields up to 95%) and very fast (reaction time less than 30 min).

The indenone motif can be found in some natural products[1,2] and in man made compounds.[3–6] Indenones have also been used as starting materials either towards biologically active molecules such as C-nor-D-homo-steroids,[7] estrogen-binding receptors,[8] gibberellins[9] or towards indanones,[3] indenes,[4] photochromic indenone oxides,[5] 2,4- and 3,4-disubstituted 1-naphthols[6] (Scheme 1).

Due to their importance, various syntheses of indenones have been reported. Classical Friedel–Crafts[10] and Grignard[11] reactions have mostly been used but more recently, cross-coupling methods have been applied to indenones synthesis.[12] Organometallics and/or metal activators have therefore always been required.[13]

Based on our work on propynones,[14] we reasoned that arylpropynones **C** could be precursors of choice towards indenones **A** (Scheme 2). Indeed, protonation in strong acids[15] would in situ generate a vinyl cation[16] (**B** in Scheme 2), which should be trapped by the adjacent aryl group leading to indenone.

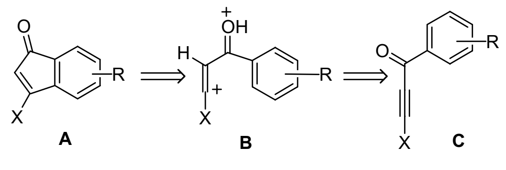


**Scheme 1.**

In this communication, we described our preliminary results based on such process and showed that aryl propynones are indeed converted to indenones in strong acid media.

To investigate this cyclization process, we prepared[14] various 1,3-diarylpropynones carrying or not various substituents on one or both aromatic rings. Dissolved in triflic acid at −30 °C or room temperature, these compounds exhibited interesting reactivities and could be distinguished into two categories (Table 1).

The 1,3-diphenyl propynone **1a** and its substituted analogues **1b–c** do not react in neat $CF_3SO_3H$ even at room temperature and after prolonged time (Table 1, entries 1, 3 and 5) while the methoxy substituted derivatives **1d–f** were cleanly converted to the corresponding 3-arylindenones **2d–f** (Table 1, entries 8–10). For the latter, quantitative transformation occurred as judged from NMR when the reaction was performed and



**Scheme 2.** Mechanistic hypothesis for the cyclization of propynones to indanones.

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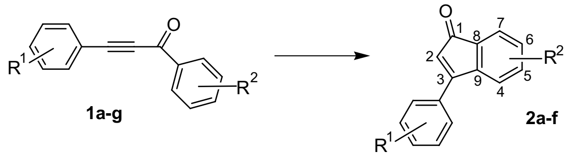
**Table 1.** Synthesis of the 3-arylindenones **2a–f** from the 1,3-diarylpropynones **1a–g**



| Entry | 1,3-Diarylpropynones | | | Reaction conditions | | | 3-Arylindenones | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Compound no. | $R^1$ | $R^2$ | Acidic medium | Time (min) | Temperature (°C) | Compound no. | $R^1$ | $R^2$ | Yields[a] |
| 1[b] | **1a** | H | H | $CF_3SO_3H$ | 30 | 25 | — | — | — | — |
| 2 | **1a** | H | H | $CF_3SO_3H/SbF_5$ (17 mol%) | 30 | 25 | **2a** | H | H | 43 |
| 3[b] | **1b** | H | 3-MeO | $CF_3SO_3H$ | 30 | 25 | — | — | — | — |
| 4 | **1b** | H | 3-MeO | $CF_3SO_3H/SbF_5$ (17 mol%) | 30 | 25 | **2b** | H | 6-MeO | 61 |
| 5[b] | **1c** | 4-Me | H | $CF_3SO_3H$ | 30 | 25 | — | — | — | — |
| 6 | **1c** | 4-Me | H | $CF_3SO_3H/SbF_5$ (17 mol%) | 30 | 25 | **2c** | 4-Me | H | 75 |
| 7 | **1c** | 4-Me | H | $HF/SbF_5$ (2 mol%) | 30 | 0 | **2c** | 4-Me | H | 60 |
| 8 | **1d** | 4-MeO | H | $CF_3SO_3H$ | 15 | −30 | **2d** | 4-MeO | H | 54 |
| 9 | **1e** | 4-MeO | 3-MeO | $CF_3SO_3H$ | 15 | −30 | **2e** | 4-MeO | 6-MeO | 95 |
| 10 | **1f** | 4-MeO | 3,4-$Me_2$ | $CF_3SO_3H$ | 15 | −30 | **2f** | 4-MeO | 5,6-$Me_2$ | 95 |
| 11[c] | **1g** | 4-MeO | 4-MeO | $CF_3SO_3H$ | 30 | −30 | — | — | — | — |

[a] Yields after preparative isolation of reaction products.

[b] No transformation, the unchanged starting compound was quantitatively isolated after reaction.

