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Article

Stereoselective Synthesis of Tri- and Tetrasubstituted Olefins via 1,6-Additions of Diazo Compounds and Their Precursors to *p*-Quinone Methides

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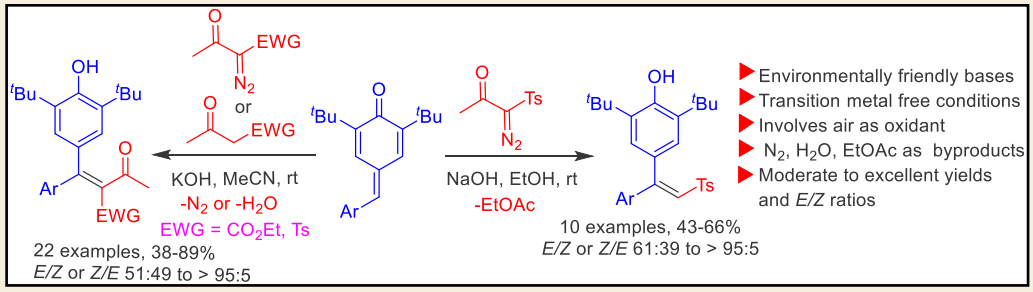

ABSTRACT: Reactions of *para*-quinone methides (*p*-QMs) with *α*-diazo-*β*-ketosulfones and their corresponding esters as well as simple *β*-dicarbonyl compounds and *β*-ketosulfones have been carried out under basic conditions. While the reaction of diazosulfone with *p*-QMs afforded trisubstituted olefins via deacylative 1,6-addition and elimination, *α*-diazo-*β*-ketoesters and various active methylene compounds such as 1,3-dicarbonyls and *β*-ketosulfones afforded tetrasubstituted olefins via 1,6-addition and aerial oxidation. These simple, environmentally benign, and mechanistically diverse protocols provided the products in moderate to excellent yields and selectivities.

KEYWORDS: *para-quinone methides, diazo compounds, 1,6-conjugate addition, aerobic oxidation, functionalized olefins*

INTRODUCTION

Formation of C═C bonds is an important process in synthetic organic chemistry.[1] In particular, synthesis of tri-and tetrasubstituted alkenes in a stereoselective manner is of tremendous interest due to their presence in a plethora of natural products of biological significance as well as in material chemistry (Figure 1).[2−10] The classical C═C bond forming reactions such as Wittig reaction and its variants, aldol condensation, Julia olefination, McMurry coupling, etc., which involve either 1,2- or 1,4-additions and more recent metal-catalyzed reactions, are useful for the construction of complex organic frameworks.[11−21] However, C═C bond forming reactions involving 1,6-addition are considerably underexplored compared to 1,2- and 1,4-additions. This is primarily due to the fact that the conjugated dienes have less positive charge density at the *δ*-carbon compared to that at the *β*-carbon. Therefore, such dienes prefer to undergo 1,4-addition rather than 1,6-addition.[22−28]

From another perspective, *para*-quinone methides (*p*-QMs) have been known for more than a century.[29] These are present in various natural products and serve as active intermediates in many pharmacological and biological processes.[30−34] Recently, *p*-QMs have emerged as attractive 1,6-acceptors due to their intrinsic electropositive character at the *δ*-carbon that leads to

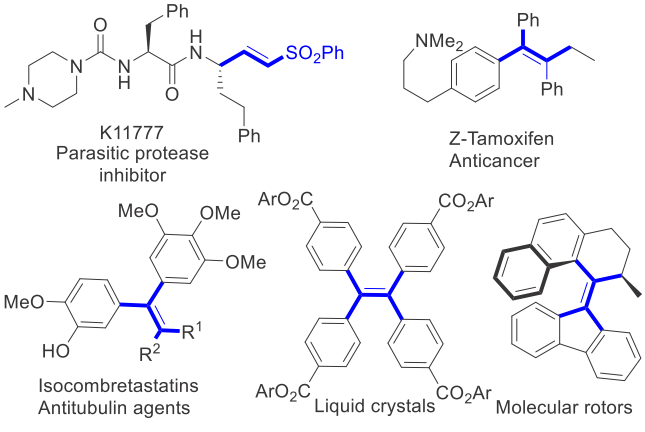

Figure 1. Importance of tri- and tetrasubstituted olefins.

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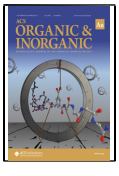
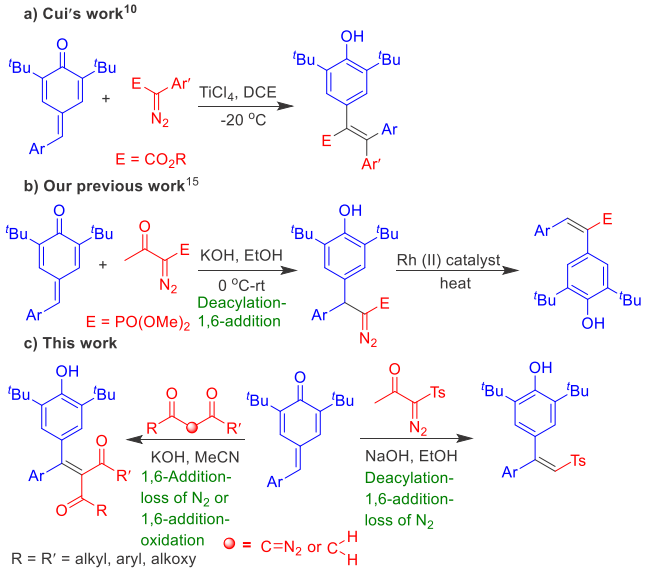


the formation of stable aromatic compounds. Therefore, 1,6-conjugate additions of various nucleophiles to *p*-QMs under a variety of conditions have been investigated.[35−40] Additions of various nucleophiles such as malonates, azlactones, indoles, boronates, α-substituted methyl tolylsulfones, etc. to *p*-QMs have also been carried out in a vinylogous Michael fashion under catalytic asymmetric conditions.[41−47] Moreover, these are also potential substrates for various dearomative annulations such as [3 + 2] annulations, [2 + 1] annulations, etc. for the construction of various spiro carbo- and heterocycles.[48−54]

Yet another class of compounds of continued interest are diazo compounds, which are precursors to carbenoids and, therefore, are employed in various reactions such as insertion, cyclopropanation, ring expansion, etc. to construct a multitude of cyclic and acyclic organic frameworks.[55,56] The utility of diazo compounds such as α-diazo-β-ketophosphonate (Bestmann−Ohira reagent) and its corresponding sulfone and ester analogues as 1,3-dipole precursors has been demonstrated in base-mediated deacylative [3 + 2] cycloaddition with conjugated electron-deficient alkenes for the synthesis of various functionalized heterocycles.[57−66] These reactions are largely based on 1,4-additions of the diazo compounds followed by cyclization in an overall [3 + 2] annulation. However, the corresponding deacylative 1,6-additions remained unexplored.

For the reaction of diazo compounds with *p*-QMs, in 2016, Cui and co-workers described a metathesis reaction involving 1,6-conjugate addition of diazoesters with *p*-QMs to form tetrasubstituted alkenes (Scheme 1a).[54] Other important 1,6-

Scheme 1. Reactivity of Diazoesters, Diazophosphonates, and Diazosulfones with *p*-QMs

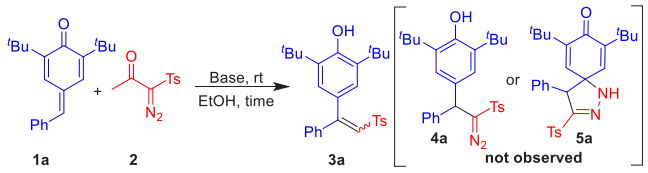


additions of diazo compounds to *p*-QMs include addition of Sayferth−Gilbert reagent[67] and aryldiazonium salts.[68] We reported the deacylative 1,6-conjugate addition of Bestmann−Ohira reagent to *p*-QMs, which afforded a new class of diazo adducts that were converted to *cis*-stilbenyl phosphonates via Rh-catalyzed diazo group elimination and 1,2-migration of the phenolic group (Scheme 1b).[69] However, in view of the limited progress in the 1,6-conjugate addition of diazo compounds, including our single report on the deacylative 1,6-addition of Bestmann−Ohira reagent to *p*-QMs, a detailed investigation on the addition of various diazo compounds to *p*-QMs appeared highly desirable. Therefore, we have described herein the 1,6-conjugate addition of α-diazo-β-ketosulfone and α-diazo-β-dicarbonyl compounds as well as the latter's precursors to *p*-QMs that led to the formation of various tri- and tetrasubstituted olefins via different mechanistic pathways (Scheme 1c).

