ORGANIC
LETTERS

XXXX
Vol. XX, No. XX
000–000

Efficient Diels–Alder Reaction of 1,2-Benzoquinones with Arynes and Its Utility in One-Pot Reactions

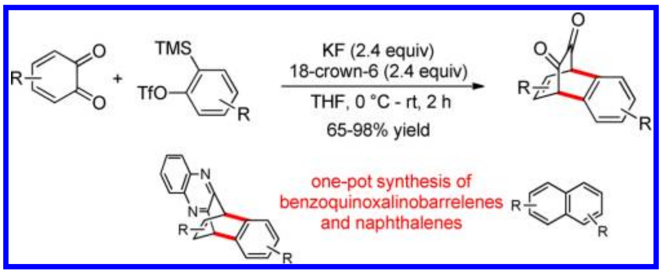
Trinadh Kaicharla, Sachin Suresh Bhojgude, and Akkattu T. Biju*

Organic Chemistry Division, CSIR-National Chemical Laboratory (CSIR-NCL),
Dr. Homi Bhabha Road, Pune-411008, India

at.biju@ncl.res.in

Received October 31, 2012

ABSTRACT



A new protocol for the efficient Diels–Alder reaction of 1,2-benzoquinones with arynes is reported. The aryne generated by the fluoride-induced 1,2-elimination of 2-(trimethylsilyl)aryl triflates undergoes a facile Diels–Alder reaction with 1,2-benzoquinones, affording the dioxobenzobicyclooctadienes in moderate to excellent yields. In addition, this methodology has been applied to the one-pot synthesis of benzoquinoxalinobarrelene and naphthalene derivatives.

1,2-Benzoquinones are a class of compounds endowed with a broad range of interesting reactivity patterns.[1] Since the first report on the Diels–Alder reaction of 1,2-benzoquinones by Smith and Hac in 1936,[2] this versatile class of compounds is known to take part in Diels–Alder reactions in four different modes: as carbodiene, heterodiene, carbodienophile, and heterodienophile.[3] Depending on the substituents and the reaction conditions, 1,2-benzoquinone can act as an excellent carbodiene or heterodiene with a variety of dienophiles. Although the reactivity of 1,2-benzoquinones as a 4π-component with a variety of dienophiles is well-documented (Scheme 1, eq 1),[3,4] application of 1,2-benzoquinones in Diels–Alder reactions with the highly electrophilic C–C triple bond of arynes has received only scant attention.[5] The latter will be attractive because it leads to the direct synthesis of dioxobenzobicyclooctadiene derivatives, which are potentially amenable to a number of synthetic transformations.[6] This includes various photochemical reactions of the bicyclo[2.2.2]-octadiene moiety as well as the reaction of the 1,2-diketo group. Herein, we report an efficient and facile Diels–Alder reaction of 1,2-benzoquinones with arynes generated by the fluoride-induced 1,2-elimination of 2-(trimethylsilyl)-aryl triflates (eq 2).[7] In addition, the synthetic utility of this methodology has been demonstrated by the one-pot

---

[1] (a) Finley, K. T. In *The Chemistry of Quininoid Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: New York, 1988; Vol. 2, p 636. (b) Kharisov, B. I.; Mendez-Rojas, M. A.; Garnovskii, A. D.; Ivakhnenko, E. P.; Ortiz-Mendez, U. *J. Coord. Chem.* **2002**, *55*, 745.

[2] (a) Smith, L. I.; Hac, L. R. *J. Am. Chem. Soc.* **1936**, *58*, 229. For a related report, see: (b) Horner, L.; Spietschka, W. *Ann.* **1953**, *579*, 159.

[3] For reviews, see: (a) Nair, V.; Menon, R. S.; Biju, A. T.; Abhilash, K. G. *Chem. Soc. Rev.* **2012**, *41*, 1050. (b) Nair, V.; Radhakrishnan, K. V. In *Science of Synthesis*; Griesbeck, A., Ed.; Georg Thieme: Stuttgart, Germany, 2006; Vol. 28, p 181. (c) Nair, V.; Kumar, S. *Synlett* **1996**, 1143.

