Olefin Functionalization

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Quinone Diazides for Olefin Functionalization**

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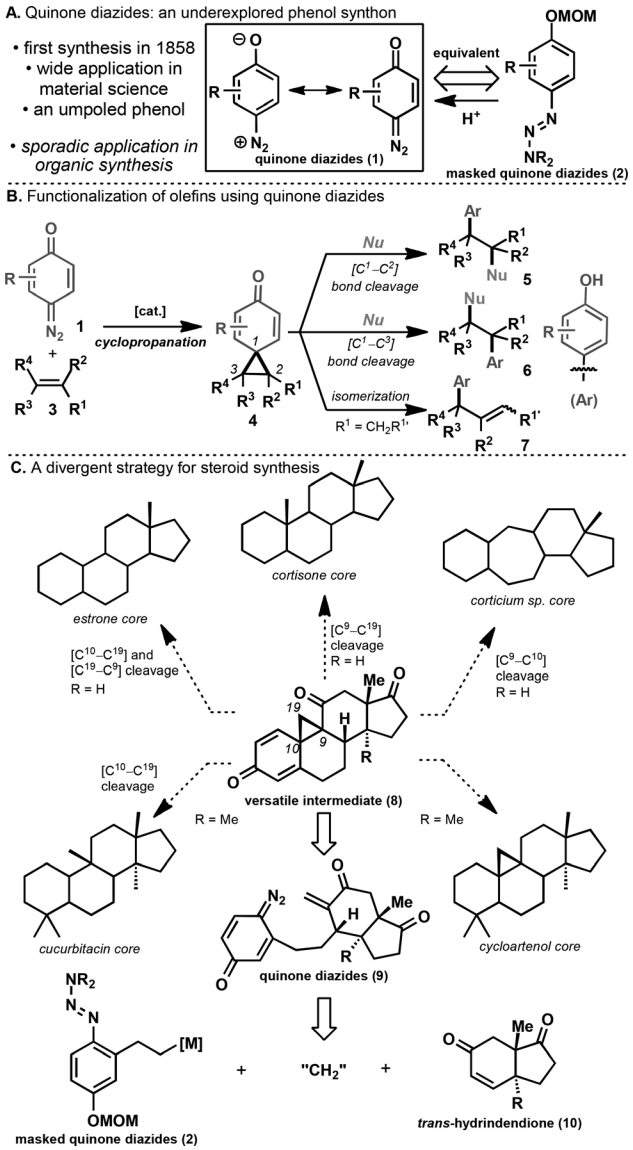
Abstract: *The utility of quinone diazides in materials science is vast and well-documented, yet this potentially useful motif has languished in the annals of organic synthesis. Herein we show that modern tools of catalysis can be employed with free or suitably masked quinone diazides to unleash the power of these classic diazo compounds in the context of both inter- and intramolecular olefin cyclopropanation.*

Quinone diazides (or arene diazo oxides; *p*-quinone diazides **1**, Scheme 1A) are among the oldest diazo compounds, with the first documented occurrence in 1858.[1] Owing to their high reactivity, a range of applications has emerged in disparate fields such as polymer chemistry,[2a] photolithography,[2b] photoaffinity labeling,[2c,d] and electronic and optical materials.[2e,f,g] Typically, they are synthesized by the diazotization of an aminophenol or functionalization of an aniline or phenol; the resulting quinone diazides can be isolated or used in situ.[1] The 1960s to 1980s represented a "golden age" of quinone diazide chemistry, with a great focus on azo coupling, thermolysis and photolysis-promoted Wolff-type rearrangements, and decomposition of the diazo moiety to the corresponding cyclohexadienone carbene.[1a,3] This final mode of reactivity presents an untapped opportunity for synthesis, since these carbenes render a phenol electrophilic at its normally nucleophilic *para* or *ortho* position. However, a lack of efficient and mild synthetic methods to manipulate quinone diazides likely contributed to the paucity of applications for the construction of complex molecules. Our interest in this underexplored species stemmed from the structurally ornate cyclopropanes that might be generated from their union with olefins (Scheme 1B). These versatile compounds could be either nucleophilically opened or isomerized. Herein, a method for harnessing the reactive carbenes derived from quinone diazides by using modern catalysts to achieve a general catalytic intermolecular functionalization of olefins with these classic species is reported.[4] In addition, a simple storage and mild release of quinone diazides in an intramolecular context has enabled a unique divergent approach to steroid synthesis (Scheme 1C).



Scheme 1. Quinone diazides and masked quinone diazides in organic synthesis.

