

Intramolecular aromatic 1,5-hydrogen transfer in preparation of oxacyclic naphthalic anhydride *via* unusual Pschorr cyclisation

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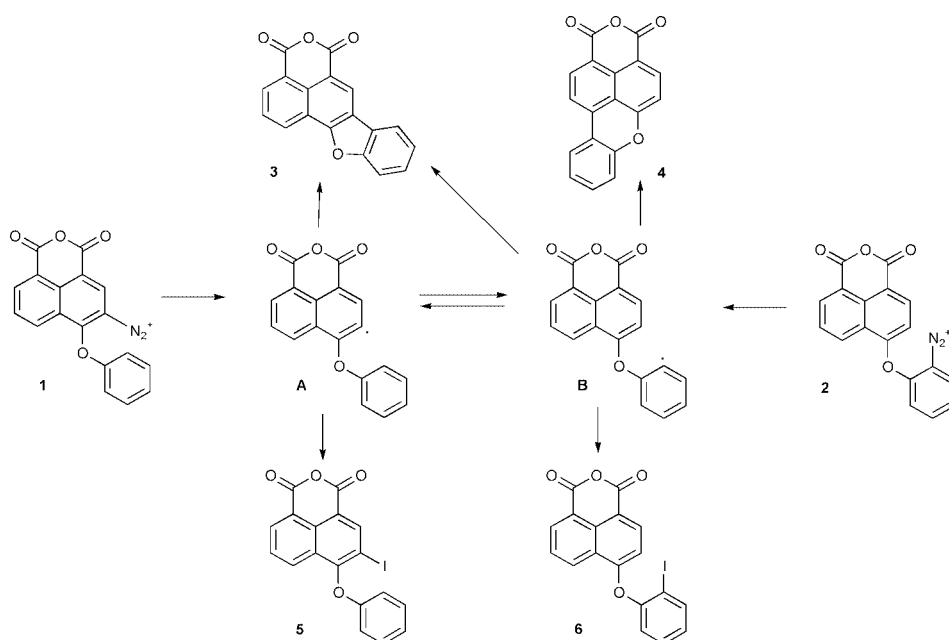
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Unusual Pschorr cyclisation *via* naphthyl radical-induced intramolecular aromatic 1,5-hydrogen transfer using the corresponding diazonium salts as starting materials gave five- and six-membered oxacyclic-fused naphthalic anhydride isomers.

Pschorr cyclisation has been widely used in the preparation of polycyclic compounds¹ for over a century.² Many applications of this reaction can be found in the pharmaceutical and dye industries. Normally, the reaction was accomplished in a three-step mechanism, namely, the diazotization of an *o*-amino group to a diazonium salt; the dediazotiation of the diazonium salt to a radical intermediate; and the closing of the ring. The rearrangements *via* radical-induced aromatic hydrogen migration to produce isomers are rarely found in Pschorr cyclisation because aromatic compounds are usually poor hydrogen donors. In contrast, radical-induced hydrogen migration is commonly seen when the migrating hydrogen originates from an aliphatic carbon or from a heteroatom.^{3,4} After a century of diazonium chemistry, phenyl radical-induced aromatic 1,5-hydrogen migration of the benzophenone derivatives was the only example of such isomerization through Pschorr cyclisation (giving two five-membered ring isomers) and Sandmeyer reaction.^{5,6} Despite the lack of reports for similar isomerizations, it has been speculated that aromatic 1,5-hydrogen transfer might be a general phenomenon in aromatic radical transformations. Recently, we found five- and six-membered oxacyclic isomers during preparation of benzoxanthene derivatives used as fluorescent probes. We report herein the naphthyl radical-induced aromatic 1,5-hydrogen transfer in Pschorr cyclisation of the corresponding diazonium salts.

The diazonium salts **1** and **2** were prepared from 4-bromo-1,8-naphthalic anhydride according to the procedure published earlier⁷ and all intermediates were characterized by ¹H-NMR, MS, IR and elemental analysis.