[4] For selected reports, see: (a) Bekele, T.; Shah, M. H.; Wolfer, J.; Abraham, C. J.; Weatherwax, A.; Lectka, T. *J. Am. Chem. Soc.* **2006**, *128*, 1810. (b) Nair, V.; Sethumadhavan, D.; Nair, S. M.; Rath, N. P.; Eigendorf, G. K. *J. Org. Chem.* **2002**, *67*, 7533. (c) Nair, V.; Maliakal, D.; Treesa, P. M.; Rath, N. P.; Eigendorf, G. K. *Synthesis* **2000**, 850. (d) Nair, V.; Kumar, S. *Tetrahedron* **1996**, *52*, 4029. (e) Nair, V.; Kumar, S.; Anilkumar, G.; Nair, J. S. *Tetrahedron* **1995**, *51*, 9155. (f) Ansell, M. F.; Gosden, A. F.; Leslie, V. J.; Murray, R. A. *J. Chem. Soc. C* **1971**, 1401.

[5] Ried, W.; Eng, J. T. S. *Liebigs Ann. Chem.* **1969**, *727*, 219.

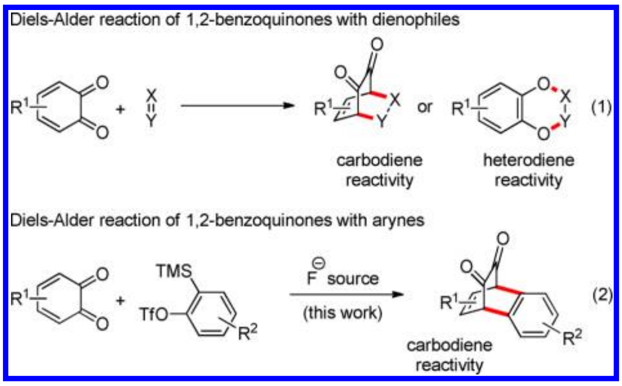
[6] (a) Boyer, J. H.; Srinivasan, K. G. *J. Chem. Soc., Perkin Trans 1.* **1976**, 1583. (b) Boyer, J. H.; Srinivasan, K. G. *J. Chem. Soc., Chem. Commun.* **1973**, 699. (c) Srinivasan, K. G.; Boyer, J. H. *J. Chem. Soc., Chem. Commun.* **1974**, 1026.

[7] For the generation of arynes from 2-(trimethylsilyl)aryl triflates, see: (a) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211. For a modified procedure for the synthesis of the triflate, see: (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.

10.1021/ol302997q

synthesis of benzoquinoxalinobarrelene and naphthalene derivatives. Interestingly, 1,2-benzoquinones manifest carbodiene-type reactivity in the Diels–Alder reactions with arynes.

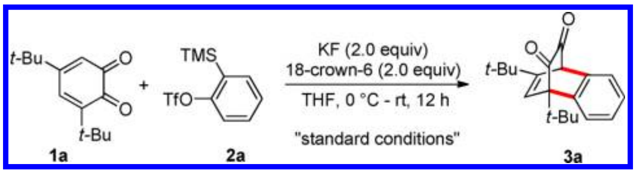
Scheme 1. Diels–Alder Reaction of 1,2-Benzoquinones



Arynes are highly reactive intermediates, which holds potential for numerous applications in organic synthesis for the construction of multisubstituted arenes of structural diversity and intricacy.[8] One of the important reactions of arynes is the Diels–Alder reaction, which is a powerful tool for constructing various carbocycles and heterocycles of synthetic importance.[9] Due to their high electrophilicity, arynes have been shown to react with a wide variety of dienes. Recently, many of the traditional aryne reactions have been revisited using Kobayashi's method for aryne generation, that is, by the treatment of 2-(trimethylsilyl)aryl triflates with a fluoride source, and this protocol has led to a general enhancement in yields.[7,10] We have recently developed an efficient and practical Diels–Alder reaction of pentafulvenes with arynes leading to the formation of benzonorbornadiene derivatives in high yields and broad scope.[11]