RESULTS AND DISCUSSION

In order to investigate the 1,6-addition of α-diazo-β-ketosulfones and esters, *p*-QM **1a** was selected as the model 1,6-acceptor and diazosulfone **2** as the donor. The reaction was conducted using 2 equiv of Cs_2CO_3 as base in ethanol as solvent. From our previous experience (Scheme 1b),[69] a 1,6-adduct **4a** or a spirocyclic product **5a** was expected, but surprisingly, it led to the formation of α,α-diarylvinyl sulfone **3a** in 40% yield and 70:30 *Z*/*E* ratio (Table 1, entry 1). In

Table 1. Reaction of Diazosulfone with *p*-QM: Optimization Studies[a]



entry	base (equiv)	time (h)	yield (%)[b]	*Z*/*E*[c]
1	Cs_2CO_3 (2)	2	40	70:30
2	NaOH (2)	2	42	70:30
3	KOH (2)	1.5	38	70:30
4	NaOEt (2)	2	25	70:30
5	DBU (2)	2	*d*	
6	K_2CO_3 (2)	3	35	64:36
7[e]	Cs_2CO_3 (3)	2	62	72:28
8[e]	NaOH (3)	2	51	70:30
9[e]	**NaOH (4)**	**1**	**66**	**70:30**
10[e,f]	NaOH (4)	1	66	68:32

[a]Reaction scale: *p*-QM **1** (0.2 mmol), diazosulfone **2** (0.2−0.3 mmol, 1−1.5 equiv), and base (2−4 equiv) in EtOH (3 mL). [b]After silica gel column chromatography. [c]Determined by ^{1}H NMR. [d]Starting materials decomposed. [e]1.5 equiv of diazosulfone **2** was used. [f]Carried out at 0 °C.

order to further improve the yield and selectivity, various other conditions were screened. For this purpose, stronger inorganic bases such as NaOH, KOH, and NaOEt were employed, which could not improve the yield or selectivity significantly and afforded product **3a** in 42, 38, and 25% yields, respectively, in identical *Z*/*E* ratio (entries 2−4). The strong organic base DBU also provided unsatisfactory results as it led to the decomposition of starting materials (entry 5). A weaker base such as K_2CO_3 could afford product **3a** only in low (35%) yield and selectivity (*Z*/*E* = 64:36, entry 6). As the screening of various bases could not produce any significant improvement in the product yield, the reaction was carried out using a slight excess of diazosulfone **2** as well as base so that the side reactions affecting the yield could be minimized. To our delight, a considerable increase in the yield was observed when the reaction was performed using 1.5 equiv of diazosulfone **2** and 3 equiv of Cs_2CO_3 (62%, *Z*/*E* = 72:28, entry 7). However, conducting the experiment using NaOH instead of Cs_2CO_3

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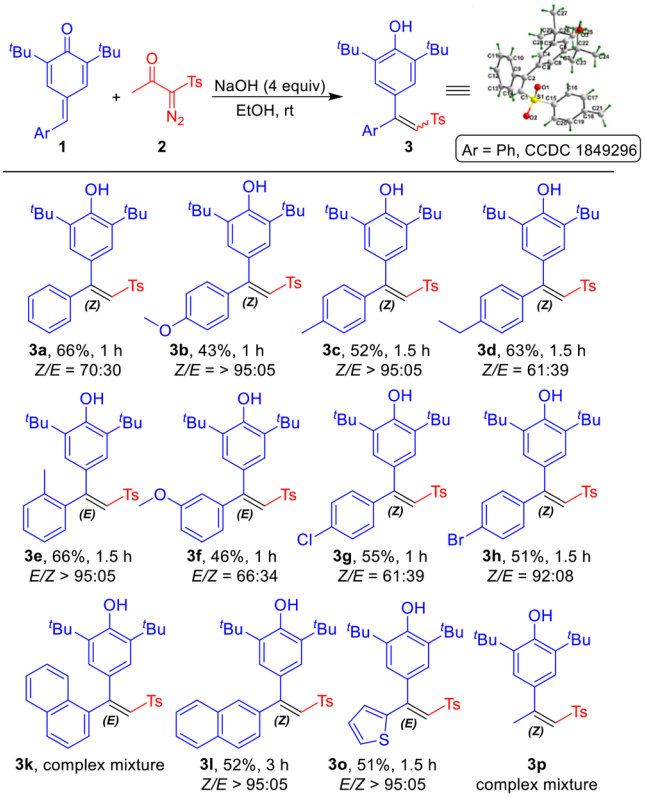
ACS Org. Inorg. Au 2021, 1, 51−59

under the same conditions caused a considerable decrease in the yield of **3a** (51%, *Z*/*E* = 70:30, entry 8). Later, the reaction was performed using 4 equiv of NaOH that afforded product **3a** in 66% yield (*Z*/*E* = 70:30, entry 9). For further improvement in the yield, the reaction was carried out at 0 °C, which resulted in product **3a** in 66% yield and marginally lower selectivity (*Z*/*E* = 68:32, entry 10). Therefore, entry 9 was regarded as the optimized condition for further generalization of the methodology.

As mentioned above, the electronically neutral parent phenyl *p*-QM **1a** afforded product **3a** in 66% yield as a 70:30 *Z*/*E* mixture. However, electron-releasing *p*-anisyl derivative **1b** afforded exclusively the *Z* isomer of product **3b** though in lower yield (43%, Scheme 2). Weakly electron-releasing *p*-tolyl

Scheme 2. Scope of *p*-QM in the Synthesis of Trisubstituted Olefins[a,b,c,d]



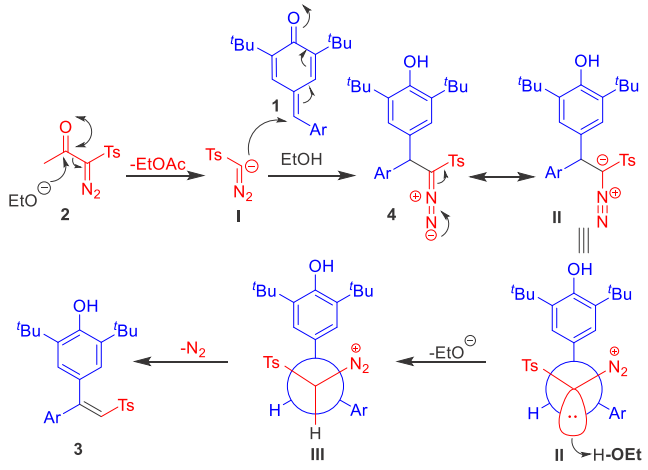
[a]Reaction scale: *p*-QM **1** (0.2 mmol), diazosulfone **2** (0.3 mmol, 1.5 equiv), and NaOH (0.8 mmol, 4 equiv) in EtOH (3 mL). [b]Isolated yields after silica gel column chromatography. [c]*Z*/*E* ratio was determined by ^{1}H NMR. [d]In all of the cases, 5−10% of the ethoxide addition product was observed as a side product.

1c and *p*-ethylphenyl **1d** derivatives afforded products **3c** and **3d**, respectively, in moderate to good yields and moderate to excellent selectivities (52%, *Z*/*E* > 95:05 and 63%, *Z*/*E* = 61:39). Sterically hindered *o*-tolyl *p*-QM **1e** afforded exclusively the *E* isomer of product **3e** in 66% yield, which suggested that the steric factor was playing a significant role in controlling the geometry of the olefins. However, mild electron-withdrawing *m*-anisyl derivative **1f** delivered product **3f** in moderate yield (46%) as well as a moderate *E*/*Z* ratio (66:34). Later, the scope of the reaction was also investigated with various halogenated *p*-QMs. When the reaction was performed with *p*-chlorophenyl *p*-QM derivative **1g**, it afforded product **3g** in 55% yield and 61:39 *Z*/*E* ratio, whereas the corresponding 4-bromophenyl derivative **1h** afforded product **3h** in 51% yield (*Z*/*E* = 92:08). To our surprise, a drastic difference in the reactivity of sterically hindered *α*-naphthyl *p*-QM **1k** and *β*-naphthyl *p*-QM **1l** was observed as the reaction of **1k** with diazosulfone **2** led to a complex reaction mixture, whereas **1l** afforded product **3l** in moderate yield (52%) but in excellent *Z*/*E* ratio (*Z*/*E* = >95:05). Similarly, the heterocyclic thienyl derivative **1o** afforded product **3o** in 51% yield as exclusively the *E* isomer, whereas the corresponding aliphatic methyl *p*-QM **1p** afforded a complex mixture instead of the expected **3p**, which is attributable to strong basic conditions.

