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Facile Photochemical Synthesis of 1,1′-Binaphthyls

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The photochemical synthesis of highly functionalized 1,1′-binaphthyls **9** by photodehydro-Diels–Alder reaction of esters **8** is reported. It was found that π-stacking interactions between a naphthyl moiety already present in the reactants **8** and an aryl group tethered in the propargyl position of these esters clearly influence the regio- and diastereoselectivity of the reaction. The formation of undesired phenanthrenes **10** could be suppressed by introduction of a blocking methoxy group in the 2-position of the naphthyl moiety. In one case, a diastereomeric ratio of 32:68 was achieved. This is the first example of an atropselective synthesis of biaryls by a photodehydro-Diels–Alder reaction.

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Biaryls, i.e. compounds containing at least two aromatic rings connected by a single bond, are widespread in natural products[1] and the development of new methods for their preparation is still a worthwhile research topic.[2] If the rotation around the bond joining the two aryl moieties is hindered owing to more or less bulky substituents in the *ortho*-position of these moieties and if they are asymmetrically substituted, a special isomerism phenomenon occurs called atropisomerism or axial chirality. The stereoselective synthesis of such axially chiral biaryls is a considerable challenge for chemists and to date numerous powerful methods have been developed.[3] Among biaryls 1,1′-binaphthyls and their derivatives have deserved exceptional attention owing to their outstanding importance as chiral catalysts and auxiliaries.[4] Standing out in this compound class, 2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl (BINAP)[5] and 2,2′-dihydroxy-1,1′-binaphthyl (BINOL)[6] should be mentioned here.

Many methods for the stereoselective synthesis of 1,1′-binaphthyls are based on linking the two already existing naphthyl moieties in the critical step,[3] whereas relatively few methods are reported where one of the naphthyl moieties is just constructed in this step.[7] In past years, we have intensively investigated the photodehydro-Diels–Alder (PDDA) reaction,[8] which is characterized in that a new naphthalene system is always formed. Very recently, we reported on the first application of the PDDA on the synthesis of 1,1′-binaphthyls.[8d] In a continuation of this work, we herein report on the synthesis of highly functionalized 1,1′-binaphthyls, especially on the influence of additional substituents on the regio- and stereoselectivity of the ring closure.

As a result of favourable experiments with 3-phenylpropiolic acid esters, we chose esters **8** as the subject of our investigations. The synthesis of compounds **8**, which is based on two different routes, is summarized in Scheme 1. According to route A, aldehydes **4** were converted to propargylic alcohols **6** by treatment with lithium trimethylsilylacetylide, giving **5**, followed by desilylation with K_2CO_3/MeOH. The Sonogashira coupling[9] of either iodonaphthalene (yielding **7a**,**c**,**d**) or 2-methoxy-1-iodonaphthalene (yielding **7f**–**i**) under standard conditions afforded the naphthalene derivatives **7**. Alternatively, **7** could also be prepared by reaction of aldehydes **4** with lithiated 1-ethynylnaphthalenes **3** (route B). Besides the known compound **3a**,[10] the β-naphthoic acid derivative **3b** was also required, which could be easily prepared from the commercially available 1-hydroxy-2-naphthoic acid **1** via the triflate **2**.[11] In the final step, the alcohols **7** were coupled with 3-phenylpropiolic acid using *N*,*N*′-dicyclohexyl-carbodiimide (DCC)/*N*,*N*-dimethyl-4-pyridinamine (DMAP). The yields of compounds **7** and **8** are summarized in Table 1.

With compounds **8** in hand, we first investigated the dependence of the regioselectivity of the PDDA reaction on the substitutent R^1. If the 2-position of the naphthalene moiety in **8** is not substituted (as in **8a**–**e**), two different products can be formed. Besides the desired 1,1′-binaphthyls **9** (route A, see Scheme 2), the phenanthrenes **10** (route B) are expected. We found that the *tert*-butyl group in **8a** has only a marginal influence on the ratio **9**:**10**, with a slightly preferred formation of **10a**. However, reactants **8b**–**e** bearing an aryl group as R^1 afforded a clear excess of 1,1′-binaphthyls **9** (ratio **9**:**10** = 60:40–69:31). Obviously, the steric hindrance between of the *tert*-butyl group and the 1-naphthyl moiety is not sufficient to prevent the formation of **9** on irradiation. The preferred formation of 1,1′-binaphthyls **9** from **8b**–**e** could be explained by an attractive interaction between the aryl groups and 1-naphthyl moiety based on π-stacking (Scheme 2, Table 2).