In the context of our interest in the chemistry of arynes, the present study was initiated with the treatment of 3,5-di-*tert*-butyl 1,2-benzoquinone **1a** with the aryne generated in situ from 2-(trimethylsilyl)aryl triflate **2a** using 2.0 equiv each of KF and 18-crown-6. Interestingly, the reaction afforded the 1,3-di-*tert*-butyl-1,4-dihydro-1,4-ethano naphthalene-9,10-dione **3a** in 94% yield (based on ^{1}H NMR spectroscopy, Table 1, entry 1). Other fluoride sources, such as CsF, furnished comparable results (entry 2), but the use of tetrabutylammonium fluoride (TBAF) was not found to be helpful (entry 3). Increasing the amount of **1a** improved the yield of **3a** (entry 4). Finally, increasing the amount of aryne precursor **2a** to 1.2 equiv and employing 2.4 equiv each of KF and 18-crown-6 improved the reactivity, with **3a** isolated in 98% yield (entry 5).[12,13]

Table 1. Optimization of the Reaction Conditions[a]



entry	variation from the standard conditions[a]	yield of **3a** (%)[b]
1	none	94
2	CsF instead of KF and 18-crown-6, CH_3CN as the solvent	91
3[c]	TBAF instead of KF and 18-crown-6	<5
4	1.2 equiv of **1a** instead of 1.0 equiv	97
5[d]	1.2 equiv of **2a** instead of 1.0 equiv, 2.4 equiv each of KF and 18-crown-6	>99 (98)

[a] Standard conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), KF (2.0 equiv), 18-crown-6 (2.0 equiv), THF (1.0 mL), 0 °C to rt and 12 h. [b] Yields were determined by ^{1}H NMR analysis of crude products using CH_2Br_2 as the internal standard. Isolated yield at 0.50 mmol scale in parentheses. [c] Decomposition of **1a** was observed. [d] Reaction mixture stirred at rt for 2 h.

With these optimized reaction conditions in hand, we then examined the substrate scope of this 1,2-benzoquinone aryne Diels–Alder reaction (Scheme 2).[14] The 3,5-di-*tert*-butyl 1,2-benzoquinone **1a** worked well, and disubstitution

---

(8) For reviews, see: (a) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (b) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (c) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (d) Okuma, K. *Heterocycles* **2012**, *85*, 515. (e) Chen, Y. Larock, R. C. In *Modern Arylation Methods*; Ackermann, L., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2009; p 401. (f) Sanz, R. *Org. Prep. Proced. Int.* **2008**, *40*, 215. (g) Yoshida, H.; Ohshita, J.; Kunai, A. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 199. (h) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502. (i) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701. (j) Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, p 483. For highlights, see: (k) Bhojgude, S. S.; Biju, A. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 1520. (l) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579. For a recent account, see: (m) Yoshida, H.; Takaki, K. *Synlett* **2012**, *23*, 1725.