The double bond geometry of the vinyl sulfones **3** was initially assigned by ^{1}H−^{1}H NOESY analysis of a representative compound **3l**. A positive correlation between the protons *ortho* to the sulfonyl group appearing as a doublet at 7.29 ppm with the aromatic protons of the phenolic moiety appearing as a singlet at 6.90 ppm confirmed this assignment. This was further unambiguously established by single-crystal X-ray analysis of the major isomer of compound **3a**.[70]

The reaction of *α*-diazo-*β*-ketosulfone **2** with *p*-QMs **1** in ethanol is an example of deacylative 1,6-addition in which the in situ generated ethoxide ion deacylates the diazosulfone **2** to generate the 1,3-dipolar synthon **I**, which subsequently adds to *p*-QM **1** in a 1,6-fashion to form intermediate **4** (Scheme 3).

Scheme 3. Plausible Mechanism for the Formation of Trisubstituted Olefins from Diazosulfone and *p*-QM



Further protonation of intermediate **4**, as shown in the conformational structure II, generates intermediate **III**, which subsequently undergoes elimination of N_2 to afford product **3** in which the phenolic and tosyl groups are on the same side of the double bond. Formation of this geometrical isomer is attributable to the *anti*-orientation of the two electron-rich moieties, the phenolic group, and the lone pair in the intermediate **II**. However, the lower *E*/*Z* selectivities in certain cases can be ascribed to the *α*-elimination of N_2 followed by 1,2-C−H insertion.

After the scope of diazosulfone **2** was investigatied, the reactivity of diazoester **6** with a representative *p*-QM **1a** was investigated under basic conditions (Scheme 4). In this case, the ethoxide addition product **8a** was isolated instead of the desired deacylative 1,6-adduct both at room temperature and at lower temperature. In order to prevent such competitive

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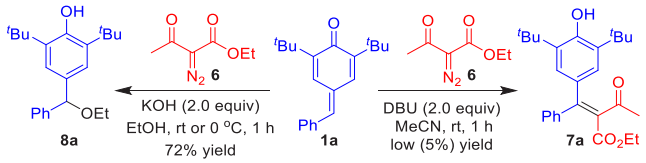
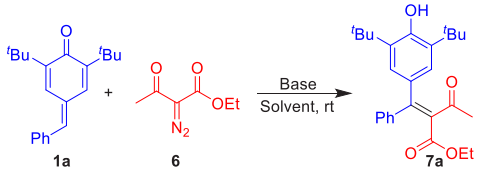
Scheme 4. KOH-Mediated Reaction of *p*-QM with Diazoester in EtOH



reactions, it was envisaged to carry out further reactions using polar aprotic solvents. To our surprise, the reaction of phenyl *p*-QM **1a** with *α*-diazo-*β*-ketoester **6** in polar aprotic solvent MeCN using DBU as base led to the formation of a tetrasubstituted olefin **7a** in a trace amount. Being inspired by the result, we screened various conditions to improve the yield, which is briefly described below.

As mentioned above, the reaction of *p*-QM **1a** with diazoester **6** using 2 equiv of DBU in MeCN afforded the tetrasubstituted olefin **7a** in 5% yield (Scheme 4 and Table 2, entry 1). Later, the reaction was carried out using 4 equiv of DBU, which resulted in a marginal improvement in the yield (8%, entry 2). Further, the reaction was performed by changing the stoichiometry of starting materials, which caused a considerable increase in the yield to 50% (entry 3). Later, the reaction was carried out using 4 equiv of Cs_2CO_3 which, to our dismay, afforded inferior results (45%, entry 4). Replacing Cs_2CO_3 by KOH turned out to be beneficial as the yield of **7a** improved substantially (65%, entry 5). Upon changing the base to NaOH, the yield of **7a** dropped drastically to 30%, which was attributed to the poor solubility of NaOH in MeCN (entry 6). Decreasing the temperature to 0 °C had a detrimental effect on the KOH-mediated reaction in terms of both the reaction rate and the yield (3 h, 30%, entry 7). Further, screening of various other polar aprotic solvents such as DMF, DCM, and THF produced unsatisfactory results (entries 8–10). Therefore, entry 5 was considered optimal for investigating the scope of the reaction.

Table 2. Reaction of Diazoester with *p*-QM: Optimization Studies[a]

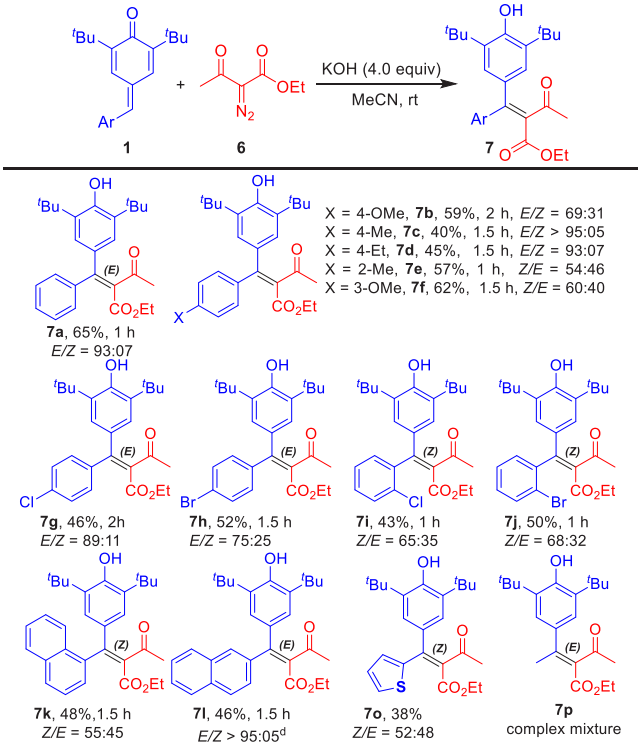


entry	base (equiv)	solvent	time (h)	yield (%)[b]
1	DBU (2.0)	MeCN	1	5
2	DBU (4.0)	MeCN	1	8
3[c]	DBU (4.0)	MeCN	1	50
4	Cs_2CO_3 (4.0)	MeCN	12	45
5	**KOH (4.0)**	MeCN	**1**	**65**[d]
6	NaOH (4.0)	MeCN	3	30
7[e]	KOH (4.0)	MeCN	3	50
8	KOH (4.0)	DMF	1	50
9	KOH (4.0)	DCM	12	27
10	KOH (4.0)	THF	1	28

[a]Reaction scale: 1 equiv (0.2 mmol) of *p*-QM **1a** and 1.2 equiv (0.24 mmol) of *α*-diazo-*β*-ketoester **6**. [b]After silica gel column chromatography. [c]Performed using 1.2 equiv (0.24 mmol) of *p*-QM **1a** and 0.8 equiv (0.16 mmol) of diazoketoester **6**. [d]*E*/*Z* = 93:07. [e]Performed at 0 °C.