Pschorr cyclisation of **1** initiated by CuSO₄, CuO, or ferrocene produced two isomeric fluorescent compounds **3** and **4** in over 9:1 ratio (Table 1, entry 1–3). The most plausible explanation for the 9:1 ratio of the isomers is that the initially formed radical **A** rearranged itself to radical **B** by 1,5-hydrogen transfer and that these two radicals in some equilibrium were then converted to the products **3** and **4** (Scheme 1). It has been demonstrated that Pschorr cyclisation and Sandmeyer iododediazotiation of benzophenone derivatives gave cyclized isomers in nearly equal amounts and some iodinated isomers, respectively.⁵ However, in our case, the ratio of the cyclized isomers was far from 1:1 and the iodinated isomers were hardly found. The iododediazotiation of diazonium salts **1** and **2** gave only iodinated compounds **5** and **6**, respectively (entry 6 and 7). It seems that the 1,5-hydrogen transfer rate between **A** and **B** is slower than that between benzophenone radicals according to the literature.⁵ Under similar reaction conditions to entry 1, diazonium salt **2** gave also **3** and **4** in the ratio of 7:93 (entry 5). This suggests that radical **B** could be also rearranged into radical **A** and the rate of formation of **B** from **A** is faster than that of **A** from **B**. This indicates that radical **B** is more stable than radical **A**. Even so, the structure of major product and the ratio of isomers still mainly depended on the starting compounds, as the rate of cyclisation to five- and six-membered rings is obviously faster than that of hydrogen transfer. Beyond what we expected, the mode of radical generation had obvious effects on hydrogen transfer, as various initiation methods



Scheme 1

Table 1 Pschorr cyclisation and Sandmeyer iododediazoniatio of diazonium salts

Entry	Substrate	Reaction	Products	Ratio ^a	Yield ^b (%)
1	1	CuSO ₄ , AcOH, H ₂ O, reflux	3:4	90:10	90 ^c
2	1	Ferrocene, acetone, rt	3:4	94:6	75 ^c
3	1	CuO, H ₂ SO ₄ , rt	3:4	92:8	80 ^c
4	1	CuSO ₄ , AcOH, rt	3:4	83:17	85 ^c
5	2	CuSO ₄ , AcOH, H ₂ O, reflux	3:4	7:93	86 ^c
6	1	KI, I ₂ , H ₂ O, rt	5		73
7	2	KI, I ₂ , H ₂ O, rt	6		88

^a The ratio was determined by HPLC/MS (Hypersil DDS2 column, H₂O + MeOH + AcOH eluent, retention time: **3**, 32 min, **4**, 29 min).^b The yield was based on the corresponding amino compounds.^c The yield was obtained in **3** + **4** mixture.

produced a different ratio of isomers (entries 1–4). It suggests that the rate of 1,5-hydrogen transfer between **A** and **B** is sensitive to the environment and can be enhanced (the ratio of **3** and **4** is 83:17) under the conditions of entry 4. This is different from the case of benzophenone derivatives,⁵ where solvent showed no effect on the rate of hydrogen transfer.

Molecular modeling using Pmodel 6.0 showed some differences in their conformations between these 4-phenoxy-naphthalic anhydride radicals and the benzophenone radicals, although they were in an aromatic conjugated system. Two aromatic rings next to ether O atom for radicals **A** and **B** were not in the same plane, while for the benzophenone radicals, the carbonyl and two aromatic rings were in the same plane. These conformational differences can be used to explain their differences in the efficiency of radical-induced 1,5-hydrogen transfer, the ratio of isomers, and the solvent effects.

In conclusion, our investigation not only provided the first example of isomerization *via* naphthyl radical-induced aromatic 1,5-hydrogen transfer in naphthalene derivatives during Pschorr cyclisation, but also implied that radical induced-aromatic hydrogen transfer possibly was more common than previously thought in many other aromatic free radical reactions.

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Notes and references

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