

HIGHLY SELECTIVE OXIDATIVE CROSS-COUPLING
OF SUBSTITUTED 2-NAPHTHOLS: A CONVENIENT APPROACH
TO UNSYMMETRICAL 1,1'-BINAPHTHALENE-2,2'-DIOLS

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Summary: Oxidative cross-coupling of several differently substituted 2-naphthols mediated by Cu(II)-amine complexes is described. The influence of substituents was examined and possible mechanism explaining the observed selectivity has been proposed.

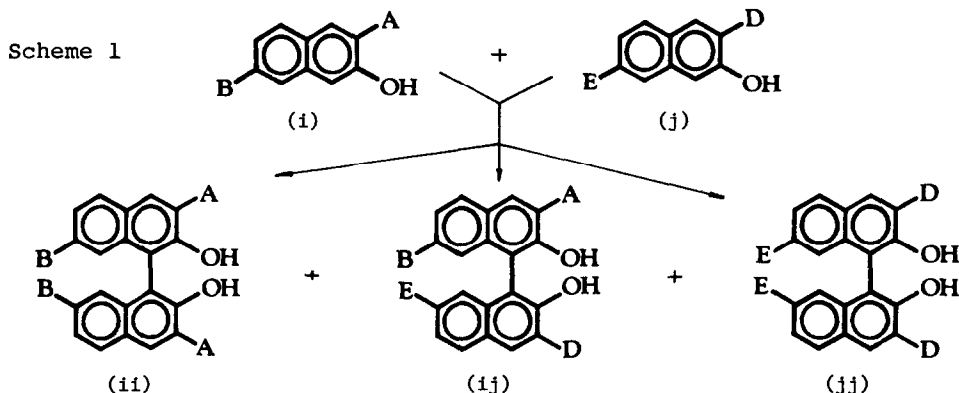
Over the last several years a number of papers has appeared describing the use of axially-chiral derivatives of 1,1'-binaphthalene-2,2'-diol as a chirality transfer agent.¹⁻¹⁰

The synthesis of these binaphthol-derived systems mostly includes three steps: (1) construction of the 1,1'-binaphthyl skeleton by internuclear C-C bond formation, (2) optical resolution of the racemic substance¹¹ and (3) appropriate functional group manipulation.

Oxidative coupling of substituted 2-naphthols represents a well established method for the preparation of 1,1'-binaphthalene-2,2'-diols. Various oxidants such as FeCl₃,^{12,13} Mn(acac)₃,^{14,15} K₃Fe(CN)₆¹⁶ and Cu(II)-amine complexes¹⁷⁻¹⁹ have been so far used to promote the coupling reaction. In particular, the last mentioned Cu(II)-derived agents proved to be very effective. The papers by Wynberg and Feringa^{17,18} and especially by Brussee et al.¹⁹ provide a simple synthetic protocol for the Cu(II)-mediated couplings.

Most of the work on the oxidative coupling of phenols published to date deals only with the oxidative dimerization leading to symmetrical binaphthol molecules. A literature search revealed that the subject of cross-coupling reactions affording unsymmetrical binaphthols remained almost unexplored. In 1956 Haynes et al.²⁰ reported a crossing experiment in which a mixture of 2,6-dimethyl- and 2,6-dimethoxyphenol was treated with alkaline $K_3Fe(CN)_6$; however, only the symmetrical tetramethyl- and tetramethoxy-substituted products were isolated. On the other hand, Japanese authors²¹ recently described a successful cross-coupling of 9-phenanthrol with 3-methoxymethoxy-2-naphthol (Cu(II)-1,2-diphenylethylamine complex as an oxidant) giving the crossed product in a 67% yield.

Herein we wish to report that Cu(II)-mediated cross-coupling may be induced effectively also between two differently substituted 2-naphthols (Scheme 1.). At the same time we wish to report that the selectivity of the reaction depends remarkably on the substitution of both partners (Table 1). All couplings were performed under strictly anaerobic conditions using in situ formed complexes of $CuCl_2$ with $tBuNH_2$ ²² or $EtNH_2$ in methanol.²³



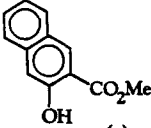
As Table 1 shows, five out of the six reaction investigated proceed with a very high selectivity (81-92%). Inspection of the results indicates that a synthetically useful degree of selectivity is achieved specifically in such situations where the difference in electron density between the reacting partners is substantial.