The above optimized conditions (entry 5) have been employed to synthesize a series of tetrasubstituted olefins **7** (Scheme 5). While phenyl *p*-QM **1a** afforded product **7a** in 65% yield and a 93:07 *E*/*Z* ratio, electron-releasing *p*-anisyl analogue **1b** furnished product **7b** in marginally lower (59%) yield and a substantially lower (69:31) *E*/*Z* ratio. Similarly, the weakly electron-donating aryl derivatives **1c** and **1d** delivered the corresponding products **7c** and **7d** in 40 and 45% yields, respectively, in excellent *E*/*Z* selectivities. However, the sterically hindered *o*-tolyl derivative **1e** and weakly electron-withdrawing *m*-anisyl derivative **1f** provided products **7e** and **7f**, respectively, in moderate yields (57 and 62%) and moderate *Z*/*E* ratios (54:46 and 60:40). Later, the scope of various halogenated *p*-QMs was investigated. Weakly electron-withdrawing *p*-chloro- and *p*-bromophenyl derivatives **1g** and **1h**, respectively, afforded products **7g** and **7h** in 46% (*E*/*Z* = 89:11) and 52% (*E*/*Z* = 75:25) yields. However, sterically hindered *o*-chloro- and *o*-bromophenyl derivatives **1i** and **1j**, respectively, afforded products **7i** and **7j** in lower yields (43 and 50%) along with moderate *Z*/*E* selectivities. A similar trend was also observed in the case of bulky *α*- and *β*-naphthyl *p*-QMs **1k** and **1l**, which furnished the corresponding products **7k** and **7l**, respectively, in moderate yields (48 and 46%) and moderate to excellent selectivities (*Z*/*E* = 55:45 and *E*/*Z* > 95:05). Later, the reaction was performed using thienyl *p*-QM

Scheme 5. Scope of *p*-QM in the Synthesis of Tetrasubstituted Olefins Using Diazoester (Method A)[a,b,c]



[a]Reaction scale: *p*-QM **1** (0.2 mmol), diazoketoester **6** (0.24 mmol, 1.2 equiv), and KOH (0.8 mmol, 4 equiv) in CH_3CN (3 mL). [b]Isolated yields after silica gel column chromatography, 5–10% of di-*tert*-butylquinone was isolated in all of the cases (see Scheme 8). [c]*E*/*Z* ratio was determined by ^{1}H NMR. [d]After recrystallization of 75:25 mixture from chloroform.

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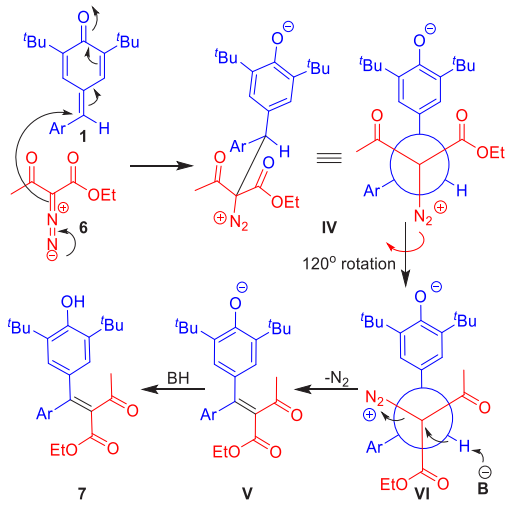
1o that afforded the desired olefin **7o** in moderate yield and lower selectivities (38%, *Z*/*E* = 52:48), whereas the reaction of aliphatic *p*-QM **1p** led to a complex mixture under the optimized conditions. Detailed analysis of the substrate scope reveals that the yields and selectivities were marginally affected by the electronic effect of substituents but considerably affected by their steric influence.

The proposed mechanism of the reaction involves 1,6-addition of diazoester **6** to *p*-QM **1** that forms the intermediate **IV** (Scheme 6). Bond rotation by 120° in intermediate **IV**

Scheme 6. Plausible Mechanism for the Formation of Tetrasubstituted Olefins from Diazoester and *p*-QM

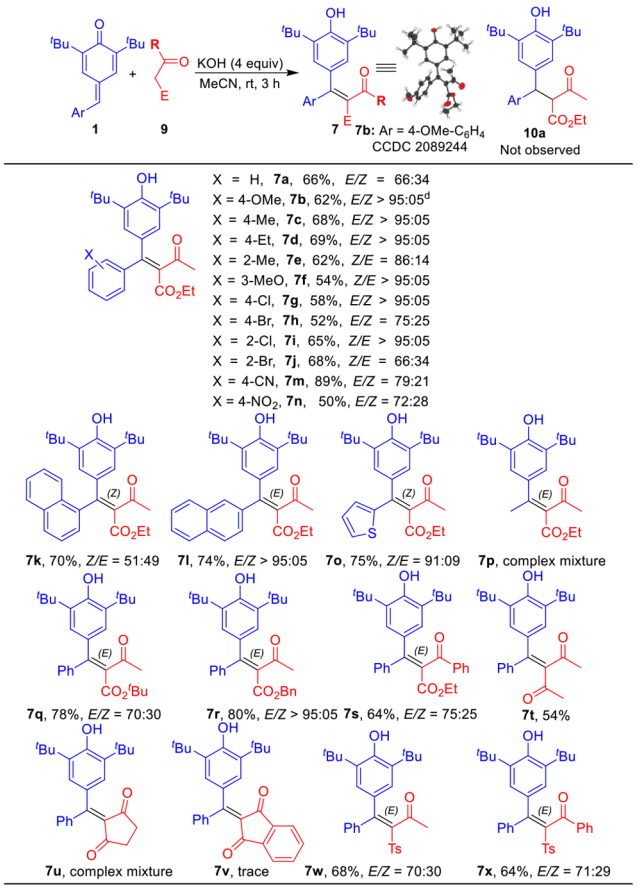


generates conformer **VI**, in which the bulky ester moiety and the di-*tert*-butyl phenol moiety are *anti* to each other. This conformer **VI** then undergoes a base-mediated denitrogenative E_2 elimination to form intermediate **V**, which on protonation affords product **7**.

Having synthesized tri- and tetrasubstituted olefins from diazosulfone **2** and diazoester **6**, we wished to examine the outcome of the addition of their immediate precursors, for instance, *β*-ketoester **9a** to *p*-QM **1**. Thus, addition of ketoester **9a** to *p*-QM **1a** under the conditions employed for the addition of diazoester **6** to *p*-QM **1**, viz. KOH/MeCN at room temperature, surprisingly gave the same product that was obtained from diazoester **6** and *p*-QM **1**, that is, tetrasubstituted olefin **7a** in comparable yield but different *E*/*Z* ratio. Even though addition of 1,3-dicarbonyl compounds to *p*-QM **1** to form 1,6-adducts of type **10a** is well-established in the literature,[71−73] the formation tetrasubstituted olefin **7a** via 1,6-addition of active methylene compounds is not reported, to the best of our knowledge. Inspired by these results, several tetrasubstituted olefins have been synthesized by this alternative method under KOH/MeCN conditions in varying yields and selectivities as described below (Scheme 7).

In addition to the synthesis of **7a** from phenyl *p*-QM **1a** and *β*-ketoester **9a** in 66% yield and 66:34 *E*/*Z* ratio, analogous products **7b**, **7c**, and **7d** have been synthesized in good yields (62, 68, and 69%, respectively) and excellent *E*/*Z* selectivities (>95:05) by treating *p*-QMs **1b−d** bearing electron-releasing groups at the *para*-position of the phenyl ring, such as methoxy, methyl, and ethyl, with *β*-ketoester **9a**. Similarly, the sterically hindered *o*-tolyl *p*-QM **1e** afforded product **7e** in 62% yield and in 86:14 *E*/*Z* ratio, whereas weakly electron-

Scheme 7. Scope of *p*-QM in the Synthesis of Tetrasubstituted Olefins Using Active Methylene Compounds (Method B)[a,b,c]



[a]Reaction scale: 0.3 mmol each of *p*-QM **1** and active methylene compound **9** and 1.2 mmol of KOH. [b]Isolated yields after silica gel column chromatography. [c]*E*/*Z* ratio was determined by ^{1}H NMR. [d]After recrystallization of original the 80:20 mixtures from ethyl alcohol/petroleum ether (20:80).

