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Lewis Acid-Promoted Annulation of *o*-Quinonediimines by Allylstannane: A Facile Synthesis of Quinoxaline Derivatives†

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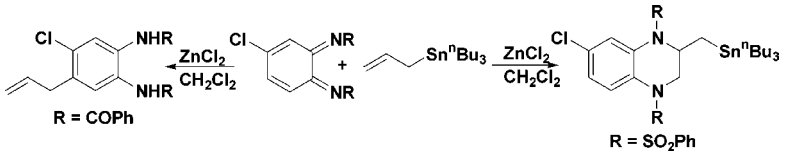
ABSTRACT



Lewis acid-promoted addition of allyltri-*n*-butylstannane to *o*-quinonediimines afforded tetrahydroquinoxaline derivatives or allylated amides depending on the nature of the substituent on imine nitrogen.

The chemistry of *o*-benzoquinones, especially their involvement in cycloadditions, has been the subject of extensive investigations in recent years.[1,2] In contrast, their aza analogues, viz.,*o*-quinonediimines, have received only scant attention,[3] the available information on their cycloaddition being mainly concerned with their participation in Diels−Alder reaction with alkenes[4] and fulvenes.[5] In the context of our general interest in the dipolar cycloaddition of quinonoids,[6] and in view of the reported proclivity of allylstannane to manifest dipolar reactivity,[7] we have examined the reaction of allyltri-*n*-butyltin with *o*-quinonediimines, in anticipation of a dihydroindole synthesis. No dipolar cycloaddition occurred, but the reaction led to a facile synthesis of tetrahydroquinoxaline derivatives. It is noteworthy that tetrahydroquinoxaline derivatives are important from a therapeutic point of view since promising anti HIV agents,[8] glucogen receptor antagonists[9] and angiotensin receptor antagonists[10] possess this ring system. The results of our preliminary investigations are presented in this letter.

The present studies were initiated by exposing a solution of 4-chloro-*o*-quinonedibenzenesulfonimide[11] **1a** to allyltri-*n*-butyltin **2a** in the presence of $ZnCl_2$. A facile reaction occurred, and the reaction mixture on usual processing[12] afforded the tetrahydroquinoxaline derivative **3a**, instead of the expected dihydroindole derivative **3a′**, as a colorless crystalline solid in 98% yield (Scheme 1).

† Dedicated with best wishes to Professor Minoru Isobe on the occasion of his 60th birthday.

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§ National Chemical Laboratory.

(1) For a review on the chemistry of quinones, see: *The Chemistry of Quinonoid Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons: New York, 1988; Vol. 2, Parts 1 and 2.

(2) (a) Nair, V.; Kumar, S. *Synlett* **1996**, 1035. (b) Nair, V.; Kumar, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1341. (c) Nair, V.; Kumar, S. *J. Chem. Soc., Perkin Trans. 1* **1996**, 443.

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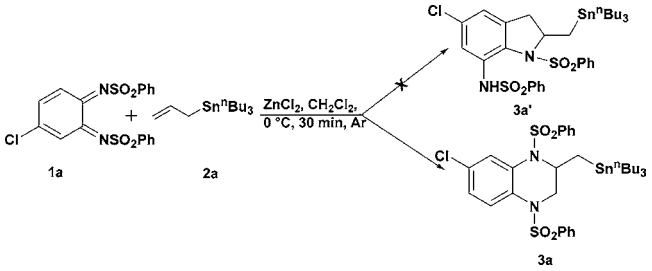
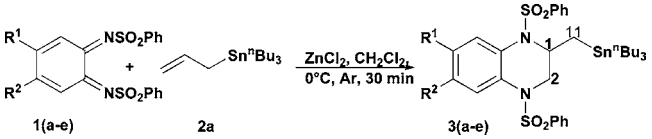
Scheme 1



Similar reactivity was displayed with other substituted *o*-quinonedibenzenesulfonimides, and the results are summarized in Table 1.

