



The preparation of 1,3,5-tris(1,1'-binaphthoyl)benzene via amine-catalyzed alkyne trimerization

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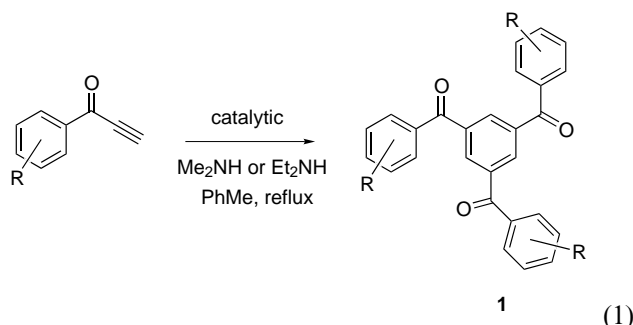
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Abstract—Three 1,1'-bi-2-naphthol moieties have been positioned about a central aromatic ring by alkyne cyclotrimerization of an optically pure 3-substituted binaphthyl ethynyl ketone. The cyclotrimerization proceeds in good yield and with complete regioselectivity to afford a 1,3,5-substituted arene exclusively. © 2001 Elsevier Science Ltd. All rights reserved.

The 1,1'-bi-2-naphthol (BINOL) framework is well recognized as an important component of chiral catalysts that are routinely utilized in asymmetric synthesis.¹ In addition, binaphthol derivatives have been applied in host–guest chemistry for the enantioselective binding of targeted substrates.² The propensity of various substituted BINOLs to form diastereomerically pure crystalline inclusion complexes also has proven beneficial in the resolution of racemic mixtures.³

Recently, advances in asymmetric catalysis and molecular recognition have been described that entail the use of ligands and molecular receptors composed of multiple covalently linked binaphthol units.⁴ For example, Shibasaki and Kobayashi have prepared chiral catalysts in which two BINOL moieties connected at the 3-position by an alkyl or alkyl ether chain serve as ligating groups for Lewis acidic metal centers.⁵ Similarly, various chiral salen-type ligands have been assembled from two formylated binaphthols and ethylene diamine-derived linkers.⁶ In the area of host–guest chemistry, several artificial molecular receptors possessing up to four BINOL fragments have been recently reported. Such receptors appear to be particularly well suited for enantioselective solution-phase binding of carbohydrate substrates.⁷ Consequently, given the potential for widespread application of covalently linked BINOL oligomers in asymmetric synthesis and molecular recognition, the development of new methods for incorporating multiple binaphthol fragments into discrete molecular assemblies is of general interest.

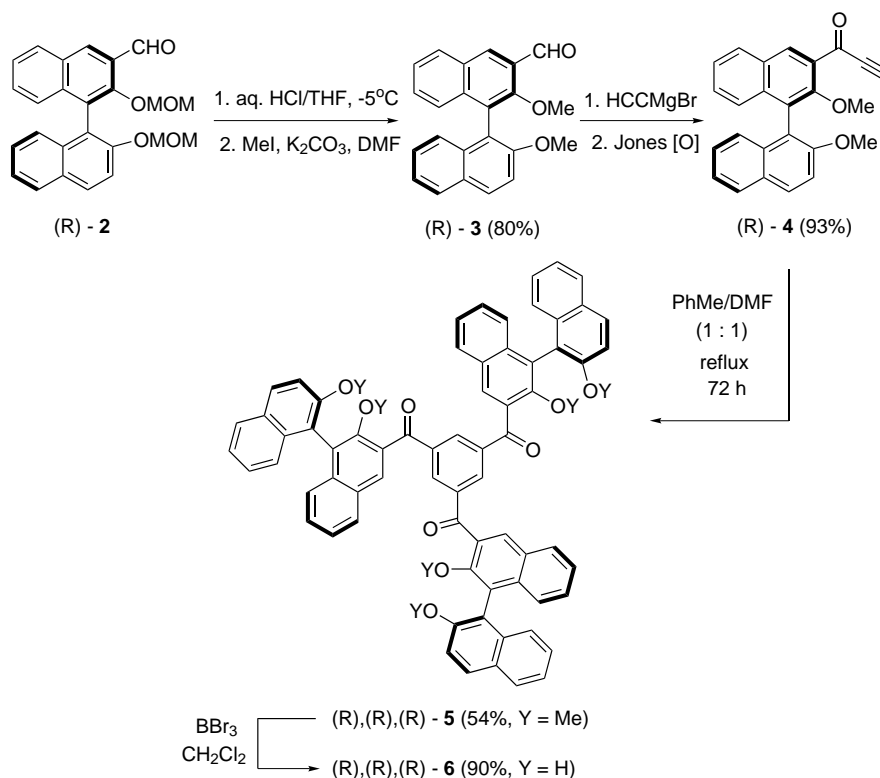
We have recently reported the preparation and inclusion complexation behavior of various substituted 1,3,5-triaroylbenzene derivatives (**1**).⁸ Such compounds are easily accessed via amine-catalyzed cyclotrimerization of aryl ethynyl ketones, as shown in Eq. (1).⁹ Extension of this reaction to include cyclotrimerization of optically pure ethynyl ketones derived from 1,1'-binaphthols would afford novel 1,3,5-tris(binaphthoyl) analogs. Potentially, such BINOL trimers may ultimately serve not only as a source of new multidentate chiral ligands but also as building blocks for enantio- and/or diastereoselective molecular receptors.



