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Synthesis of [3a,7a]-Dihydroindoles by a Tandem Arene Cyclopropanation/3,5-Sigmatropic Rearrangement Reaction

Sidney M. Wilkerson-Hill, Brandon E. Haines, Djamaladdin G. Musaev, Huw M. L. Davies
Department of Chemistry, Emory University, 1515 Dickey Dr. Atlanta GA, 30329

Abstract

Donor/acceptor carbenes provide a powerful platform for building molecular complexity, but the majority of their reactions have been limited to aryl and vinyl donor groups. We found that a N-containing donor/acceptor carbene precursor, 4-phthalimido-*N*-methanesulfonyl-1,2,3-triazole, reacts with unactivated arenes resulting in a mixture of [3+2]-cycloadducts, [3a,7a]-dihydroindoles, and formal C–H functionalization products in up to 82% yield upon heating. We also demonstrate that the formal C–H functionalization products arise from ring-opening of the [3+2]-cycloadducts. Computational studies suggest that the formal cycloaddition process takes place through a tandem arene cyclopropanation/ 6π electrocyclization/ 6π electrocyclic ring opening/3,5-sigmatropic rearrangement reaction, which also accounts for the distinctive regioselectivity of the formal cycloaddition reaction.

Graphical Abstract

INTRODUCTION

Aromatic hydrocarbons (benzenes) are ubiquitous chemical feedstocks produced yearly on metric ton scale; consequently, their use as starting materials for small molecule synthesis is common and logical.¹ As a result of their availability, the functionalization of aromatic hydrocarbons is well established, but still continues to be an area of active research. In the last four decades, cross-coupling technologies, have revolutionized the way bonds (C–C, C–heteroatom and others) are formed to arenes and have resulted in numerous applications.^{2–3}

Corresponding Author: hmdavie@emory.edu.

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ASSOCIATED CONTENT

Supporting Information

Supporting Information: Experimental data on ring opening studies of compound 4a, X-ray crystallographic data, computational details and ¹H and ¹³C NMR spectroscopic data.

Although cross-coupling reactions now allow for the facile decoration of C–H bonds on the periphery of the aromatic ring, the use of benzenes as a C₆ fragment to directly form sp³-centers (i.e., dearomatization reactions) is much less general and represents an area for significant development.

Due to the resonance stabilization energy of benzenes (approximately 30 – 36 kcal/mol) redox neutral⁴ reactions that directly use the double bonds of the arene are scarce. Some traditional strategies exist to dearomatize benzenes such as photocycloaddition reactions,⁵ stoichiometric complexation to early transition metals,⁶ and metal-catalyzed cyclopropanation⁷ reactions. Recently, methods for using arenes as dienes in [4+2] cycloaddition reactions with allenes (Himbert reaction),⁸ and using arenes as dieneophiles with aza-o-xylylenes⁹, as well as epoxy and aziridinyl enolsilanes¹⁰ have surfaced as strategies for generating complex sp³-rich chemotypes from arenes. Additionally, recent studies have demonstrated a direct [4+2] cycloaddition reaction to unactivated arenes using triazoline diones and visible light.¹¹ Work from our group has demonstrated the utility of donor/acceptor carbenes for a variety of applications, so we surmised that these intermediates could be used to facilitate dearomatization reactions.^{12,7b}

4-Aryl-*N*-sulfonyl-1,2,3-triazoles have been utilized extensively as precursors to donor/acceptor α -diazocarbonyls due to their ability to undergo ring-opening isomerism in solution.¹³ As such, *N*-sulfonyltriazoles have been used in many transformations similar to those developed for their α -diazocarbonyl congeners.^{14,15} For example in 2012, the Davies group reported the dearomatization reaction of indoles with 4-aryl-*N*-sulfonyltriazoles to afford enantioenriched pyrroloindolines (Figure 1, A).^{15h} In 2014, Murakami and co-workers showed that rhodium-carbenes generated from 4-alkyl-*N*-sulfonyltriazoles react with tethered arenes to give dihydroindoles (Figure 1, B), however this transformation was limited to intramolecular cases.¹⁶ The Anbarasan and Lee groups in 2014 and 2015, respectively showed that *N*-sulfonyltriazoles could undergo formal C–H insertion reactions with anilines and phenolic compounds, which presumably proceeds through dearomatized intermediates in an electrophilic aromatic substitution reaction (Figure 1, C).¹⁷ Recent work by Murakami and Miura has shown that this transformation can be accomplished with unactivated alkyl benzenes, albeit using 4-acetyl-*N*-sulfonyltriazoles that give highly electrophilic acceptor/acceptor rhodium carbenes.^{16c}