Quinone diazides can be classified as carbonyl diazo compounds bearing two electron-acceptor groups.[5,6] This class of diazo substrates possesses higher stability, thus making them less susceptible toward metal-catalyzed decomposition. Therefore, harsh conditions, such as elevated temperature or reactive catalysts, are often required for the formation of metal carbenoids.[5a,d,6] Furthermore, these highly electrophilic carbenoids are prone to side reactions such as carbene dimerization and hydride transfer to form zwitterionic intermediates. In addition to these potential challenges, the resulting cyclopropanes **4** (Scheme 1B) are

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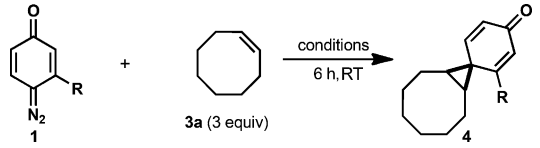
prone to undergo C–C cleavage-induced rearomatization. Thus, to promote this two-step olefin functionalization, mild conditions for the cyclopropanation step and selective conditions for the cleavage step are required. With this in mind, optimization was initially focused on the intermolecular cycloaddition of quinone diazide **1a** and cyclooctene **3a** (Table 1). Monosubstituted quinone diazide **1a** was selected

Table 1: Optimization of the cyclopropanation of quinone diazides **1** and olefin **3a**.



Entry	**1**	Cat. (5 mol%)	Solvent	Conv. [%][a]	Yield [%]
1	**1a** (R = Br)	–	CH_2Cl_2	NR	–
2	**1a** (R = Br)	$[Rh_2(OAc)_4]$	CH_2Cl_2	< 5	–
3[b]	**1a** (R = Br)	$[Rh_2(OPiv)_4]$	CH_2Cl_2	40	10
4	**1a** (R = Br)	$[Rh_2(hfb)_4]$	CH_2Cl_2	20	5
5	**1a** (R = Br)	$[Rh_2(esp)_2]$	CH_2Cl_2	full conv	35
6[c]	**1a** (R = Br)	$[Cu(acac)_2]$	CH_2Cl_2	NR	–
7	**1a** (R = Br)	$AgSbF_6$	CH_2Cl_2	NR	–
8	**1a** (R = Br)	$[Rh_2(esp)_2]$	hexanes	< 20	–
9	**1a** (R = Br)	$[Rh_2(esp)_2]$	Et_2O	< 30	–
10[d]	**1a** (R = Br)	$[Rh_2(esp)_2]$	benzene	full conv	–
11[e]	**1a** (R = Br)	$[Rh_2(esp)_2]$	CH_2Cl_2	full conv	66[f]
12[e]	**1a′** (R = H)	$[Rh_2(esp)_2]$	CH_2Cl_2	full conv	44

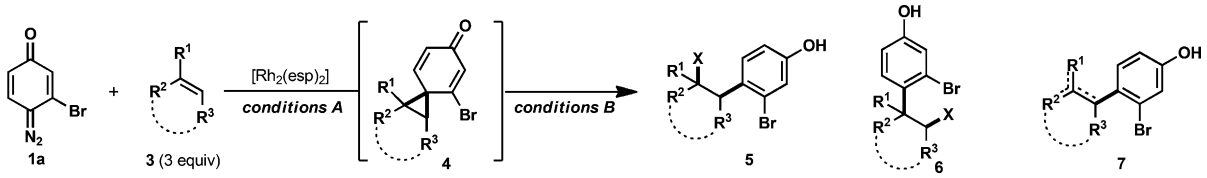
[a] Consumption of **1** determined by ^{1}H NMR spectroscopic analysis of crude materials. [b] Catalyst decomposed. [c] Stoichiometric loading. [d] Only a by-product resulting from reaction with the solvent was obtained. [e] Molecular sieves (4 Å MS) were used as the additive; slow addition of quinone diazide **1** over 5 h, then additional 4 h at RT. [f] A single diastereomer was obtained. Piv = pivaloyl, esp = α,α,α',α'-tetramethyl-1,3-benzenedipropionate, acac = acetyl acetonate, hfb = heptafluorobutyrate, NR = no reaction.