(9) For selected recent reports, see: (a) Xie, C.; Zhang, Y. *Org. Lett.* **2007**, *9*, 781. (b) Shou, W.-G.; Yang, Y.-Y.; Wang, Y.-G. *J. Org. Chem.* **2006**, *71*, 9241. (c) Criado, A.; Peña, D.; Cobas, A.; Guitián, E. *Chem.—Eur. J.* **2010**, *16*, 9736. (d) Buszek, K. R.; Luo, D.; Kondrashov, M.; Brown, N.; VanderVelde, D. *Org. Lett.* **2007**, *9*, 4135. (e) Ikawa, T.; Takagi, A.; Kurita, Y.; Saito, K.; Azechi, K.; Egi, M.; Kakiguchi, K.; Kita, Y.; Akai, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5563. (f) Dockendroff, C.; Sahil, S.; Olsen, M.; Milhau, L.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 15028. (g) Li, J.; Wang, N.; Li, C.; Jia, X. *Org. Lett.* **2012**, *14*, 4994. (h) Im, G.-Y.; Bronner, S. M.; Goetz, A. E.; Paton, R. S.; Cheong, P. H.-Y.; Houk, K. N.; Garg, N. K. *J. Am. Chem. Soc.* **2010**, *132*, 17933.

(10) For selected recent reports, see: (a) Rodríguez-Lojo, D.; Cobas, A.; Peña, D.; Pérez, D.; Guitián, E. *Org. Lett.* **2012**, *14*, 1363. (b) Fang, Y.; Rogness, D. C.; Larock, R. C.; Shi, F. *J. Org. Chem.* **2012**, *77*, 6262. (c) Li, P.; Wu, C.; Zhao, J.; Rogness, D. C.; Shi, F. *J. Org. Chem.* **2012**, *77*, 3149. (d) Rogness, D. C.; Markina, N. A.; Waldo, J. P.; Larock, R. C. *J. Org. Chem.* **2012**, *77*, 2743. (e) Lu, C.; Dubrovskiy, A. V.; Larock, R. C. *J. Org. Chem.* **2012**, *77*, 2279. (f) Kim, J. M.; Stoltz, B. M. *Tetrahedron Lett.* **2012**, *53*, 4994. (g) Pirali, T.; Zhang, F.; Miller, A. H.; Head, J. L.; McAusland, D.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2012**, *51*, 1006. (h) Markina, N. A.; Dubrovskiy, A. V.; Larock, R. C. *Org. Biomol. Chem.* **2012**, *10*, 2409. (i) Zhao, J.; Li, P.; Wu, C.; Chen, H.; Ai, W.; Sun, R.; Ren, H.; Larock, R. C.; Shi, F. *Org. Biomol. Chem.* **2012**, *10*, 1922.

(11) Bhojgude, S. S.; Kaicharla, T.; Bhunia, A.; Biju, A. T. *Org. Lett.* **2012**, *14*, 4098.

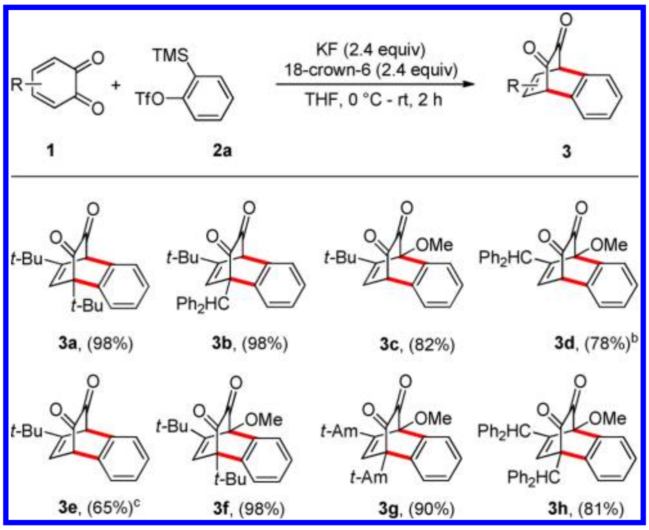
(12) For details, see the Supporting Information.

(13) The same yield was obtained from a 2.0 mmol scale reaction.