Critically, the ring-opening equilibrium of these 4-substituted *N*-sulfonyltriazoles permits for the development of reactions with donor/acceptor carbenes containing heteroatom donor groups (i.e., N or O) that have yet to be accessed by standard diazo transfer reactions. Indeed, studies in the Davies group showed that 4-phthalimido-*N*-sulfonyltriazoles can function as donor/acceptor diazocarbonyl precursors for thermal cyclopropanation reactions of styrene derivatives (Figure 1, D), and these phthalimidotriazole reagents have not been extensively studied in other transformations.¹⁸ To our knowledge, our work provided the first synthetic application of a donor/acceptor carbene containing a nitrogen atom donating groups.^{19,20} Herein, we report that 4-phthalimido-*N*-sulfonyl-1,2,3-triazole reacts thermally with unactivated arenes to give [3a,7a]-dihydroindoles with alkyl substitution at the ring fusion. The reaction results in the formation of sp³-rich products containing nitrogen atoms directly from commercially available arene feedstock substrates (Figure 1, E).

RESULTS AND DISCUSSION

To this end, we began our studies by reacting 4-phthalimido-*N*-sulfonyl-1,2,3-triazole (**1a**) with disubstituted arenes such as p-xylene (Table 1). Gratifyingly, heating triazole **1a** with arene **3a** in 1,2-dichloroethane resulted in the formation of a mixture of dihydroindole **4a** and arene **5a** as a side-product. X-ray crystallographic analysis of **4a** confirmed the unusual regioselectivity of the cycloaddition reaction.²¹ After a solvent screening campaign we found that chlorinated solvents were optimal for this transformation (Entries 1 – 3). Specifically, performing the reactions in chloroform produced the highest combined isolated yield of isomers **4a** and **5a** (82% yield, Entry 3). The ratio of these isomers could be controlled through solvent effects. We observed that polar solvents such as acetonitrile and dioxane (Entries 7 and 16) resulted in moderate combined isolated yields products **4a** and **5a** (22%, 64% yields respectively), however the aromatized isomer **5a** was favored under these conditions. When using ethanol as a solvent (Entry 10), we observed the formation of a formal O–H insertion product in 88% by ¹H NMR.²² Conversely nonpolar solvents typically gave higher ratios of **4a** compared to **5a**, however the combined isolated yield of these was much lower (Entries 4, 9, and 17). We attributed this result to the low solubility of triazole **1a** in hydrocarbon solvents as well as their diminished ability to undergo ring-to-chain opening in apolar solvents. Due to the ability of **4a** to convert to **5a** thermally (vide infra), we chose Entry 3 as our optimal reaction conditions.

With these conditions in hand, we investigated the scope of this reaction with various symmetrical and unsymmetrical disubstituted arenes (Figure 2). Symmetrical arenes such as 1,4-diethylbenzene and 1,4-diisopropyl benzene participated in the formal cycloaddition reaction to give predominantly cycloadducts **4c** (46% yield), **4d**, (24% yield) respectively in addition to their formal C–H insertion side-products **5c** and **5d**.²² Changing the sulfonyl group from mesyl (**1a**) to tosyl (**1b**), resulted in diminished yields of dihydroindole products (35% yield). We observed that during the formation of cycloadduct **4d** unreacted triazole remained after 1.5 h of heating, due to the decreased dielectric constant of the reaction medium from using more nonpolar hydrocarbon substrates. We found that unsymmetrical arenes, such as p-cymene, could produce the desired [3+2] adduct **4e** and **4e'** in moderate yields (55% combined) as a mixture of regioisomers (4.5:1) favoring the depicted isomer with the smaller alkyl group (methyl group) at the ring fusion position of the dihydroindole. Using a tosyl protecting group did not significantly change the regioselectivity of **4f** to **4f'** (4.5:1). Unsymmetrical arenes such as 4-ethyltoluene also participated in the formal cycloaddition reaction to give product **4g** and **4g'**; however, the regioselectivity of the cycloaddition reaction was diminished because of the similar steric demands of a methyl and ethyl group (1.6:1 rr). Increasing the size of one of the substituents on the aromatic partner permitted the regioselective formation of dihydroindole **4h** (> 20:1 rr). Disubstituted arenes such as ethyl 4-methylbenzoate and 4-bromotoluene, which contain at least one electron withdrawing group, performed poorly in the reaction to give compound **4i** and **4j**, respectively, in low isolated yields (34% and 14% yield respectively). However, no ring-opened products were detected by ¹H NMR analysis of the crude reaction mixture in these cases. Interestingly, when m-xylene (**3k**) was used, the ring-opened enamine **5k** predominated (see, Eq 1). We surmise that these data suggest the formation of zwitterionic