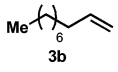
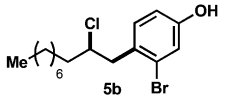
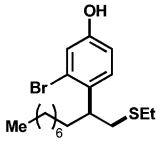
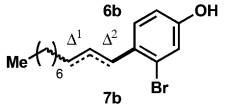
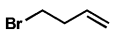
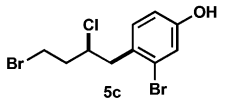
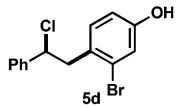
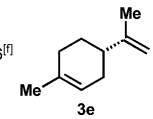
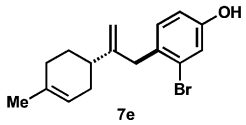
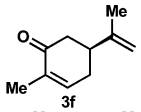
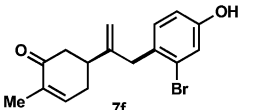
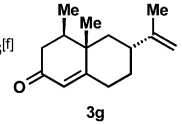
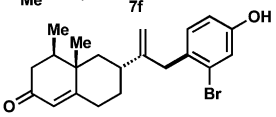
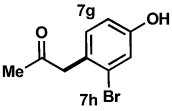
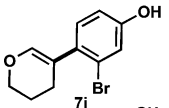
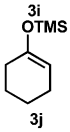
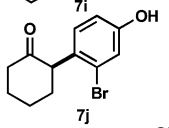
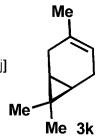
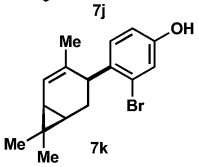
due to its ease of synthesis from the corresponding aminophenol, and the synthetic versatility of the products. In the first experiments, the uncatalyzed reaction between quinone diazide **1a** and cyclooctene (**3a**; 3 equiv) did not occur, and a catalytic amount of $[Rh_2(OAc)_4]$ proved to be ineffective (entries 1 and 2). Encouragingly, when the more soluble $[Rh_2(OPiv)_4]$ was employed, a substantial amount of decomposition of **1a** was observed, together with a small amount of the desired cyclopropane adduct **4a** (R = Br; entry 3). It is notable that the coupling product between **1a** and pivalate anion was also isolated, thus indicating decomposition of the catalyst. Strikingly, when the more reactive $[Rh_2(hfb)_4]$ catalyst was employed, nitrogen extrusion from quinone diazide **1a** was less effective (entry 4 versus entry 3).[5a] To our delight, when the more stable $[Rh_2(esp)_2]$ was employed, the decomposition of the diazo moiety occurred efficiently with substantial improvement in the yield of the isolated desired coupling adduct **4a** (entry 5 versus entry 4).[7] Other metal catalysts, $[Cu(acac)_2]$ and $AgSbF_6$, did not promote the desired reaction under the same conditions even with the use of stoichiometric loading (entries 6 and 7). The use of CH_2Cl_2 as solvent and a slow addition procedure, in combination with the use of molecular sieves, improved the yield of the isolated cyclopropanation product (entries 8–11). In addition, under these optimal conditions, unsubstituted quinonediazide **1a'** reacted with **3a** to yield **4a′** (R = H) in good yield (entry 12).

Next, the substrate scope including the proposed selective C–C bond cleavage was investigated (Table 2). Cycloaddition of monosubstituted olefin **3b** under optimized conditions proceeded smoothly even with a lower catalyst loading (2 mol%). Selective C–C bond cleavage was investigated in a one-pot procedure. Thus, immediately after the cyclopropanation, exposure of the mixture to HCl initiated an S_N1-type reaction, thereby leading to the formation of **5b** in an excellent yield. This reaction represents a rare example of a direct olefin chloroarylation.[8] In another example of unique olefin difunctionalization, the use of a sulfur-based nucleophile on cyclopropane **4b** led to the selective cleavage of the other C–C bond (presumably through an S_N2-type mechanism) to give **6b** in high yield. As a testament to the versatility of quinone diazide/olefin adducts, formal isomerization of **4b** could be achieved (TMSOTf/Et_3N) to give unsaturated products **7b** in high yield. Other monosubstituted olefins, including aliphatic bromide **3c**, also participated in the one-pot, two-step sequence to give good yields of the difunctionalized products (**5c** and **5d**). The functionalization of 1,1-disubstituted olefins was investigated with the use of readily available terpenes (**3e–g**). Under optimized conditions, the coupling of these natural products and quinone diazide **1a** proceeded smoothly to yield formal allylic oxidation adducts (**7e–g**). It is thought that in situ formed cyclopropanes (**4e–g**) readily undergo isomerization to these phenolic coupling products. Hetero-substituted olefins such as **3h–j** also resulted in phenolic products (**7h–j**) with good yields under mild conditions. Trisubstituted olefins such as **3j** and **3k** are less reactive under the same reaction conditions, and the more nucleophilic **3j** gave a higher yield than **3k**.