(14) The 1,2-benzoquinones were synthesized by the Friedel–Crafts alkylation of catechol derivative followed by the oxidation using $NaIO_4$. For details, see ref 3b.

at various positions of the 1,2-benzoquinones was well-tolerated and led to dioxobenzobicyclooctadienes in good to excellent yield (**3a**–**3d**). Interestingly, monosubstituted 1,2-benzoquinone resulted in the smooth formation of cycloadduct **3e** in 65% yield. Moreover, trisubstituted 1,2-benzoquinones also furnished good to excellent yields of the desired products, further expanding the scope of this 1,2-benzoquinone aryne Diels–Alder reaction. It is noteworthy, however, that in preliminary experiments commercially available 1,2-benzoquinones such as *o*-chloranil failed to undergo this cycloaddition under the optimized reaction conditions.[15]

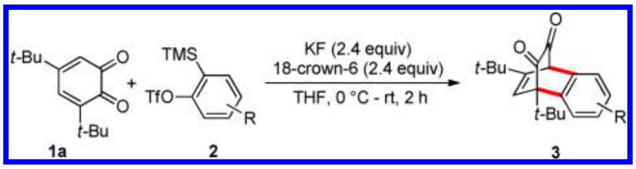
Scheme 2. Diels–Alder Reaction of 1,2-Benzoquinones with Benzyne[a]

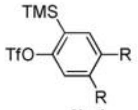
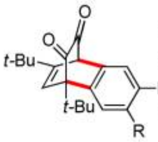
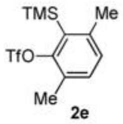
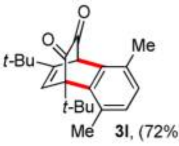
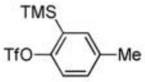
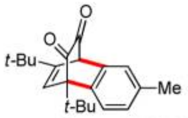
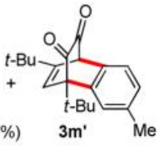
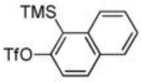
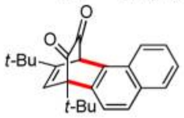
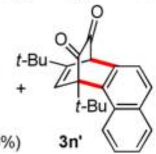


[a] General conditions: **1** (0.50 mmol), **2a** (0.60 mmol), KF (2.4 equiv), 18-crown-6 (2.4 equiv), THF (2.0 mL), 0 °C to rt and 2 h. Yields of the isolated products are given. [b] ^{1}H NMR yield of the product is given. [c] Reaction was carried out using 1.0 equiv of **2a** and 1.5 equiv of **1e** and 2.0 equiv each of KF and 18-crown-6.

In view of these interesting results, we next examined the effect of varying the substituents on the aryne precursor **2** (Table 2). Electronically dissimilar 4,5-disubstituted symmetrical aryne precursors **2b**–**d** readily furnished the dioxobenzobicyclooctadienes **3i**–**k** in good to excellent yields (entries 1–3). Moreover, the 3,6-dimethyl-substituted symmetrical aryne precursor **2e** worked well to afford product **3l** in 72% yield (entry 4). Additionally, the reaction of the unsymmetrical aryne generated from **2f** resulted in the formation of an inseparable mixture of regioisomers **3m/3m′** in a 1:1 ratio (entry 5). Furthermore, the unsymmetrical naphthalyne derived from **2g** underwent efficient cycloaddition to deliver an inseparable mixture of regioisomers **3n** and **3n′** in 95% overall yield (entry 6).

Table 2. Diels–Alder Reaction of 3,5-Di-*tert*-butyl 1,2-Benzoquinone with Arynes



entry	aryne precursor	product(s), yield (%)
1 2 3	 **2b-d**	 **3i**, R = Me, (97%)[b] **3j**, R = $O(CH_2)O$, (92%)[c] **3k**, R = F, (66%)[c,d]
4	 **2e**	 **3l**, (72%)[b]
5	 **2f**	 **3m** +  **3m′** [1:1][e], (97%)
6	 **2g**	 **3n** +  **3n′** [2:1][e], (95%)

[a] General conditions: **1** (0.50 mmol), **2a** (0.60 mmol), KF (2.4 equiv), 18-crown-6 (2.4 equiv), THF (2.0 mL), 0 °C to rt and 2 h. Yields of the isolated products are given. [b] Reaction mixture stirred for 3 h at rt. [c] Reaction was run on 0.25 mmol scale. [d] 1.5 equiv of **2d** was used. [e] The regioisomer ratio was determined by ^{1}H NMR analysis of the crude reaction mixture.