Table 1.



entry	subsrate	yield (%)
1	**1a**, R^1 = Cl, R^2 = H	98
2	**1b**, R^1 = Br, R^2 = H	72
3	**1c**, R^1 = CH_3, R^2 = H	72
4	**1d**, R^1 = Cl, R^2 = Cl	82
5	**1e**, R^1 = Me, R^2 = Me	44

The tetrahydroquinoxaline structure of **3a** was assigned on the basis of spectroscopic analysis. In ^{1}H NMR, the C-2 proton was discernible as a multiplet at δ 4.64. The C-3 protons afforded two separate signals: one at δ 3.75 (dd, J = 12.4 Hz, 3.4 Hz) and the other at δ 3.01 (dd, J = 12.4 Hz, 4.0 Hz). The C-11 protons and the protons of the *n*-butyl group were discernible as a multiplet between δ 1.51−0.87. In the ^{13}C NMR, the two carbons adjacent to nitrogen were seen at δ 53.7 and 50.7. The exocyclic carbon was discernible at δ 13.3.

Conclusive evidence for the structure of **3a** was obtained by single-crystal X-ray analysis (Figure 1).

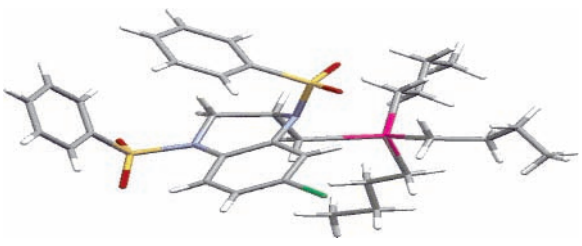
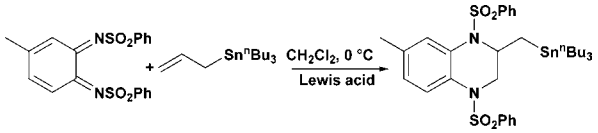


Figure 1. Single-crystal X-ray structure of **3a**.

Although the products are formally Diels−Alder adducts, it is noteworthy that in the absence of Lewis acids, no cycloaddition was observed. The reaction most likely occurs via a stepwise ionic mechanism (vide infra). In a limited screening of the Lewis acids, it was found that $AlCl_3$, Me_2AlCl, BF_3·OEt_2, and $TiCl_4$ also mediated the above transformation, but less efficiently than $ZnCl_2$. The results are summarized in Table 2.

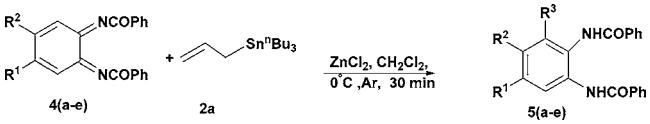
Table 2.



entry	Lewis acid	yield (%)
1	0	<5
2	$AlCl_3$	53
3	Me_2AlCl	38
4	BF_3·OEt_2	48
5	$TiCl_4$	28
6	$ZnCl_2$	72

Subsequently, we studied the reaction of allylstannane with *o*-quinonedibenzimides.[13] The $ZnCl_2$-catalyzed reaction of *o*-quinonedibenzimide **4a** and allylstannane **2a** resulted in the formation of allylated amide **5a**. In the case of other substituted *o*-quinonedibenzimides, allylation of the imide took place in a 1,4- or 1,6-manner depending on the ring substituents, and the results are presented in Table 3.

Table 3.



entry	substrate	product	yield (%)
1	**4a**, R^1 = R^2 = H	**5a**, R^1 = R^3 = H, R^2 = allyl	61
2	**4b**, R^1 = CH_3, R^2 = H	**5b**, R^1 = CH_3, R^3 = H, R^2 = allyl	68
3	**4c**, R^1 = Cl, R_2 = H	**5c**, R^1 = Cl, R^3 = H, R^2 = allyl	68
4	**4d**, R^1 = R^2 = Cl	**5d**, R^1 = R^2 = Cl, R^3 = allyl	77
5	**4e**, R^1 = R^2 = CH_3	**5e**, R^1 = R^2 = CH_3, R^3 = allyl	69

The structural assignments of the products **5a**−**e** were made on the basis of spectroscopic data, especially ^{1}H NMR. The presence of a singlet at δ 7.03 is suggestive of C-3-allylated structure for **5a**.