The steroid skeleton was targeted to evaluate the use of quinone diazides in the context of complex molecule synthesis. Steroids are ubiquitous and can be classified on the basis of the structure of various core skeletons: estrone (estranes), cortisone (cholestanes, cholanes, pregnanes, and androstanes), corticium sp., cycloartenol, and cucurbitacin (Scheme 1C). A divergent strategy to access different steroid scaffolds by a single pathway is challenging. In this context, intermediate **8** was envisioned to be a versatile precursor to access these different skeletons through selective C–C bond cleavage and isomerization events. Synthesis of this steroid skeleton, potentially accessible from quinone diazide **9**, would require a method to store and generate a quinone diazide moiety under extremely mild conditions. A practical precursor of a quinone diazide that could be both easily installed and unveiled was therefore designed. Since its resonance structure is an oxyaryldiazonium zwitterion (Scheme 1A), it was anticipated that methoxymethyl (MOM) and triazene groups would effectively shield the oxyanion and diazo species, respectively, and be easily unmasked under mildly acidic conditions.[9] This masked quinone diazide was anticipated to arise from the union of triazenes **2** with *trans*-bicyclic

Table 2: Substrate scope for functionalization of olefin **3b–k** with quinone diazide **1a**.



Entry[a]	Olefins	Conditions B	Products	Yield [%] (isomer ratio)
1[b]	 **3b**	HCl	 **5b**	93 (33:1)
2[c]	**3b**	EtSH	 **6b**	63 (3.5:1)
3[d]	**3b**	TMSOTf/Et_3N	 **7b**	79 (Δ^1:Δ^2 = 3.3:1)
4[b]	 **3c**	HCl	 **5c**	53
5[e]	 **3d**	LiCl	 **5d**	56
6[f]	 **3e**	None	 **7e**	67
7[f]	 **3f**	none	 **7f**	57
8[f]	 **3g**	none	 **7g**	46
9[g,h]	 **3h**	none	 **7h**	69
10[f,i]	 **3i**	none	 **7i**	39
11[g,i]	 **3j**	none	 **7j**	48
12[f,j]	 **3k**	none	 **7k**	24

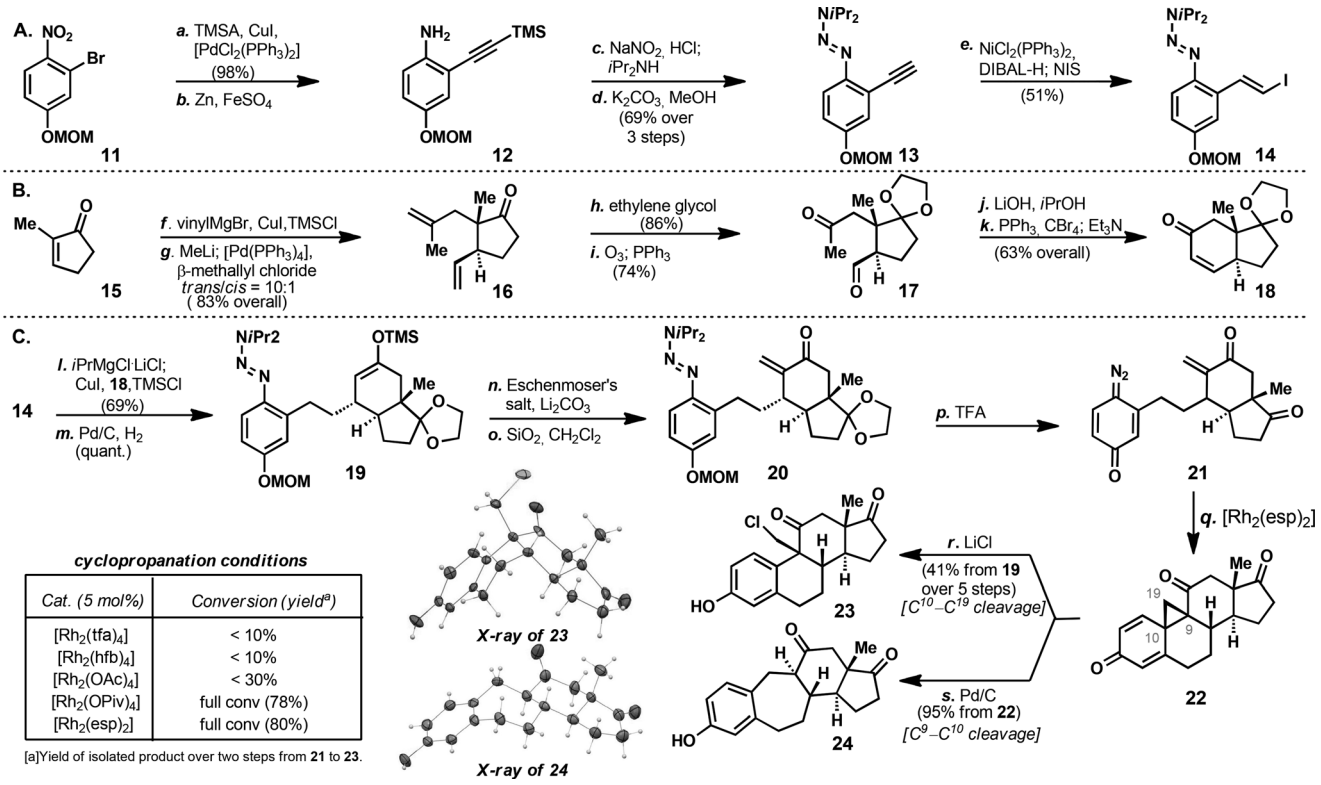
[a] Conditions A: Slow addition of **1a**, $[Rh_2(esp)_2]$ (2–5 mol%), CH_2Cl_2, 15–45 °C. Conditions B: [b] HCl (2 equiv), −78 °C to RT. [c] EtSH (25 equiv), −78 °C to RT. [d] TMSOTf (10 equiv), Et_3N (14 equiv), 0 °C to RT. [e] LiCl, −78 °C to RT. [f] Isomerization occurred during the course of the reaction and/or quenching. [g] Hydrolysis during quenching. [h] 2 equiv of **3h** was used. [i] 1.5 equiv of **3i** and **3j** was used. [j] 5 equiv of **3k** was used.