The synthetic utility of the aryne Diels–Alder reaction has been demonstrated by the efficient one-pot synthesis of benzoquinoxalinobarrelene derivatives.[16] Thus treatment of 1,2-benzoquinones **1** with aryl triflates **2** under the optimized reaction conditions followed by the addition of 1,2-phenylenediamine resulted in the one-pot synthesis of benzoquinoxalinobarrelenes **4** in good to excellent yields (Scheme 3). The disubstituted 1,2-benzoquinones and even monosubstituted 1,2-benzoquinones worked well in the one-pot operation, leading to good to excellent yield of the product (**4a**, **4b**).[17] In addition, a symmetric aryne precursor **2c** derived from sesamol resulted in the smooth conversion to the bicyclic product in 95% yield (**4c**), further expanding the scope of this one-pot reaction. Evidently, the one-pot reaction has advantages over the two-step reaction as it allows the rapid construction of benzoquinoxalinobarrelenes, thus reducing labor, waste, affording the same/better yield compared to a stepwise

---

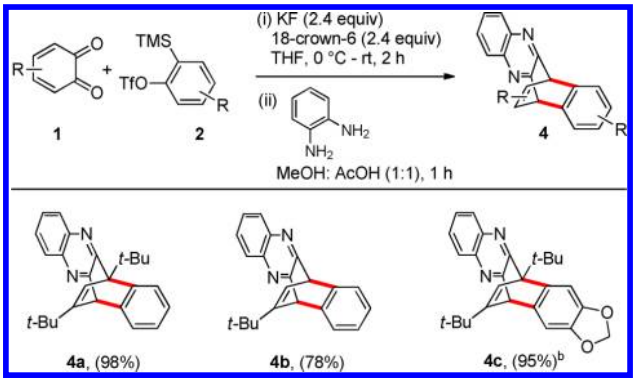
(15) It may be noted that commercially available 1,2-quinones such as acenaphthenequinone and phenanthrenequinone did not show any heterodiene reactivity with arynes under the optimized conditions.

(16) Benzoquinoxalinobarrelenes are potential candidates for photochemical rearrangement reactions. For details, see refs 6a and 6c.

(17) Interestingly, the synthesis of **4b** from the corresponding 1,2-benzoquinone resulted in 65% overall yield for the two steps, whereas the one-pot operation afforded the product in 78% yield.

process, and utilizing the use of more readily available starting materials.[18]

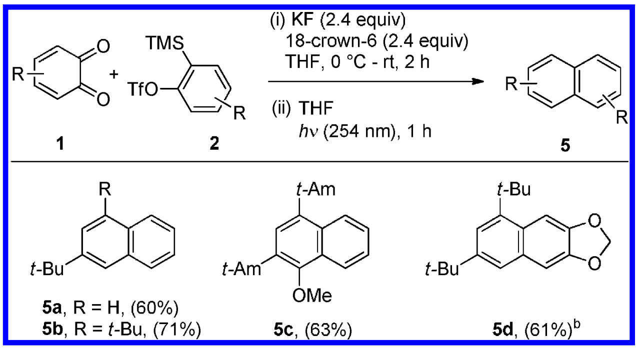
Scheme 3. One-Pot Synthesis of Benzoquinoxalinobarrelenes from 1,2-Benzoquinones and Triflates **2**[a]



[a] General conditions: **1** (0.50 mmol), **2a** (0.60 mmol), KF (2.4 equiv), 18-crown-6 (2.4 equiv), THF (2.0 mL), 0 °C to rt and 2 h, followed by addition of *o*-phenylenediamine (1.5 equiv) in MeOH/AcOH (1:1). Yields of the isolated products are given. [b] Reaction was run on 0.25 mmol scale.