An initial approach to a first-generation tris(binaphthol) triaroylbenzene is illustrated in Scheme 1 and begins with the readily available MOM-protected 3-formyl-1,1'-bi-2-naphthol (*R*)-**2**.¹⁰ At the outset, the successful trimerization of a binaphthyl ethynyl ketone was not a forgone conclusion, as it was feared that steric demands inherent to the binaphthyl framework might impede the cyclization process. This concern was heightened when attempted cyclotrimerization of the MOM-protected ethynyl ketone prepared directly from (*R*)-**2** (and analogous to (*R*)-**4**) produced a complicated

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Scheme 1.

reaction mixture devoid of the desired triaroylbenzene product. In the hope that an alternate protecting group would be compatible with alkyne trimerization, MOM-protected (*R*)-**2** was converted to the dimethoxy binaphthol derivative (*R*)-**3**. Treatment of (*R*)-**3** with ethynyl magnesium bromide followed by oxidation of the resulting alcohol afforded alkynyl ketone (*R*)-**4** in good overall yield.¹¹ The key benzanulation reaction was then successfully effected by simply heating to reflux a 0.2 M solution of (*R*)-**4** in 1:1 PhMe:DMF.¹² After 72 h, TLC analysis indicated complete consumption of the starting alkyne and the expected trimer (*R*),(*R*),(*R*)-**5** was isolated in 54% yield after flash column chromatography (SiO₂, CH₂Cl₂).^{11,13} Trimer **5** was then easily converted to the tris(BINOL) analog (*R*),(*R*),(*R*)-**6** by removal of the methyl protecting groups with excess BBr₃.^{11,13} Thus, 3-propynoyl substituted dimethoxy binaphthol can indeed undergo regioselective trimerization to yield a structurally intriguing 1,3,5-tris(binaphthoyl)benzene derivative. Moreover, the trimerization event proceeds without any apparent epimerization of the starting axially chiral binaphthyl framework as determined by spectroscopic comparison of (*R*),(*R*),(*R*)-**5** and (*R*),(*R*),(*R*)-**6** with a diastereomeric mixture of cyclotrimers (±)-**5** and (±)-**6** (prepared from racemic **4**).¹⁴ Further evidence of stereochemical integrity was secured by conversion of (*S*)-**2** to tris-

(BINOL) (*S*),(*S*),(*S*)-**6**, which exhibited an optical rotation of comparable magnitude (but opposite sign) to that of the (*R*)-enantiomer.¹⁵

In conclusion, the ability to assemble three BINOL moieties around a central arene connector in a concise and efficient manner has been demonstrated. The use of optically pure tris(BINOL) **6** as a ligating group for various catalytically relevant metal ions is currently under investigation. In addition, the preparation of isomeric BINOL-containing triaroylbenzenes, as well as unsymmetrically substituted derivatives designed to function as molecular receptors, is also being pursued.¹⁶

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11. All new compounds exhibited spectral (^1H and ^{13}C NMR) and analytical (combustion analysis and/or HRMS) data consistent with the assigned structures.
12. The small amount of dimethylamine generated from slight decomposition of DMF under the reaction conditions⁹ is sufficient to catalyze the cyclotrimerization.
13. (R),(R),(R)-5: Beige solid; mp 228–235°C (dec.); ^1H NMR (300 MHz, CDCl_3): δ 2.96 (s, 9H), 3.76 (s, 9H), 7.18–7.49 (m, 21H), 7.80–7.83 (m, 3H), 7.94 (d, $J=9.0$ Hz, 3H), 7.96 (d, $J=9.0$ Hz, 3H), 8.14 (s, 3H), 8.59 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 56.62, 61.53, 113.40, 118.22, 123.78, 125.11, 125.58, 125.72, 125.79, 127.14, 127.97, 128.01, 129.00, 129.13, 130.11, 130.27, 130.84, 132.68, 133.95, 134.33, 135.78, 138.64, 153.50, 155.02, 195.45; $[\alpha]_{\text{D}}^{25}=+168.2$ (c 0.005, CHCl_3); Anal. calcd for $\text{C}_{75}\text{H}_{54}\text{O}_9 \cdot 0.5\text{H}_2\text{O}$: C, 81.28; H, 5.00; found C, 81.20; H, 4.98. (R),(R),(R)-6: Yellow powder; mp 205–212°C (dec.); ^1H NMR (300 MHz, CDCl_3): δ 5.14 (s, 3H), 7.14–7.44 (m, 21H), 7.89–7.96 (m, 9H), 8.48 (s, 3H), 8.59 (s, 3H), 10.81 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 113.48, 116.41, 117.99, 121.12, 123.85, 124.64, 125.15, 125.33, 127.08, 127.49, 128.61, 129.54, 130.55, 130.80, 131.53, 133.48, 133.58, 137.64, 138.00, 139.04, 151.71, 155.31, 199.23; $[\alpha]_{\text{D}}^{25}=+54.6$ (c 0.0062, CHCl_3); HRMS (FAB⁺, NBA) calcd for $\text{C}_{69}\text{H}_{43}\text{O}_9$ ($[\text{M}+\text{H}]^+$) 1015.2907, found 1015.2900.
14. Cyclotrimerization of racemic **4** produced an inseparable statistical mixture of all possible diastereomers (i.e. $[\text{R},\text{R},\text{R}]/[\text{S},\text{S},\text{S}]$ and $[\text{R},\text{R},\text{S}]/[\text{S},\text{S},\text{R}]$) as determined by ^1H NMR spectroscopy.
15. $[\alpha]_{\text{D}}^{25}=-48.8$ (c 0.014, CHCl_3).
16. For examples of unsymmetrical triaroylbenzenes, see: Pigge, F. C.; Ghasedi, F. *Tetrahedron Lett.* **2000**, 41, 6545.