enones **10** by conjugate addition followed by trapping with a one-carbon electrophile (Scheme 1C).

The synthesis of triazene **14** commenced from bromophenol derivative **11** (Scheme 2A). In the event, **11** underwent coupling with trimethylsilylacetylene (TMSA) under standard Sonogashira reaction conditions to afford the desired nitro product in 98% yield. After reduction of the nitro group, triazene formation was achieved by diazotization of the resulting amine moiety followed by trapping with iPr_2NH.[9a] Removal of the TMS group gave triazene **13** in 69% yield over 3 steps. Lastly, vinyl iodide **14** was synthesized from alkyne **13** by nickel-catalyzed hydroalumination, followed by in situ trapping with NIS (51% yield).[10]

The precursor to the right-hand side of intermediate **8**, *trans*-hydrindenone **18** was prepared in a concise sequence (Scheme 2B) inspired by past successes to access such scaffolds from the Denmark as well as Nakamura and Kuwajima research groups.[11] Thus, copper-catalyzed conjugate addition of vinylmagnesium bromide to enone **15** followed by trapping with TMSCl was conducted. Allylation of the resulting silyl enol ether was achieved under Tsuji–Trost conditions to give *trans* ketone **16** in high yield (83% yield over 2 steps) with high diastereoselectivity (*trans*/*cis* = 10:1).[12] Ketone **16** was then protected with ethylene glycol (86% yield), followed by ozonolysis of both terminal olefinic moieties to give keto-aldehyde **17** (74% yield), thereby setting the stage for the key intramolecular aldol reaction step. This aldol condensation is challenging owing to a potential isomerization of the α-hydrogen atom to a thermodynamically more stable *cis* isomer. This issue was overcome by treating **17** with LiOH in *i*PrOH, followed by bromination and elimination, which resulted in a 63% overall yield of the desired *trans* isomer (6% yield of *cis* isomer).[13]

After extensive screening of different conjugate addition methods to merge vinyl iodide **14** and enone **18** (Scheme 2C),[14] it was discovered that the vinylmagnesium species, derived from magnesium–iodine exchange of vinyl iodide **14** and *i*PrMgCl·LiCl (Knochel's reagent), was ideally suited for this purpose.[15] After generation, it underwent copper(I)-catalyzed conjugate addition to enone **18**, followed by trapping with TMSCl to give the corresponding 1,4-adduct in 69% yield. The olefin moiety of the coupling product was selectively reduced (Pd/C, H_2) to yield silyl enol ether **19** in quantitative yield. A final carbon atom was added by



cyclopropanation conditions

Cat. (5 mol%)	*Conversion (yield[a])*
$[Rh_2(tfa)_4]$	< 10%
$[Rh_2(hfb)_4]$	< 10%
$[Rh_2(OAc)_4]$	< 30%
$[Rh_2(OPiv)_4]$	full conv (78%)
$[Rh_2(esp)_2]$	full conv (80%)

[a]Yield of isolated product over two steps from **21** to **23**.