withdrawing *m*-anisyl *p*-QM **1f** delivered product **7f** in slightly lower yield (54%) but excellent *Z*/*E* selectivity (>95:05). The reaction was further performed with various halogenated aryl *p*-QMs, *p*-chlorophenyl **1g**, and *p*-bromophenyl **1h** derivatives, which led to products **7g** and **7h** in 58 and 52% yields and in 95:05 and 75:25 *E*/*Z* ratios, respectively. Sterically crowded *o*-halo derivatives **1i** and **1j** afforded products **7i** and **7j** in comparable yields (65 and 68%) but in varying selectivities (*Z*/*E* = >95:5 and 66:34). The reaction of sterically hindered *α*-naphthyl **1k** and *β*-naphthyl **1l** *p*-QMs with *β*-ketoester **9a** was also remarkably different. While the *α*-naphthyl *p*-QM **1k** delivered product **7k** in 70% yield as a mixture of isomers (*Z*/*E* = 51:49), the corresponding *β*-naphthyl derivative **1l** afforded product **7l** in 74% yield as a single isomer (*E*/*Z* > 95:05). The lower *E*/*Z* selectivities in the case of *o*-bromophenyl **7j** and *α*-naphthyl **7k** derivatives are attributable to severe steric hindrance. Later, the reaction was performed by employing electron-withdrawing aryl *p*-QMs **1m** and **1n**, which led to the corresponding products **7m** and **7n** in 89 and 50% yields and good selectivities (*E*/*Z* = 79:21 and 72:28). The reaction also worked well with a heteroaryl *p*-QM, viz. thienyl derivative **1o**, which afforded product **7o** in 75% yield and 91:09 *Z*/*E* ratio. Although the aliphatic methyl *p*-QM **1p** reacted vigorously

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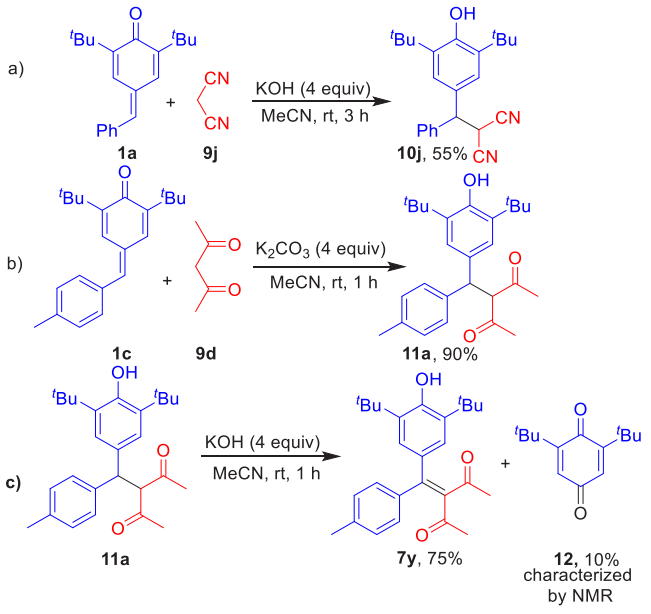
under the optimized conditions, it afforded only a complex mixture.

After the scope of *p*-QMs **1** using *β*-ketoester **9a** was demonstrated, other *β*-ketoesters, *tert*-butyl acetoacetate **9b**, benzyl acetoacetate **9c**, and ethyl benzoyl acetate **9d**, were treated with *p*-QM **1a**. These reactions led to corresponding products **7q**, **7r**, and **7s** in 78, 80, and 64% yields, respectively. The *E*/*Z* selectivities in these cases were also good to excellent (70:30, >95:5, and 75:25). Later, the reaction was performed using symmetrical 1,3-dicarbonyl compounds, acetylacetone **9e**, cyclopentan-1,3-dione **9f**, and indane-1,3-dione **9g**. While **9e** delivered product **7t** in moderate (54%) yield, the other two did not provide any positive results presumably due to their greater rigidity and steric hindrance. The suitability of other selected active methylene compounds, acetyl sulfone **9h** and benzoyl sulfone **9i**, was investigated. Pleasingly, both of them reacted with *p*-QM **1a** and afforded the corresponding olefins **7w** and **7x** in good yields (68 and 64%) and selectivities (*E*/*Z* = 70:30 and 71:29).

The double bond geometry in olefins **7** was initially assigned by ^{1}H−^{1}H NOESY analysis of a representative compound **7l** in that the two aromatic protons of the phenolic moiety appearing as a singlet at 7.00 ppm show a positive correlation with that of the acetyl methyl singlet appearing at 1.94 ppm. This was further confirmed by single-crystal X-ray analysis of compound **7b**.

In order to understand the mechanism of the above transformation, the following control experiments were conducted (Scheme 8). Initially, the reaction of *p*-QM **1a**

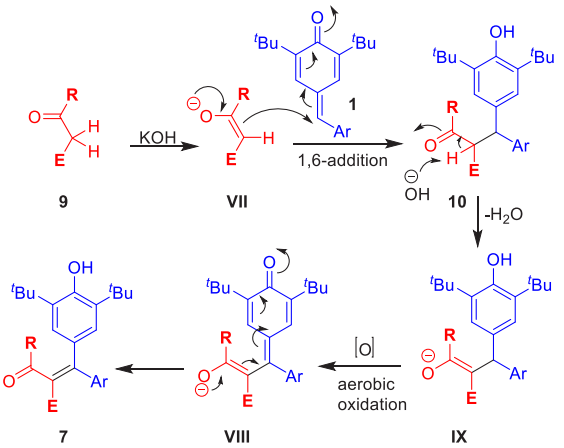
Scheme 8. Control Experiments



was performed with malononitrile **9j** under the standard conditions which led to the formation of 1,6-adduct **10j** in 55% yield (Scheme 8a). This suggested that the presence of a carbonyl group was essential for the formation of olefin **7**. Further, a reaction of *p*-QM **1a** with acetylacetone **9d** was conducted using K_2CO_3 as base, which led to the formation of 1,6-adduct **11a** (Scheme 8b). This confirmed the necessity of stronger base for the formation of olefin **7**. Therefore, 1,6-adduct **11a** was treated with KOH in MeCN, which resulted in tetrasubstituted olefin **7y** in 75% yield along with quinone **12** as the side product (Scheme 8c). The formation of olefin **7y** as the major product and quinone **12** as the side product indicated that aerial oxidation of **11a** to **7y** followed by oxidative cleavage of **7y** took place under our reaction conditions.

Based on the above observations, the following mechanism is proposed (Scheme 9). Initially, the base (KOH) abstracts a

Scheme 9. Plausible Mechanism for the Formation of Tetrasubstituted Olefins from Active Methylene Compounds and *p*-QM



proton from the active methylene compound **9** to generate the enolate ion **VII**, which then adds to *p*-QM **1** in a 1,6-fashion to form adduct **10**. Further deprotonation of **10** and stabilization of the resulting enolate **IX** via keto−enol tautomerism weakens the doubly benzylic C−H bond, thereby facilitating aerial oxidation to corresponding quinone **VIII**.[74] Later, the quinone **VIII** undergoes rearomatization to afford the tetrasubstituted olefin **7**.

Later, we decided to investigate the reactivities of the diazo compounds **2** and **6** and 1,3-dicarbonyl compound **9a** with a disubstituted *p*-QM (e.g., *N*-methyl isatin derived *p*-QM **13**) under the respective optimized conditions (Scheme 10).[75] Initially, *p*-QM **13** was treated with diazosulfone **2** in the presence of NaOH in ethanol, which unfortunately afforded a complex mixture instead of the expected diazo adduct **14**. On the contrary, *p*-QM **13** smoothly reacted with diazoester **6** under the previously optimized conditions (KOH, MeCN) and afforded the diazo adduct **15** in 63% yield. Unlike in the previous case (see Scheme 5), this reaction proceeds via deprotonation of the acetyl methyl group of diazoester **6** followed by its 1,6-addition to *p*-QM **13**. Finally, the reaction of ethyl acetoacetate with *p*-QM **13** under the optimized conditions (KOH, MeCN) afforded a complex mixture instead of the expected 1,6-adduct **16**.

