Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Synthetic Applications of Oxidative Aromatic Coupling—From Biphenols to Nanographenes

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1. Synthesis of small-molecule targets

Intramolecular oxidative coupling of arenes is a convenient method for the synthesis of small-molecule targets such as natural products and drug intermediates, among others. This method is most commonly used for the preparation of 6-membered (benzene) rings, however, in recent years multiple examples of oxidative ring closures of 5-, 7- and 8-membered rings have been reported. The most interesting examples will be discussed in this section.

As demonstrated by Waldvogel and co-workers, $MoCl_5$ and other Mo^V reagents are versatile oxidants for both inter- and intramolecular oxidative couplings of arenes.[S1] Recently it was shown that fluorene derivatives **S1**-**S4** can be readily synthesized from the corresponding diarylmethanes *via* Mo^V-mediated oxidative closure of 5-membered rings (Figure S1).[S2] In general, electron-rich aromatic moieties are required for this reaction to occur. Using $MoCl_5$ as an oxidant, a series of symmetrically or unsymmetrically substituted spirobifluorenes of type **S1** have been prepared in excellent yields. In addition, the authors obtained 9,9-dimethyl-2,3,6,7-tetramethoxyfluorene (**S2**) and spiro-lactam **S3**. $MoCl_5$ or its analogue with two chlorides substituted with the hexafluoroisopropoxide ligands ($MoCl_3[OCH(CF_3)_2]_2$) have also been used in the synthesis of a library of 9-monosubstituted, unsymmetrical fluorenes of the type **S4** (Figure S1).[S3]

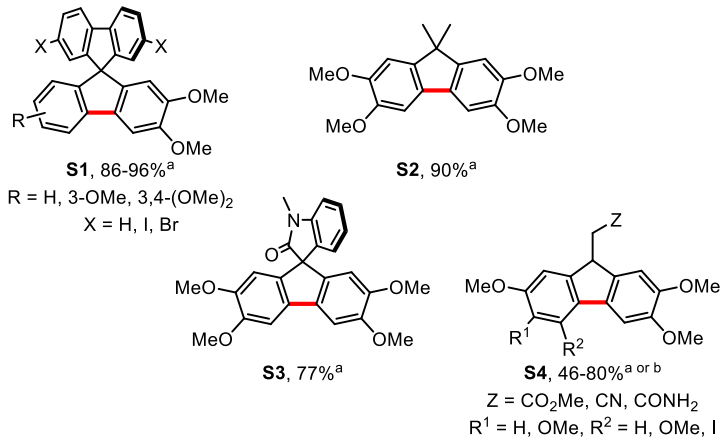
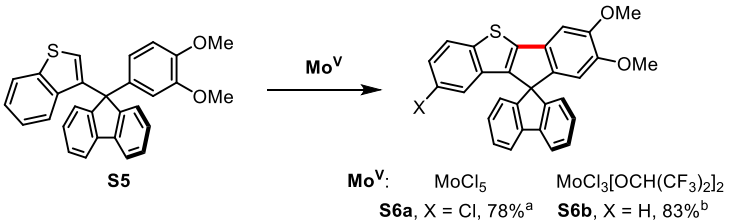


Figure S1. Cyclization conditions: a) $MoCl_5$ (2.2-3.9 eq.), CH_2Cl_2, RT; b) $MoCl_3[OCH(CF_3)_2]_2$ (3 eq.), CH_2Cl_2, RT.

The HFIP-modified oxidant generally leads to higher yields of the corresponding fluorenes with reduced amounts of chlorinated side-products, which had been demonstrated earlier on a broader scope of inter- and intramolecular oxidative couplings.[S4] A very good example is the oxidation of benzothienyl-substituted fluorene **S5**, which with $MoCl_5$ proceeds with the formation of chlorinated spiro-bifluorene analogue **S6a** in high yield, whereas $MoCl_3[OCH(CF_3)_2]_2$ efficiently yields the non-chlorinated product **S6b** (Scheme S1).[S5] Similar to fluorenes, carbazoles can also be synthesized from the corresponding di- or triarylamines by Mo^V-mediated oxidative closure of 5-membered ring.[S6]



Scheme S1. Reaction conditions: a) $MoCl_5$ (3 eq.), CH_2Cl_2, RT; b) $MoCl_3[OCH(CF_3)_2]_2$ (2 eq.), CH_2Cl_2, RT.