Scheme 2. Convergent approach to **22** and divergent synthesis of steroidal skeletons **23** and **24**. Reagents and conditions: a) $[PdCl_2(PPh_3)_2]$, CuI, TMSA, toluene, Et_3N, 60 °C, 9 h; 98 %. b) $FeSO_4$, NH_4Cl, Zn, EtOH, 50 °C, 2 h. c) HCl, $NaNO_2$, 0 °C, 30 min; iPr_2NH, K_2CO_3, 0 °C, 15 min. d) K_2CO_3, MeOH, RT, 4 h, 69 % over 3 steps. e) $[NiCl_2(PPh_3)_2]$, DIBAL-H, THF, RT, 22 h; NIS, −5 °C, 1 h, 51 %. f) vinylMgBr, CuI, −5 °C; TMEDA, TMSCl, Et_3N, **15**, −78 to 4 °C, 24 h. g) LiCl, MeLi, THF, −20 °C, 100 min; β-methallyl chloride, $[Pd(PPh_3)_4]$, −25 °C, 24 h, *trans*/*cis* = 10:1, 83 %. h) Ethylene glycol, TsOH·H_2O, $HC(OMe)_3$, C_6H_6, RT, 12 h, 86 %. i) O_3, CH_2Cl_2, −78 °C; PPh_3, −78 °C to RT, 10 h, 74 %. j) LiOH, *i*PrOH, RT, 1 h. k) CBr_4, PPh_3, CH_2Cl_2, 0 °C, 40 min; Et_3N, 63 % *trans*-**18** and 6 % *cis*-**18**. l) *i*PrMgCl·LiCl, THF, −78 to −50 °C, 5 h; −20 °C, 1 h; CuI·0.75 Me_2S, TMEDA, TMSCl, Et_3N, **18**, −78 to 0 °C over 15 h, 69 %. m) Pd/C, EtOAc, H_2 450 psi, RT, 3 h, quant. n) Li_2CO_3, Eschenmoser's salt, MeCN, RT, 6 h. o) SiO_2, CH_2Cl_2, RT, 3 h. p) TFA, CH_2Cl_2, 0 °C; K_2CO_3. q) 2 mol % $[Rh_2(esp)_2]$, CH_2Cl_2, RT, 1 h. r) LiCl, THF, RT, 41 % over 5 steps from **19**. s) Pd/C, MeCN, H_2, RT, 95 %. DIBAL-H = diisobutylaluminum hydride, NIS = *N*-iodosuccinimide, TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, TMS = trimethylsilyl, Ts = 4-toluenesulfonyl, TFA = trifluoroacetic acid.

treatment of silyl enol ether **19** with Eschenmoser's salt in the presence of Li_2CO_3,[16] followed by simply treating the crude material with silica gel in CH_2Cl_2 to furnish the desired enone **20**. Quinone diazide **21** was gently unmasked from **20** under acidic conditions followed by in situ treatment with K_2CO_3. Notably, the masked quinone diazide motif was stable under strongly basic conditions, mildly Lewis-acidic conditions, heterogeneous and homogeneous reductive conditions, and exposure to strong electrophiles. Next, the intramolecular cyclopropanation to construct the steroidal structure was examined (see table within Scheme 2). Metal-catalyzed cyclopropanation of such highly electrophilic diazo carbonyl compounds with electron-deficient enone systems is challenging and, to our knowledge, unprecedented in the context of rhodium or copper catalysis.[5a,17] Encouragingly, when $[Rh_2(OAc)_4]$ was employed, the desired product was formed in trace quantities; in contrast, $[Rh_2(tfa)_4]$ and $[Rh_2(hfb)_4]$ were not effective in decomposing the quinone diazide moiety.[18] To our delight, both $[Rh_2(OPiv)_4]$ and $[Rh_2(esp)_2]$ efficiently catalyzed the cyclopropanation to give **22** in high yield.[19]

With key intermediate **22** in hand, selective C–C bond cleavage of the cyclopropane was explored. In the presence of LiCl, cleavage of the C^{10}–C^{19} bond took place to generate aromatic steroid **23** (41 % overall yield over 5 steps).[4c,d] This reaction was thought to proceed by a nucleophilic substitution triggered by Lewis acid activation of the cross-conjugated dienone system. X-ray analysis of **23** confirmed the stereochemistry of the cyclopropanation event. Interestingly, under heterogeneous hydrogenation conditions, the C^9–C^{10} bond underwent selective cleavage to form **24**, which contains a seven-membered ring, in high yield, and the stereochemistry was confirmed by X-ray crystallographic analysis. The current convergent synthesis of versatile intermediate **22**, and the divergent approach to steroid skeletons **23** and **24** through selective C–C bond cleavage presented a unique strategy to quickly achieve complexity and diversity, thus highlighting the synthetic utilities of quinone diazides and the corresponding masked form in organic synthesis.