A comparison of the reactivity of *α*-diazo-*β*-ketophosphonate (Bestmann−Ohira reagent), its corresponding diazosulfone **2**, and ester **6** with *p*-QM under similar conditions (NaOH or KOH/EtOH) shows that while the phosphonate analogue gives a product arising from deacylative 1,6-addition (Scheme 1b), the sulfone analogue **2** provides trisubstituted alkene **3** arising from deacylative 1,6-addition and diazo elimination (Schemes 2 and 3), and the ester analogue **6** furnishes undesired ethoxide adduct **8a** (Scheme 4). In order to facilitate the ester analogue **6** to take part in 1,6-addition

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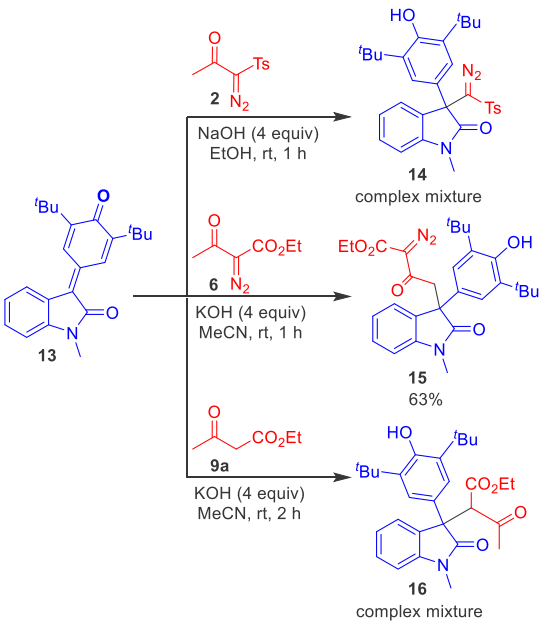
ACS Org. Inorg. Au 2021, 1, 51−59

Scheme 10. Reaction of Diazosulfone, Diazoester, and a 1,3-Dicarbonyl with *N*-Methyl Isatin Derived *p*-QM



and prevent a side reaction, EtOH had to be replaced by CH_3CN (Schemes 5 and 6). This resulted in the formation of tetrasubstituted alkenes **7** via nondeacylative 1,6-addition and diazo elimination (Schemes 5 and 6). This divergent reactivity and product profile can be attributed to better stabilization of the formal negative charge on the diazo carbon in the deacylated diazophosphonate intermediate and also in the diazophosphonate adduct (Scheme 1b) as compared to their sulfone counterparts (intermediates **I** and **4**, Scheme 3). Therefore, elimination of N_2 from the initial sulfone adduct **4** takes place to form alkene **3**.

CONCLUSIONS

In conclusion, we have demonstrated a base-promoted method for the synthesis of tri- and tetrasubstituted alkenes by both deacylative and nondeacylative 1,6-addition of α-diazocarbonyl compounds and their precursors to the *p*-QMs. The reaction possesses a wide range of substrate scope, and the products were isolated in moderate to excellent yields and selectivities. We have further demonstrated the reaction of active methylene compounds with *p*-QMs that led to the formation of tetrasubstituted alkenes. The reaction proceeds through base-mediated 1,6-addition of active methylene compounds and subsequent one-pot aerobic oxidation of the 1,6-adducts to the desired alkenes in moderate to excellent yields and selectivities.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsorginorgau.1c00012.

Experimental procedures and characterization data, copies of NMR spectra (PDF)

FID of compounds **3a–o**, **7a–o**, **8a**, **10j**, **11a**, **12**, and **15** (ZIP)

Accession Codes

CCDC 1849296 and 2089244 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

S.P. performed the reaction of *p*-QMs with diazosulfone and 1,3-dicarbonyls. S.R. performed the reaction of *p*-QMs with diazoester. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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ABBREVIATIONS

p-QM: *para*-quinone methide; DBU: 1,8-diazabicyclo[5.4.0]-undec-7-ene

REFERENCES

(1) Piva, O.; Katritzky, A. R.; Taylor, R. J. K. One or More C:C bond(s) by Elimination of Hydrogen, Carbon, Halogen, or Oxygen Functions. *Comprehensive Organic Functional Group Transformations II*; Elsevier, 2005; Vol. *1*, pp 581−600.

(2) Xia, Y.; Qiu, D.; Wang, J. Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810−13899.

(3) Marinozzi, M.; Pertusati, F.; Serpi, M. λ5-Phosphorus-Containing α-Diazo Compounds: A Valuable Tool for Accessing Phosphorus-Functionalized Molecules. *Chem. Rev.* **2016**, *116*, 13991−14055.

(4) Back, T. G.; Clary, K. N.; Gao, D. Cycloadditions and Cyclizations of Acetylenic, Allenic, and Conjugated Dienyl Sulfones. *Chem. Rev.* **2010**, *110*, 4498−4553.

(5) Nielsen, M.; Jacobsen, C. B.; Holub, N.; Paixao, M. W.; Jørgensen, K. A. Asymmetric Organocatalysis with Sulfones. *Angew. Chem., Int. Ed.* **2010**, *49*, 2668−2679.

(6) Shindo, M.; Matsumoto, K. Stereoselective Synthesis of Tetrasubstituted Alkenes *via* Torquoselectivity-Controlled Olefination of Carbonyl Compounds with Ynolates. *Top. Curr. Chem.* **2012**, *327*, 1−32.