[c] No 3-arylindenone formation, the 1,3-diarylpropynone was completely transformed into mixture of oligomeric material.

followed in NMR tubes. The products were isolated with yields up to 95% after reaction time of only 15 min, even at low temperature (−30 °C).

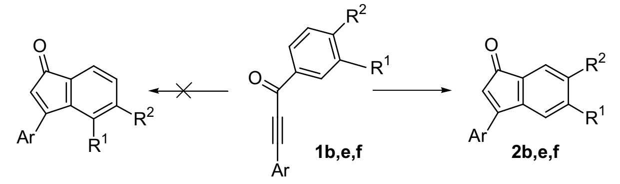
This discrepancy can be correlated with the electron density of the propynone system. When located on the aromatic group adjacent to the acetylenic group like in **1d–f**, the strong electron-donating property of the methoxy group induces an increase of the propynone electron density. This effect would thus favor the O,C-diprotonation of the propynone system[17] (proposed intermediate **B** in Scheme 2) and facilitate the subsequent cyclization to indenones **2d–f**. On the other hand, the unsubstituted **1a** or derivatives substituted by a less donating group (**1b–c**) may lack electron density and are thus not basic enough to be additionally C-protonated at the acetylene group by triflic acid.

If this is true, acids stronger than triflic acid would nevertheless O,C-diprotonate the propynone fragment and induce the expected ring closure. Increasing the acidity of the reaction medium from $H_0 = -14.1^5$ for neat $CF_3SO_3H$ up to $H_0 = -19$ or $-20^{15}$ for mixtures of $CF_3SO_3H$ and $SbF_5$ (17 mol%) or of HF and $SbF_5$ (2 mol%), respectively, indeed allows the reaction to proceed. The indenones **2a–c** were thus obtained but the yield was slightly lower than for the formation of **2e–f** (Table 1, entries 2, 4, 6 and 7 vs 9 and 10). We found that such compounds are surprisingly sensitive, especially to nucleophiles, heat and light.

To further check the effect of methoxy substituent, we prepared **1g** bearing a methoxy group at both *para*-positions of both aromatic substituents and submitted it to triflic acid. In a few minutes at −30 °C, **1g** was completely consumed but a mixture of oligomeric materials was produced from which it was impossible to detect the expected indenone. It seems that such methoxy substitution renders the propynone system too reactive.

It is worth noting that a single regioisomer is always formed when the aromatic ring is not symmetrically substituted. The diarylpropynones **1b**,**e**,**f** only gave the indenones **2b**,**e**,**f**, although two compounds could have been produced (Scheme 3).

In conclusion, we have developed a new, simple and efficient method for the synthesis of 3-arylindenones by intramolecular cyclization of 1,3-diarylpropynones in superacidic media. Moreover, this one-pot reaction does not require metal catalysts or reagents and is very fast,



**1b** Ar = Ph; $R^1$ = OMe, $R^2$ = H
**1e** Ar = 4-Me$OC_6H_4$; $R^1$ = OMe, $R^2$ = H
**1f** Ar = 4-Me$OC_6H_4$; $R^1$ = $R^2$ = Me

**Scheme 3.**

with reaction times lower than 30 min (usually 15 min). Mechanistic studies are now underway in order to detect the in situ formation of vinyl cation.

## Typical procedure

Propynone **1a–f** (0.5 mmol) was added to a mixture of triflic acid $CF_3SO_3H$ (2 mL, 3.4 g, 22.5 mmol) and $SbF_5$ (980 mg, 4.5 mmol, 17 mol% in the mixture $CF_3SO_3H–SbF_5$) or to triflic acid $CF_3SO_3H$ (2 mL, 3.4 g, 22.5 mmol) at −30 °C or at room temperature (see Table 1) with vigorous magnetic stirring. Color of solutions became intensively red or violet. After stirring during 15–30 min (see Table 1), the reaction mixture was slowly added dropwise to a vigorously stirred ice–water mixture (~30 mL). The product **2a–f** was then isolated either after extraction with $CH_2Cl_2$ and flash-chromatography on silica gel or after filtration when a solid formed after water quenching. This solid was then recrystallized from $MeOH/CH_2Cl_2$.

*6-Methoxy-3-(4-methoxyphenyl)indenone* ***2e***: Yield 95%. Red-orange crystals, mp 155–157 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 3.82 (s, 3H), 3.86 (s, 3H), 5.84 (s, 1H), 6.77 (dd, $J = 8.1, 2.5$ Hz, 1H), 6.98 (d, $J = 8.9$ Hz, 2H), 7.08 (d, $J = 2.5$ Hz, 1H), 7.26 (d, $J = 8.1$ Hz, 1H), 7.62 (d, $J = 8.9$ Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 55.44, 55.73, 110.24, 114.34, 115.32, 120.22, 122.60, 125.74, 129.13, 135.14, 135.53, 161.16, 161.63, 163.32, 196.67. MS: m/z ($I_{rel.}$, %) 266 (100) $M^+$, 159 (72), 135 (59). Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.76; H, 5.27.

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