In conclusion, this work represents the first systematic study of quinone diazides, a ubiquitous entity in materials science, in the context of organic synthesis. The most significant findings resulting from this inquiry include: 1) a general rhodium-catalyzed intermolecular cyclopropanation of quinone diazides with a variety of different olefin classes, 2) divergent manipulations of the resulting cyclohexadienone adducts, 3) a strategy to enlist quinone diazides in complex

intramolecular settings using a triazene-enabled "mask", and 4) application to a fundamentally different approach to the steroid skeleton.

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[1] For books and book chapters, see a) V. V. Ershov, G. A. Nikiforvo, C. R. H. I. De Jonge, *Studies in Organic Chemistry: Quinonediazides*, Elsevier, Amsterdam, **1981**; b) A. G. Griesbeck, E. Zimmermann in *Science of Synthesis*, *Vol. 28* (Ed.: A. G. Griesbeck), Thieme, Stuttgart, **2000**, pp. 807 – 830.

[2] a) H. Mori, I. Tando, H. Tanaka, *Macromolecules* **2010**, *43*, 7011 – 7020; b) G. M. Wallraff, W. D. Hinsberg, *Chem. Rev.* **1999**, *99*, 1801 – 1822; c) J. D. Olszewski, M. Marshalla, M. Sabat, R. J. Sundberg, *J. Org. Chem.* **1994**, *59*, 4285 – 4296; d) M. J. Bouchet, A. Rendon, C. G. Wermuth, M. Goeldner, C. Hirth, *J. Med. Chem.* **1987**, *30*, 2222 – 2227; e) T. Ohno, N. Martín, B. Knight, F. Wudl, T. Suzuki, H. Yu, *J. Org. Chem.* **1996**, *61*, 1306 – 1309; f) B. Knight, N. Martín, T. Ohno, E. Ortí, C. Rovira, J. Veciana, J. Vidal-Gancedo, P. Viruela, R. Viruela, F. Wudl, *J. Am. Chem. Soc.* **1997**, *119*, 9871 – 9882; g) M. Eckert-Maksić, D. Margetić, *High Pressure Res.* **2007**, *27*, 109 – 114.

[3] a) G. F. Koser, W. H. Pirkle, *J. Org. Chem.* **1967**, *32*, 1992 – 1994; b) J. C. Fleming, H. Shechter, *J. Org. Chem.* **1969**, *34*, 3962 – 3969; c) S. Nakazawa, K. Hirakawa, S. Fujimori, K. Iwasaki, *J. Chem. Soc. Perkin Trans. 1* **1979**, 2052 – 2056; d) R. S. Ward, K. S. Thatcher, *Tetrahedron Lett.* **1981**, *22*, 4831 – 4834; e) A. S. Kende, P. Hebeisen, P. J. Sanfilippo, B. H. Toder, *J. Am. Chem. Soc.* **1982**, *104*, 4244 – 4245; f) G. A. Kraus, J. O. Nagy, J. DeLano, *Tetrahedron* **1985**, *41*, 2337 – 2340; g) H. D. Becker, T. Elebring, *J. Org. Chem.* **1985**, *50*, 1319 – 1322; h) A. S. Kende, P. Hebeisen, *Tetrahedron Lett.* **1985**, *26*, 3769 – 3772.

[4] Metal-catalyzed cyclopropanations employing quinone diazides have been sporadically reported with a limited scope of quinone diazides and olefins: a) R. J. Sundberg, E. W. Baxter, *Tetrahedron Lett.* **1986**, *27*, 2687 – 2690; b) R. J. Sundberg, E. W. Baxter, W. J. Pitts, R. Ahmed-Schofield, T. Nishiguchi, *J. Org. Chem.* **1988**, *53*, 5097 – 5107; c) R. J. Sundberg, W. J. Pitts, *J. Org. Chem.* **1991**, *56*, 3048 – 3054; d) D. L. Boger, P. Mesini, *J. Am. Chem. Soc.* **1994**, *116*, 11335 – 11348; e) D. L. Boger, T. J. Jenkins, *J. Am. Chem. Soc.* **1996**, *118*, 8860 – 8870; f) P. V. Murphy, T. J. O'Sullivan, N. W. Geraghty, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2109 – 2119.