(7) Hu, Y.; Zhang, X. P. Selective Olefination of Carbonyl Compounds *via* Metal-Catalyzed Carbene Transfer from Diazo Reagents. *Top. Curr. Chem.* **2012**, *327*, 147−162.
(8) Siau, W.-Y.; Zhang, Y.; Zhao, Y. Stereoselective Synthesis of Z-Alkenes. *Top. Curr. Chem.* **2012**, *327*, 33−58.
(9) Buttard, F.; Sharma, J.; Champagne, P. A. Recent Advances in the Stereoselective Synthesis of Acyclic All-Carbon Tetrasubstituted Alkenes. *Chem. Commun.* **2021**, *57*, 4071−4088.
(10) Ettari, R.; Bonaccorso, C.; Micale, N.; Heindl, C.; Schirmeister, T.; Calabro, M. L.; Grasso, S.; Zappala, M. Development of Novel Peptidomimetics Containing a Vinyl Sulfone Moiety as Proteasome Inhibitors. *ChemMedChem* **2011**, *6*, 1228−1237.
(11) Basiak, D.; Barbasiewicz, M. Olefination with Sulfonyl Halides and Esters - Sulfur-Based Variant of the Horner-Wadsworth-Emmons Reaction. *ARKIVOC* **2020**, *2021*, 118−135.
(12) Ali, W.; Prakash, G.; Maiti, D. Recent Development in Transition Metal Catalyzed C-H Olefination. *Chem. Sci.* **2021**, *12*, 2735−2759.
(13) Thiemann, T. Wittig- and Horner-Wadsworth-Emmons Olefination in Aqueous Media with and without Phase Transfer Catalysis. *Mini-Rev. Org. Chem.* **2018**, *15*, 412−432.
(14) Gueyrard, D. Extension of the Modified Julia Olefination on Carboxylic Acid Derivatives: Scope and Applications. *Synlett* **2018**, *29*, 34−45.
(15) Armstrong, R. J.; Aggarwal, V. K. 50 Years of Zweifel Olefination: A Transition-Metal-Free Coupling. *Synthesis* **2017**, *49*, 3323−3336.
(16) Bag, S.; Maiti, D. Palladium-Catalyzed Olefination of Aryl C-H Bonds by Using Directing Scaffolds. *Synthesis* **2016**, *48*, 804−815.
(17) Blakemore, P. R. Olefination of Carbonyl Compounds by MainGroup Element Mediators. In *Comprehensive Organic Synthesis*, 2nd ed.; Molander, G. A., Knochel, P., Eds.; Elsevier Ltd.: Oxford, 2014; Vol. *1*, pp 516−608.
(18) Cachatra, V.; Rauter, A. P. Revisiting Wittig Olefination and Aza-Wittig Reaction for Carbohydrate Transformations and Stereocontrol in Sugar Chemistry. *Curr. Org. Chem.* **2014**, *18*, 1731−1748.
(19) Chatterjee, B.; Bera, S.; Mondal, D. Julia-Kocienski Olefination, a Key Reaction for the Synthesis of Macrolides. *Tetrahedron: Asymmetry* **2014**, *25*, 1−55.
(20) Heravi, M. M.; Faghihi, Z. McMurray Coupling of Aldehydes and Ketones for the Formation of Heterocycles *via* Olefination. *Curr. Org. Chem.* **2012**, *16*, 2097−2123.
(21) Zajc, B.; Kumar, R. Synthesis of Fluoroolefins *via* Julia-Kocienski Olefination. *Synthesis* **2010**, *2010*, 1822−1836.
(22) Belot, S.; Quintard, A.; Krause, N.; Alexakis, A. Organocatalyzed Conjugate Addition of Carbonyl Compounds to Nitrodienes/Nitroenynes and Synthetic Applications. *Adv. Synth. Catal.* **2010**, *352*, 667−695.
(23) Enders, D.; Wang, C.; Greb, A. Asymmetric Synthesis of 2,3,4-Trisubstituted Functionalized Tetrahydrofurans *via* an Organocatalytic Michael Addition as Key Step. *Adv. Synth. Catal.* **2010**, *352*, 987−992.
(24) Chauhan, P.; Chimni, S. S. Facile Construction of Vicinal Quaternary and Tertiary Stereocenters *via* Regio- and Stereoselective Organocatalytic Michael Addition to Nitrodienes. *Adv. Synth. Catal.* **2011**, *353*, 3203−3212.
(25) Shaw, S.; White, J. D. Regioselective and Enantioselective Addition of Sulfur Nucleophiles to Acyclic *α, β, γ, δ*-Unsaturated Dienones Catalyzed by an Iron (III)−Salen Complex. *Org. Lett.* **2015**, *17*, 4564−4567.
(26) Hayashi, Y.; Okamura, D.; Umemiya, S.; Uchimaru, T. Organocatalytic 1,4-Addition Reaction of *α, β-γ, δ*-Diunsaturated Aldehydes versus 1,6-Addition Reaction. *ChemCatChem* **2012**, *4*, 959−962.
(27) Csaky, A. G.; Herran, G. D. L.; Murcia, M. C. Conjugate Addition Reactions of Carbon Nucleophiles to Electron-Deficient Dienes. *Chem. Soc. Rev.* **2010**, *39*, 4080−4102.
(28) Silva, E. M. P.; Silva, A. M. S. 1,6-Conjugate Addition of Nucleophiles to *α, β, γ, δ*-Diunsaturated Systems. *Synthesis* **2012**, *44*, 3109−3128.
(29) Toteva, M. M.; Richard, J. P. The Generation and Reactions of Quinone Methides. *Adv. Phys. Org. Chem.* **2011**, *45*, 39−91.
(30) Takao, K.-I.; Sasaki, T.; Kozaki, T.; Yanagisawa, Y.; Tadano, K.-I.; Kawashima, A.; Shinonaga, H. Synthesis and Absolute Stereochemistries of UPA0043 and UPA0044, Cytotoxic Antibiotics Having a *p*-Quinone-methide Structure. *Org. Lett.* **2001**, *3*, 4291−4294.
(31) Martin, H. J.; Magauer, T.; Mulzer, J. In Pursuit of a Competitive Target: Total Synthesis of the Atibiotic Kendomycin. *Angew. Chem., Int. Ed.* **2010**, *49*, 5614−5626.
(32) Modica, E.; Zanaletti, R.; Freccero, M.; Mella, M. Alkylation of Amino Acids and Glutathione in Water by *o*-Quinone Methide. *J. Org. Chem.* **2001**, *66*, 41−52.
(33) Messiano, G. B.; da Silva, T.; Nascimento, I. R.; Lopes, L. M. X. Biosynthesis of Antimalarial Lignans from Holostylis Reniformis. *Phytochemistry* **2009**, *70*, 590−596.
(34) Awad, H. M.; Boersma, M. G.; Boeren, S.; van Bladeren, P. J.; Vervoort, J.; Rietjens, I. M. C. M. Structure-Activity Study on the Quinone/Quinone Methide Chemistry of Flavonoids. *Chem. Res. Toxicol.* **2001**, *14*, 398−408.
(35) Lima, C. G. S.; Pauli, F. P.; Costa, D. C. S.; de Souza, A. S.; Forezi, L. S. M.; Ferreira, V. F.; de Carvalho da Silva, F. *para*-Quinone Methides as Acceptors in 1,6-Nucleophilic Conjugate Addition Reactions for the Synthesis of Structurally Diverse Molecules. *Eur. J. Org. Chem.* **2020**, *2020*, 2650−2692 and references therein.
(36) Ranga, P. K.; Ahmad, F.; Nager, P.; Rana, P. S.; Vijaya Anand, R. Bis(amino)cyclopropenium Ion as a Hydrogen-Bond Donor Catalyst for 1,6-Conjugate Addition Reactions. *J. Org. Chem.* **2021**, *86*, 4994−5010.
(37) Das, D.; Ghosh, K. G.; Chandu, P.; Sureshkumar, D. Ammonium Chloride-Mediated Trifluoromethylthiolation of *p*-Quinone Methides. *J. Org. Chem.* **2020**, *85*, 14201−14209.
(38) Xiang, L.; Liu, X.; Zhang, H.; Zhao, N.; Zhang, K. Thermoresponsive Self-Healable and Recyclable Polymer Networks Based on a Dynamic Quinone Methide-Thiol Chemistry. *Polym. Chem.* **2020**, *11*, 6157−6162.
(39) Kanchupalli, V.; Shukla, R. K.; Singh, A.; Volla, C. M. R. Rh (III)-Catalyzed RedoxNeutral Cascade Annulation of Benzamides with *p*-Quinone Methides. *Eur. J. Org. Chem.* **2020**, *2020*, 4494.
(40) Xiang, L.; Liu, X.; He, Y.; Zhang, K. Eye-Readable Dynamic Covalent Click Reaction and Its Application in Polymer Synthesis. *Macromolecules* **2020**, *53*, 5434−5444.
(41) Parra, A.; Tortosa, M. *para*-Quinone Methide: a New Player in Asymmetric Catalysis. *ChemCatChem* **2015**, *7*, 1524−1526.
(42) Chauhan, P.; Kaya, U.; Enders, D. Advances in Organocatalytic 1,6-Addition Reactions: Enantioselective construction of Remote Stereogenic Centers. *Adv. Synth. Catal.* **2017**, *359*, 888−912.
(43) Chu, W.-D.; Zhang, L.-F.; Bao, X.; Zhao, X.-H.; Zeng, C.; Du, J.-Y.; Zhang, G.-B.; Wang, F. X.; Ma, X.-Y.; Fan, C.-A. Catalytic 1,6-Conjugate Addition/Aromatization of *para*-Quinone Methides: Enantioselective Introduction of Functionalized Diarylmethine Stereogenic Centers. *Angew. Chem., Int. Ed.* **2013**, *52*, 9229−9233.
(44) Li, W.; Xu, X.; Liu, Y.; Gao, H.; Cheng, Y.; Li, P. Enantioselective Organocatalytic 1,6-Addition of Azlactones to *para*-Quinone Methides: An Access to *α,α*-Disubstituted and *β,β*-Diaryl-*α*-Amino Acid Esters. *Org. Lett.* **2018**, *20*, 1142−1145.
(45) Rahman, A.; Zhou, Q.; Lin, X. Asymmetric Organocatalytic Synthesis of Chiral 3,3-Disubstituted Oxindoles *via* a 1,6-Conjugate Addition Reaction. *Org. Biomol. Chem.* **2018**, *16*, 5301−5309.
(46) Lou, Y.; Cao, P.; Jia, T.; Zhang, Y.; Wang, M.; Liao, J. Copper-Catalyzed Enantioselective 1,6-Boration of *para*-Quinone Methides and Efficient Transformation of *gem*-Diarylmethine Boronates to Triarylmethanes. *Angew. Chem., Int. Ed.* **2015**, *54*, 12134−12138.
(47) Groszek, G.; Blazej, S.; Brud, A.; Swierczynski, D.; Lemek, T. Reactions of Carbanions Derived From *α*-Substituted-Methyl Tolyl Sulfones With Quinone methides as Michael Acceptors. *Tetrahedron* **2006**, *62*, 2622−2630.