Figure S2 depicts some of the small-molecular targets which can be synthesized by oxidative closure of 6-membered rings. As reported by Pelkey and co-workers, PIFA/$BF_3{\cdot}Et_2O$ is a powerful system for the synthesis of phenanthrene derivatives of the type **S7**,[S7] as well as its heterocyclic analogues **S8** and **S9** containing indole moieties.[S8] These compounds are structurally related to the natural product staurosporine, an inhibitor of protein kinase C, and some of them show enhanced biological activities.[S7,S8]

Phenanthrene derivatives such as **S10a**-**c** are considered as synthetic intermediates for important anti-cancer alkaloids from the phenanthro-quinolizidine and -indolizidine families, i.e. tylophorine and cryptopleurine.[S9] The polymethoxy-substituted phenanthrene skeleton can be readily prepared in high yields by cyclization from the corresponding stilbene derivatives using various oxidative conditions: $MoCl_5$ or $MoCl_5/TiCl_4$,[S9] CAN,[S10] or dehydrogenation with 5% Pd on Al_2O_3 in an atmosphere of oxygen (**S10a-c**, Figure S2).[S11] The presence of $TiCl_4$ in the $MoCl_5$-mediated oxidation greatly improves the yield of phenanthrene **S10a** from 80% to 98%.[S9] Higher yields are attributed to the HCl-scavenging properties of $TiCl_4$, which minimizes unwanted chlorination.[S12] Dehydrogenation with Pd/Al_2O_3 under oxygen proved to be an excellent method for the synthesis of triphenylenes, such as **S11a**-**g**.[S11] A similar range of triphenylene derivatives can also be obtained through indirect anodic oxidation in the presence of 5 mol% of DDQ as a redox mediator.[S13]

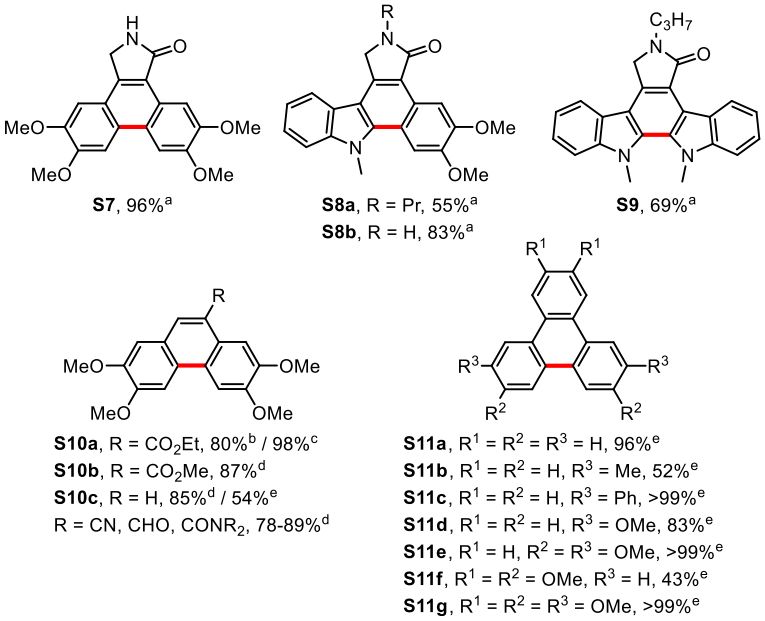


Figure S2. Selected examples of oxidative 6-membered ring closures. Reaction conditions: a) PIFA (1.1 eq.), $BF_3{\cdot}Et_2O$ (1.2 eq.), CH_2Cl_2, −40 °C; b) $MoCl_5$ (2.2 eq.), CH_2Cl_2, RT; c) $MoCl_5$ (2.2 eq.), $TiCl_4$ (2.3 eq.), CH_2Cl_2, 0 °C; d) CAN (2 eq.), $NaHCO_3$ (4 eq.), CH_3CN, RT; e) 5% Pd/Al_2O_3 (5 mol%), O_2 (1 atm), TfOH or MsOH, TFE or HFIP, RT.