In compounds **8f**–**k**, the 2-position of the naphthalene moiety is blocked and, consequently, only the formation of 1,1′-binaphthyls is expected in the PDDA reaction. Once again, we found that the *tert*-butyl group has a negligible influence on the course of the photochemical cyclization. Both diastereomers (*syn* and *anti*) were obtained in the same amounts. The aryl residues in **8g**–**k** have a clear but non-uniform influence

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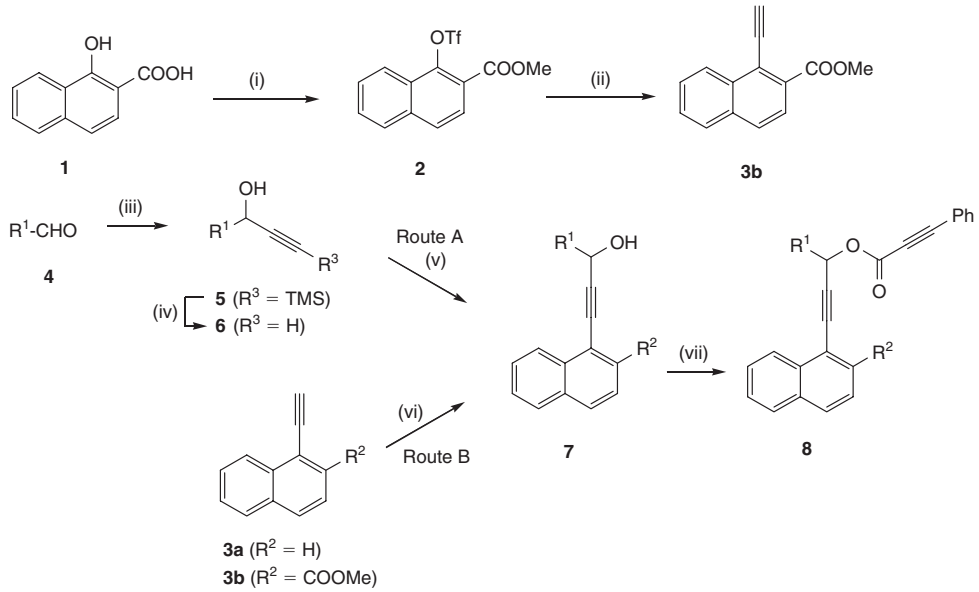


Scheme 1. (i) 1. MeOH/H^+; 2. Tf_2O; (ii) 1. trimethylsilylacetylene, $Pd(PPh_3)_2Cl_2$, Et_2NH, DMF; 2. K_2CO_3/MeOH; (iii) lithium-trimethylsilylacetylide; (iv) K_2CO_3/MeOH; (v) 2 mol-% $PdCl_2(PPh_3)_2$, 1 mol-% CuI, 1.5 eq. 1-iodonaphthalene (**7a**,**c**,**d**) or 2-methoxy-1-iodonaphthalene (**7f**–**i**), Et_3N, 50°C; (vi) 1. *n*-BuLi; 2. **4**; (vii) 3-phenylpropiolic acid, DCC, 6 mol-% DMAP, 0°C.

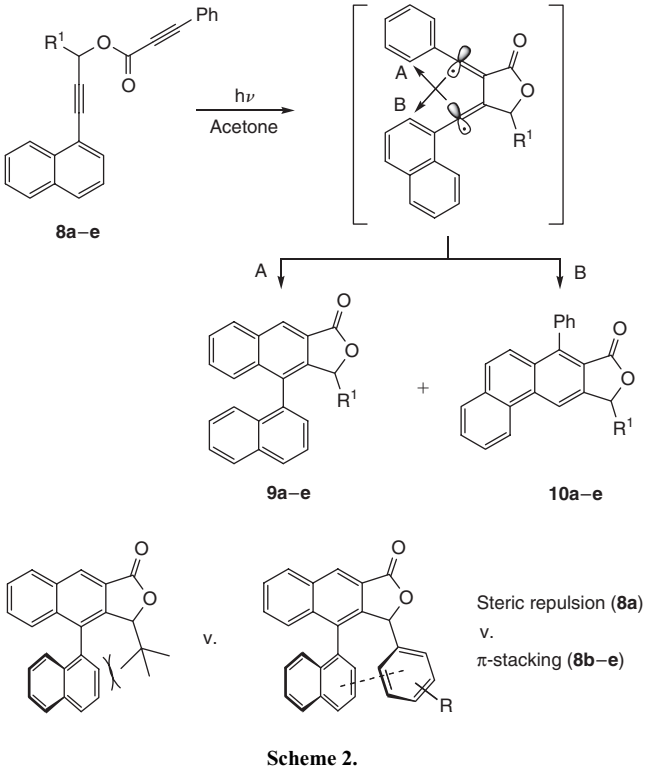
Table 1. Yields of compounds 7 and 8
Mes, 2,4,6-trimethylphenyl

	R^1	R^2	Route[A]	Yield **7** [%]	Yield **8** [%]
a	*t*Bu	H	A	53	86
b	Ph	H	B	>99	>99
c	4-CF_3-Ph	H	A	95	80
d	4-MeO-Ph	H	A	>99	>99
e	Mes	H	B	98	29
f	*t*Bu	OMe	A	44	60
g	Ph	OMe	A	53	>99
h	4-CF_3-Ph	OMe	A	73	>99
i	Mes	OMe	A	52	>99
j	Ph	COOMe	B	10	97
k	Mes	COOMe	B	>99	74

[A] See Scheme 1.