https://doi.org/10.1021/acsorginorgau.1c00012
ACS Org. Inorg. Au 2021, 1, 51−59

(48) Ma, C.; Huang, Y.; Zhao, Y. Stereoselective 1,6-Conjugate Addition/Annulation of *para*-Quinone Methides with Vinyl Epoxides/Cyclopropanes. *ACS Catal.* **2016**, *6*, 6408−6412.
(49) Yuan, Z.; Wei, W.; Lin, A.; Yao, H. Bifunctional Organo/Metal Cooperatively Catalyzed [3 + 2] Annulation of *para*-Quinone Methides with Vinylcyclopropanes: Approach to Spiro[4.5]-deca-6,9-diene-8-ones. *Org. Lett.* **2016**, *18*, 3370−3373.
(50) Kim, S.; Kitano, Y.; Tada, M.; Chiba, K. Alkylindan Synthesis *via* an Intermolecular [3 + 2] Cycloaddition Between Unactivated Alkenes and *in-situ* Generated *para*-Quinomethanes. *Tetrahedron Lett.* **2000**, *41*, 7079−7083.
(51) Zhang, X.-Z.; Du, J.-Y.; Deng, Y.-H.; Chu, W.-D.; Yan, X.; Yu, K.-Y.; Fan, C.-A. Spirocyclopropanation Reaction of *para*-Quinone Methides with Sulfonium Salts: The Synthesis of Spirocyclopropanyl *para*-Dienones. *J. Org. Chem.* **2016**, *81*, 2598−2606.
(52) Yuan, Z.; Fang, X.; Li, X.; Wu, J.; Yao, H.; Lin, A. 1,6-Conjugated Addition-Mediated [2 + 1] Annulation: Approach to Spiro[2.5]octa-4,7-dien-6-one. *J. Org. Chem.* **2015**, *80*, 11123−11130.
(53) Gai, K.; Fang, X.; Li, X.; Xu, J.; Wu, X.; Lin, A.; Yao, H. Synthesis of Spiro[2.5]octa-4,7-dien-6-one with Consecutive Quaternary Centers *via* 1,6-Conjugate Addition Induced Dearomatization of *para*-Quinone Methides. *Chem. Commun.* **2015**, *51*, 15831−15834.
(54) Huang, B.; Shen, Y.; Mao, Z.; Liu, Y.; Cui, S. Metathesis Reaction of Diazo Compounds and *para*-Quinone Methides for C−C Double Bond Formation: Synthesis of Tetrasubstituted Alkenes and Quinolinones. *Org. Lett.* **2016**, *18*, 4888−4891.
(55) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981−10080.
(56) Cheng, Q.-Q.; Deng, Y.; Lankelma, M.; Doyle, M. P. Cycloaddition of Enoldiazo Compounds. *Chem. Soc. Rev.* **2017**, *46*, 5425−5443.
(57) Baiju, T. V.; Namboothiri, I. N. N. Synthesis of Functionalized Pyrazoles *via* 1,3-Dipolar Cycloaddition of α-Diazo-β-ketophosphonates, Sufones and Esters with Electron-Deficient Alkenes. *Chem. Rec.* **2017**, *17*, 939−955 and references therein.
(58) Muruganantham, R.; Mobin, S. M.; Namboothiri, I. N. N. Base-mediated Reaction of the Bestmann−Ohira Reagent With Nitroalkenes for the Regioselective Synthesis of Phosphonylpyrazoles. *Org. Lett.* **2007**, *9*, 1125−1128.
(59) Mohanan, K.; Martin, A. R.; Toupet, L.; Smietana, M.; Vasseur, J.-J. Three-Component Reaction Using the Bestmann−Ohira Reagent: A Regioselective Synthesis of Phosphonyl Pyrazole Rings. *Angew. Chem., Int. Ed.* **2010**, *49*, 3196−3199.
(60) Pramanik, M. M. D.; Kant, R.; Rastogi, N. Synthesis of 3-Carbonyl Pyrazole-5-phosphonates *via* 1,3-Dipolar Cycloaddition of Bestmann−Ohira Reagent With Ynones. *Tetrahedron* **2014**, *70*, 5214−5220.
(61) Ahamad, S.; Gupta, A. K.; Kant, R.; Mohanan, K. Domino Reaction Involving the Bestmann−Ohira Reagent and α, β-unsaturated Aldehydes: Efficient Synthesis of Functionalized Pyrazoles. *Org. Biomol. Chem.* **2015**, *13*, 1492−1499.
(62) Mahendran, V.; Pasumpon, K.; Shanmugam, S. An Easy Access to Bipyrazoles and Unusual Demethylation of Methyl Phosphorous Ester: Exploring the Synthetic Utility of Bestmann-Ohira Reagent. *ChemistrySelect* **2017**, *2*, 2866−2869.
(63) Phatake, R. S.; Mullapudi, V.; Wakchaure, V. C.; Ramana, C. V. Fluoride-Mediated Dephosphonylation of α-Diazo-β-carbonyl Phosphonates. *Org. Lett.* **2017**, *19*, 372−375.
(64) Gupta, A. K.; Vaishanv, N. K.; Kant, R.; Mohanan, K. Rapid and Selective Synthesis of Spiropyrazolines and Pyrazolylphthalides Employing Seyferth−Gilbert Reagent. *Org. Biomol. Chem.* **2017**, *15*, 6411−6415.
(65) Du, T.; Du, F.; Ning, Y.; Peng, Y. Organocatalytic Enantioselective 1,3-Dipolar Cycloadditions Between Seyferth−Gilbert Reagent and Isatylidene Malononitriles: Synthesis of Chiral Spiro-phosphonylpyrazoline-oxindoles. *Org. Lett.* **2015**, *17*, 1308−1311.
(66) Shelke, A. M.; Suryavanshi, G. An Efficient One Pot Regioselective Synthesis of a 3, 3′-Spiro-phosphonylpyrazole-oxindole Framework *via* Base Mediated [1, 3]-Dipolar Cycloaddition Reaction. *Org. Biomol. Chem.* **2015**, *13*, 8669−8675.
(67) Gupta, A. K.; Ahamad, S.; Vaishanv, N. K.; Kant, R.; Mohanan, K. Base Mediated 1,6-Conjugate Addition of the Seyferth−Gilbert Reagent to *para*-Quinone Methides. *Org. Biomol. Chem.* **2018**, *16*, 4623−4627.
(68) Dai, L.; Mao, K.; Zhang, G.; Wang, C.; Liu, Y.; Rong, L.; Zhang, J. Ru-Catalyzed δ-Arylation of *para*-Quninone Methides with Aryl Diazonium Salts to Synthesize Fuchsones. *J. Org. Chem.* **2020**, *85*, 7238−7246.
(69) Pati, S.; Namboothiri, I. N. N. Deacylative 1, 6-Addition of Bestmann-Ohira reagent to *p*-Quinone Methides for the Synthesis of α-Diazo-β-Diarylphosphonates and Cis-Stilbenyl phosphonates. *Tetrahedron* **2019**, *75*, 2246−2253.
(70) Compound **3a** has been prepared by Lemek et al. via addition of α-chloromethyl tolylsulfone to *p*-QM followed by base-mediated elimination of HCl in low yield (12%) as part of a mixture, and its X-ray structure has been reported. See ref 47.
(71) Santra, S.; Porey, A.; Guin, J. 1,6-Conjugate Addition of 1,3-Dicarbonyl Compounds to *para*-Quinone Methides Enabled by Noncovalent N-Heterocyclic Carbene Catalysis. *Asian J. Org. Chem.* **2018**, *7*, 477.
(72) Chu, W.-D.; Zhang, L.-F.; Bao, X.; Zhao, X.-H.; Zeng, C.; Du, J.-Y.; Zhang, G.-B.; Wang, F.-X.; Ma, X.-Y.; Fan, C.-A. Asymmetric Catalytic 1,6-Conjugate Addition/Aromatization of *para*-Quinone Methides: Enantioselective Introduction of Functionalized Diarylmethine Stereogenic Centers. *Angew. Chem., Int. Ed.* **2013**, *52*, 9229.
(73) Ge, L.; Lu, X.; Cheng, C.; Chen, J.; Cao, W.; Wu, X.; Zhao, G. Amide-Phosphonium Salt as Bifunctional Phase Transfer Catalyst for Asymmetric 1,6-Addition of Malonate Esters to *para*-Quinone Methides. *J. Org. Chem.* **2016**, *81*, 9315.
(74) For a similar mechanism, see: Wang, B.-Q.; Luo, Q.; Xiao, Q.; Lin, J.; Yan, S.-J. Synthesis of Quinone Methide Substituted Neonicotinoid Derivatives via 1,6-Conjugate Addition of N-Benzyl Nitro Ketene Aminals with para-Quinone Methides Accompanying Oxidation. *ACS Sustainable Chem. Eng.* **2017**, *5*, 8382−8389.
(75) We thank one of the reviewers for suggesting these reactions.

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