Similar cyclizations involving two thienyl groups in the formation of 6-membered rings were performed using $FeCl_3$, $MoCl_5$ or DDQ as oxidants in the syntheses of various sulfur-doped PAHs.[S5,S14–S20]

DDQ[S21] or MnO_2[S22] in the presence of $BF_3{\cdot}Et_2O$ enable the efficient oxidative closure of 7- and 8-membered rings leading to compounds **S12a**-**d** and **S13a**-**d**, respectively, when precursors bearing electron-rich aryl substituents are used as the starting materials (Figure S3).

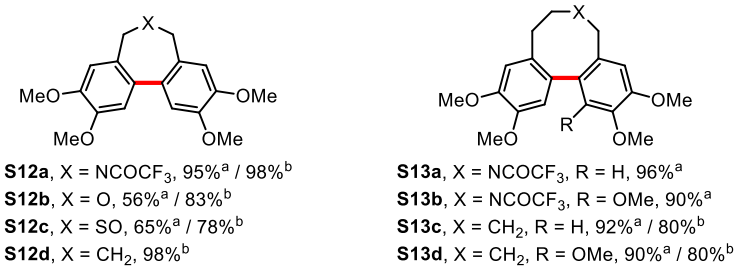
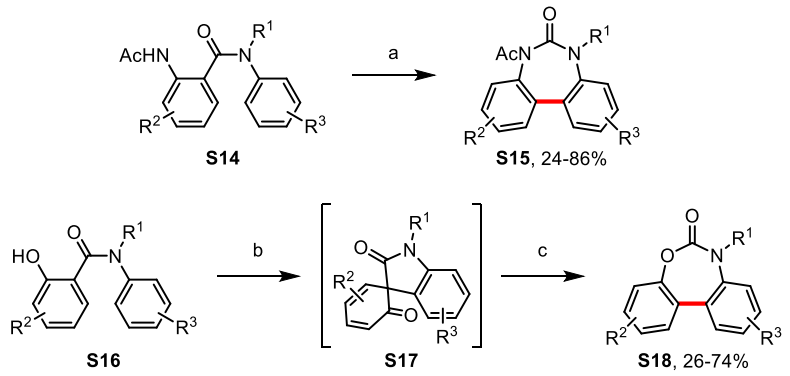


Figure S3. Oxidative closure of 7- and 8-membered rings. Reaction conditions: a) DDQ (1 eq.), $BF_3{\cdot}Et_2O$ (12 eq.), CH_2Cl_2, RT; b) MnO_2 (6 eq.), $BF_3{\cdot}Et_2O$ (3 eq.), CH_2Cl_2, RT.

An interesting method for the oxidative construction of 7-membered rings has been discovered by Du, Zhao and co-workers (Scheme S2).[S23] Upon treatment with PIDA in boiling acetonitrile, benzanilides **S14**, bearing an acetylated amino group at the *ortho*-position relative to the benzanilide carbonyl, underwent oxidative cyclization accompanied by a ring-expanding rearrangement to give biaryl-bridged, 7-membered ring-based ureas **S15** in moderate to good yields. Some mechanistic insights into this process were provided by the fact that the analogous transformation proceeds for hydroxybenzanilides **S16** with PIFA as an oxidant. In this case, however, the reaction is a two-step process and addition of $BF_3{\cdot}Et_2O$ is necessary to convert the initially forming spirocyclic intermediate **S17** into the cyclic carbamates **S18**. The authors suggested that the formation of ureas **S15** also involves a 5-membered-ring intermediate.



R^1 = Alkyl, Aryl; R^2 and R^3 = H, F, Cl, Br, OMe, Alkyl

Scheme S2. Oxidative coupling with a rearrangement to a 7-membered ring. Reaction conditions: a) PIDA (3 eq.), CH_3CN, reflux; b) PIFA (1.3 eq.), CH_2Cl_2, -35 °C or 0 °C; c) $BF_3{\cdot}Et_2O$ (0.3 eq.), RT.

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