[5] For general cyclopropanations with carbenoids, see a) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*, Wiley, New York, **1998**; b) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911 – 936; c) H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, *103*, 977 – 1050; d) H. M. Davies, R. E. Beckwith, *Chem. Rev.* **2003**, *103*, 2861 – 2904; g) J. L. Thompson, H. M. L. Davies, *J. Am. Chem. Soc.* **2007**, *129*, 6090 – 6091.

[6] For selective two-electron-acceptor diazocarbonyl compounds and their application in Rh catalysis, see a) M. P. Doyle, S. B. Davies, W. Hu, *Org. Lett.* **2000**, *2*, 1145 – 1147; b) O. Lifchits, D. Alberico, I. Zakharian, A. B. Charette, *J. Org. Chem.* **2008**, *73*, 6838 – 6840; c) O. Lifchits, A. B. Charette, *Org. Lett.* **2008**, *10*, 2809 – 2812; d) V. N. G. Lindsay, C. Nicolas, A. B. Charette, *J. Am. Chem. Soc.* **2011**, *133*, 8972 – 8981; e) R. R. Nani, S. E. Reisman, *J. Am. Chem. Soc.* **2013**, *135*, 7304 – 7311; our classification is based on the ^{13}C NMR chemical shift of the diazo groups ($C{=}N_2$): acceptor/acceptor diazocarbonyl compounds: ca. $\delta = 80$ ppm; monoacceptor and donor/acceptor diazocarbonyls: ca. $\delta = 55$ ppm; **1a**: $\delta = 79.5$ ppm.

[7] C. G. Espino, K. W. Fiori, M. Kim, J. Du Bois, *J. Am. Chem. Soc.* **2004**, *126*, 15378 – 15379.

[8] For a recent review, see M. R. Heinrich, *Chem. Eur. J.* **2009**, *15*, 820 – 833.

[9] a) H. Ku, J. R. Barrio, *J. Org. Chem.* **1981**, *46*, 5239 – 5241; b) D. B. Kimball, M. M. Haley, *Angew. Chem. Int. Ed.* **2002**, *41*, 3338 – 3351; *Angew. Chem.* **2002**, *114*, 3484 – 3498; c) A.-F. Voica, A. Mendoza, W. R. Gutekunst, J. O. Fraga, P. S. Baran, *Nat. Chem.* **2012**, *4*, 629 – 635.

[10] F. Gao, A. H. Hoveyda, *J. Am. Chem. Soc.* **2010**, *132*, 10961 – 10963.

[11] a) S. E. Denmark, J. P. Germanas, *Tetrahedron Lett.* **1984**, *25*, 1231 – 1234; b) K. Fukuzaki, E. Nakamura, I. Kuwajima, *Tetrahedron Lett.* **1984**, *25*, 3591 – 3594.

[12] E. Piers, J. Renaud, *J. Org. Chem.* **1993**, *58*, 11 – 13.

[13] K. Chen, Y. Ishihara, M. M. Galán, P. S. Baran, *Tetrahedron* **2010**, *66*, 4738 – 4744.

[14] M. Schlosser, *Organometallics in Synthesis: a Manual*, Wiley, Hoboken, NJ, USA, **2002**.

[15] H. Ren, A. Krasovskiy, P. Knochel, *Org. Lett.* **2004**, *6*, 4215 – 4217.

[16] a) S. Danishefsky, T. Kitahara, R. McKee, P. F. Schuda, *J. Am. Chem. Soc.* **1976**, *98*, 6715 – 6717; b) N. L. Holy, Y. F. Wang, *J. Am. Chem. Soc.* **1977**, *99*, 944 – 946; the use of a sub-stoichiometric amount of Li_2CO_3 was critical for the C–C bond formation.

[17] For Pd^0 and $[Mo(CO)_6]$ catalysis, see a) U. Mende, B. Radüchel, V. Skuballa, H. Vorbrüggen, *Tetrahedron Lett.* **1975**, *16*, 629 – 632; b) M. P. Doyle, J. G. Davidson, *J. Org. Chem.* **1980**, *45*, 1538 – 1539; Co catalysis: cb) A. Nakamura, A. Konishi, Y. Tatsuno, S. Otsuka, *J. Am. Chem. Soc.* **1978**, *100*, 3443 – 3448.

[18] ^1H NMR studies revealed an unproductive coordination of the catalysts with the substrate.

[19] $[Rh_2(OPiv)_4]$ gave 78% yield, and $[Rh_2(esp)_2]$ gave 80% overall yield in two steps from **21** to **23**.