Table 2. Yields of compounds 9a–e and 10a–e
Mes, 2,4,6-trimethylphenyl

	R^1	Yield **9** [%]	Yield **10** [%]	Ratio **9**:**10**
a	*t*Bu	37	47	44:56
b	Ph	39	25	61:39
c	4-CF_3-Ph	44	26	63:37
d	4-MeO-Ph	36	24	60:40
e	Mes	49	22	69:31

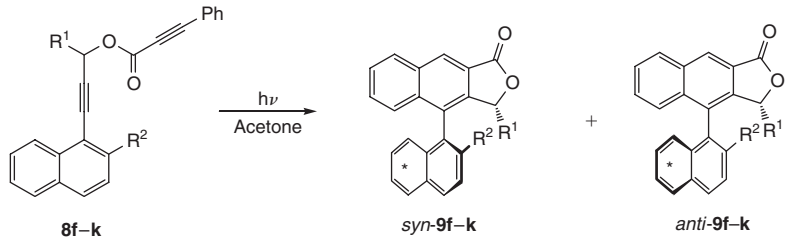


Scheme 2.

on the ratio of *syn*- and *anti*-isomers. The highest selectivity (*syn*:*anti* = 38:62) was observed in the case of compound **8i** bearing a methoxy group as R^2 and a mesityl group as R^1.

Although **8g** also gave a slight preference of the *anti*-isomer, a slightly preferred formation of the *syn*-isomer was observed with **8h**,**j**,**k** (Scheme 3, Table 3).

These results could be explained by a subtle balance between opposing attractive (π-stacking) and repulsive (steric hindrance) forces between R^1 and the naphthyl moiety impeding a reliable forecast of the preferred isomer. It should be noted that the assignment of the isolated products to *anti*- or *syn*-geometry was unambiguous from X-ray structure analysis. As an example, the crystal structure of *anti*-**9h** is depicted in Fig. 1.[12] Interestingly, the structure of *anti*-**9h** also reveals clear evidence for the above-mentioned attractive interaction between R^1 and the lower naphthyl moiety, which is considerably bent towards R^1. This is discernible in the angle between the atoms A, B, C, which amounts to only 169.2° (Fig. 1).



Scheme 3.

Table 3. Yields of compounds 9f–k
Mes, 2,4,6-trimethylphenyl

	R^1	R^2	Yield **9** [%]	d.r. **9**[A]
f	*t*Bu	OMe	86	50:50
g	Ph	OMe	36	43:57
h	4-CF_3-Ph	OMe	75	58:42
i	Mes	OMe	47	**38:62**
j	Ph	COOMe	28	52:48
k	Mes	COOMe	70	57:43

[A] *syn*:*anti* ratio (*syn* and *anti* refer to the relative position of R^1 and the benzene ring marked with an asterisk in Scheme 3).

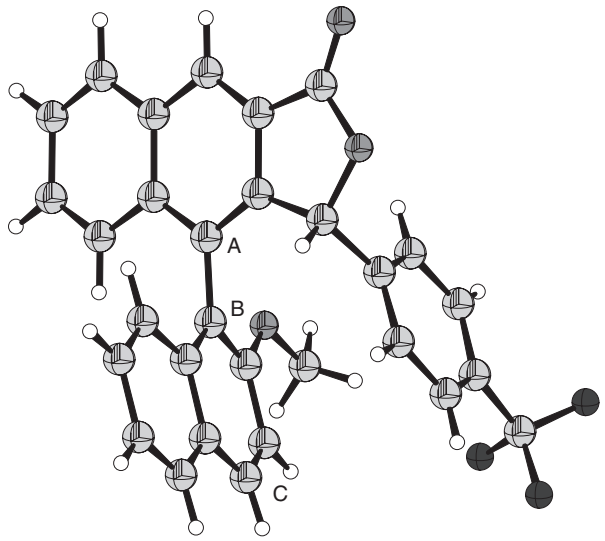


Fig. 1. X-Ray structure of *anti*-**9h**.