The synthetic potential of the 1,2-benzoquinone aryne [4 + 2] cycloaddition reaction was further examined by the one-pot synthesis of naphthalene derivatives. It should be noted that naphthalene derivatives are ubiquitously present in many natural products and pharmaceuticals.[19] The reaction of 1,2-benzoquinones **1** with triflates **2** under the optimized reaction conditions followed by the irradiation of the reaction mixture at 254 nm afforded the one-pot synthesis of naphthalene derivatives (Scheme 4).[20] This one-pot reaction works well with mono-, di-, and even trisubstituted 1,2-benzoquinones to deliver the functionalized naphthalenes in moderate to good yields (**5a**–**5c**). Moreover, the symmetric aryne precursor **2c** was also well-tolerated to furnish the tetrasubstituted naphthalene **5d** in 61% yield in a one-pot operation. It may be noted that the mechanistic details of the decarbonylation of similar adducts was known as early as 2002.[21]

Scheme 4. One-Pot Synthesis of Naphthalenes from 1,2-Benzoquinones and Triflates **2**[a]



[a] General conditions: **1** (0.50 mmol), **2a** (0.60 mmol), KF (2.4 equiv), 18-crown-6 (2.4 equiv), THF (2.0 mL), 0 °C to rt and 2 h, then dilution (THF, 12.0 mL) and irradiation at 254 nm for 1 h. Yields of the isolated products are given. [b] Reaction was run on 0.25 mmol scale.

In conclusion, we have developed an efficient and practical Diels–Alder reaction of 1,2-benzoquinones with arynes, leading to dioxobenzobicyclooctadiene derivatives in high yields. It is noteworthy that dioxobenzobicyclooctadienes are potentially amenable to a number of synthetic transformations. In addition, the application of this mild cycloaddition reaction has been demonstrated by the one-pot synthesis of benzoquinoxalinobarrelene and naphthalene derivatives. Efforts to expand the Diels–Alder reaction of arynes with challenging dienes are ongoing in our laboratory.

Acknowledgment. Generous financial support from CSIR-NCL (start-up grant to A.T.B., MLP022426), CSIR-New Delhi (Network project ORIGIN, and for the award of SPM Fellowship to T.K., and Junior Research Fellowship to S.S.B.) is gratefully acknowledged. We thank Dr. P.R. Rajamohanan (CSIR-NCL) for the NMR spectra, Dr. C.S. Gopinath (CSIR-NCL) for extending the facility for conducting the photochemical reactions, and Ms. B. Santhakumari (CSIR-NCL) for HRMS data.

Supporting Information Available. Experimental procedures and full spectroscopic data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

---

(18) For recent reviews on one-pot reactions, see: (a) Albrecht, Ł.; Jiang, H.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 8492. (b) Climent, M. J.; Corma, A.; Iborra, S. *Chem. Rev.* **2011**, *111*, 1072. (c) Walji, A. M.; MacMillan, D. W. C. *Synlett* **2007**, 1477.

(19) For selected reviews, see: (a) Kilian, P.; Knight, F. R.; Woollins, J. D. *Chem.—Eur. J.* **2011**, *17*, 2302. (b) Cai, Y.-S.; Guo, Y.-W.; Krohn, K. *Nat. Prod. Rep.* **2010**, *27*, 1840.

(20) For a related bisdecarbonylation of bicyclic adducts derived from 1,2-benzoquinones and acetylenic compounds, see: Thomas, A.; Anilkumar, G.; Nair, V. *Tetrahedron* **1996**, *52*, 2481.

(21) Nair, V.; Maliakal, D. *Res. Chem. Intermed.* **2002**, *28*, 337.