A new insight into the coupling mechanism is obtained from this observation. According to the commonly accepted view, biphenol products are formed by recombination of free phenoxy radicals.²⁴ This, however, may hardly explain why the selectivity of cross-reactions found in Table 1 (entries 1 to 5) should be so high. One is therefore tempted to suggest

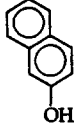
Table 1

entry	starting naphthols		react. conditions [§]		Yield (%)	molar percentage of biaryl products (%mol) ^{§§}		
	(i)	(j)	Temp. (°C)	Time (min)		(ii)	(ij)	(jj)
1	(a)	(b)	50	30	97	5	91	4
2	(a)	(c)	41	120	93	12	88	0
3	(a)	(d)	50	110	95	5	92	3
4	(a)	(e)	23	5	85	5	89	6
5	(a)	(f)	23	120	80	5	81	14
6	(b)	(d)	23	1440	80	25	48	27

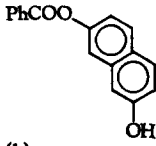
[§] for the effect of reaction variables on the selectivity, see.²⁵
^{§§} all new products gave satisfactory analytical data.



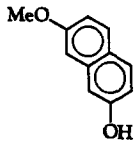
(a)



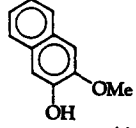
(b)



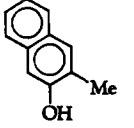
(c)



(d)

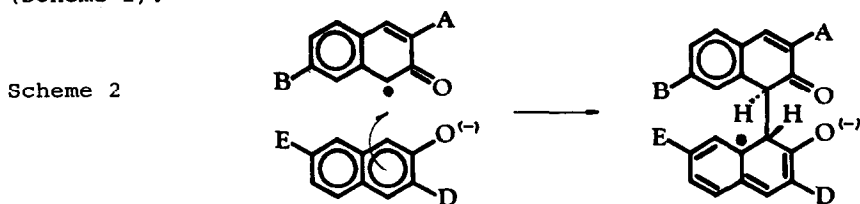


(e)



(f)

that two species of different nature are involved in the coupling step. It is proposed tentatively that a radical which is formed preferentially from the electron-rich component ((b)-(f), Table 1) having lower redox potential and an anion arising from the electron-deficient one ((a), Table 1) with higher redox potential act as partners in the reaction (Scheme 2).



Such a proposal²⁶ would explain well the observation that the crossed products (ab), (ac), (ad), (ae) and (af) derived from electron-poor naphthol (a) and its electron-rich counterparts (b) to (f) are formed with a high selectivity. In contrast reaction of the partners of similar electron density, i.e. (b) with (d), affords only statistical ratio of products.

References and Notes

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22. In the coupling reactions of methyl 3-hydroxy-2-naphthoate (a) EtNH₂ cannot be used because of competitive aminolysis of ester function. The amide so formed does not undergo the coupling reaction. Fortunately, tBuNH₂ is well compatible with the ester function even at elevated temperatures.
23. General experimental procedure: Through a magnetically stirred solution of the equimolar mixture of naphthols (i) and (j) (1 mmol of each) and CuCl₂ (538 mg, 4 mmol) in degassed methanol (20 ml) at room temperature, argon is bubbled for several minutes. Then, with a vigorous stirring, tBuNH₂ (16 ml of 1M solution in methanol) is added dropwise and the heterogeneous reaction mixture is heated as indicated in Table 1. After the completion the reaction mixture is cooled to approx. 10°C and decomposed with 6M HCl. Methanol is taken down on the evaporator and the product filtered (entry 4) or extracted with chloroform. The biaryls are separated by flash chromatography on silicagel.
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25. Several experiments with a pair of naphthols (a) and (b) were carried out varying the structure of amine (tert.butylamine, 1-aminoadamantane, pyridine), temperature (0°C, rt, 50°C) and stoichiometry (100 and 200% excess of Cu(II)(tBuNH₂)₄Cl, complex). It was found that the selectivity of the reaction is almost unaffected by these changes.
26. Very recently an analogous mechanism has been proposed for oxidative cross-coupling of trimethyl silyl ethers mediated by cerium(IV)-ammonium nitrate; Baciocchi E., Casu A., Ruzziconi R.: *Tetrahedron Lett.* 30, 3707 (1989).

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