In summary, we reported on the synthesis of highly functionalized 1,1′-binaphthyls **9** by PDDA cyclization of esters **8**. Whereas the influence of a bulky alkyl substituent as R^1 on the regio- and stereoselectivity of the cyclization is only marginal, the weak attractive π-stacking interaction between two aryl residues clearly influences the 1,1′-binaphthyl formation. The photochemical behaviour of **8b**–**e** demonstrates, however, that this interaction is not strong enough to suppress the formation of the undesired phenanthrenes **10**. This problem could be circumvented by the introduction of a blocking 2-methoxy group in the reactant **8**. In the case of the resulting esters **8f**–**k**, a weak but clear asymmetric induction from the chiral centre to the newly formed chirality axis was observed. Despite the moderate maximum diastereomeric ratio achieved (38:62, **9i**), this is the first example of a diastereomeric synthesis of a biaryl by a PDDA reaction. From this point of view, the results are very encouraging and it is to be expected that highly stereoselective biaryl synthesis by PDDA reaction will be developed soon.

Experimental

The irradiation of esters **8** was performed in acetone at a concentration of $\sim 10^{-3}$ mol L^{-1} using a high-pressure mercury arc lamp (150 W, TQ150, Heraeus Nobelight GmbH, Hanau, Germany). Light of wavelength below 300 nm was absorbed using a Pyrex glass jacket between the lamp and the reaction vessel. The reaction was monitored by TLC to determine when the reactant had completely disappeared. The solution was concentrated under reduced pressure and the products separated by flash chromatography (petrol ether/EtOAc 20:1) to give the pure photoproducts **9** and/or **10**. In some cases, the diastereomers of **9** were obtained as an inseparable mixture. The ratio of isomers was acquired by irradiation of a 4×10^{-4} M solution of **8** in the appropriate solvent for 1 h, concentration under reduced pressure and determination of the ratio by ^{1}H NMR spectroscopy of the crude reaction mixture.

Exemplarily, the analytical data of compounds *syn*-**9h** and *anti*-**9h** are given:

3-RS-$S_a$$R_a$-*4-(2-methoxy-1-naphthyl)-3-(4-trifluoromethyl phenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (*syn-***9h**): ν_{max}(KBr)/ cm^{-1} 1763, 1313, 1122, 1093. δ_H ($CDCl_3$, 300 MHz) 8.68 (1H, s), 8.17 (1H, d, ^3J 8.5 Hz), 7.96 (1H, d, ^3J 9.1 Hz), 7.66–7.56 (2H, m), 7.47–7.37 (2H, m), 7.29–7.27 (2H, m), 7.13–7.08 (1H, m), 6.80–6.72 (2H, m), 6.52–6.48 (2H, m), 6.23 (1H, s), 6.13 (1H, d, ^3J 8.5 Hz), 3.86 (3H, s). δ_C ($CDCl_3$, 75 MHz) 169.2, 154.5, 143.4, 136.2, 133.8, 132.7, 132.02, 131.6, 130.2, 130.0, 129.3, 129.1, 128.8, 128.4, 128.3, 127.7, 126.7, 124.3 (q, ^3J 4 Hz), 124.0, 123.8, 122.6, 117.3, 112.8, 82.4, 56.6. *m/z* (high resolution mass spectroscopy-electron ionization mass spectrometry) $C_{30}H_{19}F_3O_3$ $[M]^+$ Calc. 484.1286. Found 484.1286.

3-SR-$R_a$$S_a$-*4-(2-methoxy-1-naphthyl)-3-(4-trifluoromethyl phenyl)naphtho[2,3-*c*]furan-1(3*H*)-one (*anti-***9h**): ν_{max} (KBr)/ cm^{-1} 1760, 1322, 1118, 1064. δ_H ($CDCl_3$, 300 MHz) 8.69 (1H, s), 8.17 (1H, d, ^3J 8.3 Hz), 7.95–7.91 (2H, m), 7.63–7.58 (1H, m), 7.47–7.33 (4H, m), 7.24 (2H, m), 7.09–7.05 (1H, m), 6.92 (1H, d, ^3J 9.3 Hz), 6.50 (2H, d, ^3J 8.1 Hz), 5.98 (1H, s), 3.12 (3H, s). δ_C ($CDCl_3$, 75 MHz) 170.7, 154.2, 142.2, 139.9, 136.3, 133.9, 132.7, 130.7, 130.5, 130.2, 130.0, 129.2, 128.7, 128.5, 127.7, 127.5, 127.2, 126.9, 124.5 (q, ^3J 4 Hz), 123.9, 123.5, 122.6, 116.4, 111.8, 82.1, 54.9. *m/z* (HRMS-EI) $C_{30}H_{19}F_3O_3$ $[M]^+$ Calc. 484.1286. Found 484.1286.

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