The mechanistic dichotomy underlying the reaction leading to an allylated product in the case of benzimide versus

(12) A solution of allyltributyltin **2a** (79 mg, 0.24 mmol) and 4-chloro-*o*-quinonedibenzenesulfonimide **1a** (84 mg, 0.2 mmol) in 4 mL CH_2Cl_2 was cooled to 0 °C, and $ZnCl_2$ (33 mg, 0.24 mmol) was added to it. After stirring for 30 min at 0 °C, the reaction was quenched by adding ice-cold water, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with water (10 mL) and brine (10 mL) and dried over anhydrous Na_2SO_4. It was concentrated, and the residue on silica gel chromatography with 15% ethyl acetate in hexane afforded the tetrahydroquinoxaline derivative **3a** in 147 mg (98%).

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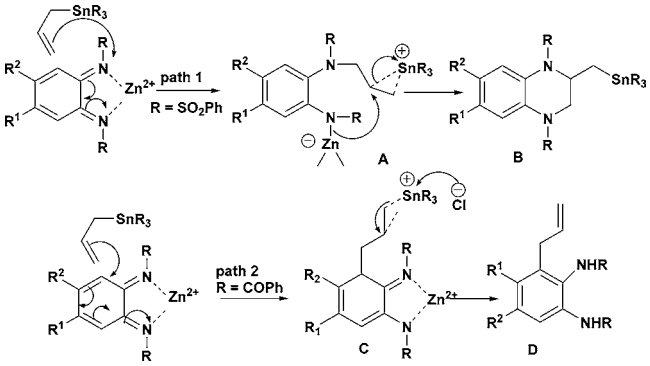
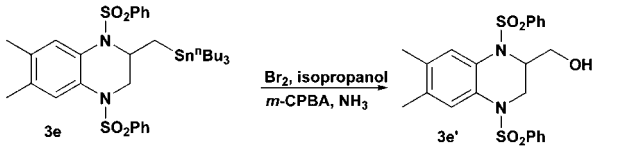
Scheme 2



Diels−Alder adducts in the case of sulfonimide may be understood by the following analysis (Scheme 2). Since the Lewis acid is crucial for the formation of tetrahydroquinoxaline derivatives, it is conceivable that an ionic mechanism is operating in this transformation. First the Lewis acid coordinates with the quinoneimine. The initial attack of allylstannane mainly depends on the basicity of the quinoneimine nitrogen. The sulfonyl substituent on nitrogen is more electrophilic, and allylstannane attacks it to form an intermediate tin-coordinated carbocation that is stabilized by hyperperconjugative interaction with the tin moiety.[7] The thus formed carbocation **A** is quenched by the N-terminus of the metal-coordinated nitrogen to furnish product **B** (path 1). When the substituent is benzoyl (imide nitrogen is more basic), the initial nucleophilic attack of the allylstannane occurs in a 1,4- or 1,6-manner depending on the substituents on the aromatic ring. The resulting carbocation **C** suffers destannylation by the nucleophile to furnish the product **D** (path 2).

As already mentioned, tetrahydroquinoxaline derivatives exhibit a wide range of pharmacological properties, and for this methodology to be effective in the construction of desirable systems, destannylation of the tetrahydroquinoxaline derivatives is essential. We have found that destannylation can be effected by combining the procedures reported by Gielen[14] and Herndon,[15] cleanly leading to the corresponding alcohol **3e′** in 86% yield (Scheme 3).

Scheme 3



In conclusion, we have encountered a facile Lewis acid-catalyzed Diels−Alder reaction of *o*-quinone dibenzenesulfonimides with allylstannane thus constituting a facile synthesis of tetrahydroquinoxaline derivatives with potential biological activities. *o*-Quinonedibenzimides provide access to allylated amides with generous substitution under similar conditions.

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Supporting Information Available: Detailed experimental procedure and characterization data for all compounds, including the CCDC deposition number of compound **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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