intermediates during the course of the reactions (*vide infra*). Of note, we were unable to detect carbene insertion into the activated benzylic C–H bonds of these substrates.

(Eq 1)

The transformation was then extended to monosubstituted arenes (Figure 3). Our preliminary results show that reacting triazole **1a** with toluene resulted in the formation of two formal cycloaddition products **7a** and **8a** as well as the formal C–H insertion product **9a**. The connectivity of compounds **7a** and **8a** were assigned unambiguously based on X-ray crystallographic analysis. Other arenes, such as *tert*-butylbenzene and biphenyl, produced analogous products **7b**, **8b**, and **8c**, **9c**, respectively. X-ray crystallographic analysis of *tert*-butyl compound **7b** demonstrates that sterically demanding groups can also be incorporated at the ring-fusion position. Electron-deficient arenes such as bromobenzene lead to non-specific decomposition of triazole **1a**, whereas arenes with strongly electron-donating groups, such as anisole, produced exclusively formal C–H insertion products *ortho*-**9d** and *para*-**9d** in a 1:1 ratio (Eq 2).

(Eq 2)

We then sought to further understand the factors that control the selectivity between the [3+2] adducts and the C–H insertion products. Our initial hypothesis was that C–H insertion product **5a** could arise from **4a** through a ring-opening event. Thus, taking compound **4a** in CDCl_3 and heating to 70°C , we found that **5a** was produced over time (Figure 4), which conclusively establishes one of the paths leading to **5a**. When the same transformation was attempted in C_6D_6 , less than five percent conversion was observed after 150 min. Using acetonitrile as solvent, the rate of formation of **5a** is faster. These data suggest that **5a** arises from **4a** through a zwitterionic intermediate, which would be stabilized in more polar solvents. This is also supported by the preference for **5a** when the reaction is performed in MeCN (Table 1, Entry 7) as well as the preferred formation of **5k** starting from *meta*-xylene and *para*-**9d** and *ortho*-**9d** starting from anisole.

The discovered transformation presented interesting mechanistic questions regarding the regioselectivity of the formation of dihydroindole **4a**. Specifically, the formation of **4a**

suggested the possibility of a [3,5]-sigmatropic rearrangement from azavinylnorcaradiene intermediates as a possible reaction pathway, which occurs preferentially over a [1,3]-sigmatropic rearrangement to obtain dihydroindole products containing alkyl substitution at the ring-fusion position (Scheme 1, A).²³

We envisioned that upon heating, triazole **1a** undergoes thermal ring-opening to produce intermediate *a*-diazimine **A** that undergoes thermal decomposition to give free carbene **B**, which could then cyclopropanate an arene (such as *p*-xylene) to give norcaradiene *endo*-**C**, in accord with the observed selectivity for thermal cyclopropanation reactions with donor/acceptor carbenes with aryl²⁴ and nitrogen¹⁸ donor groups. Intermediate *endo*-**C**, however, does not possess the correct geometry to undergo a [3,5]-sigmatropic rearrangement to give **4a**. To achieve the correct geometry, we hypothesize that *endo*-**C** can equilibrate to *exo*-**C** by a norcaradiene to cycloheptatriene equilibrium as preceded by Jones and coworkers for the analogous vinylnorcaradiene systems.^{23,25} Intermediate *exo*-**C**, then possesses the correct geometry to undergo a [3,5]-sigmatropic rearrangement to give **4a**, which aromatizes to **5a**. To probe this mechanistic scenario, we studied this process using density functional theory (DFT) calculations²⁶ and found the [3,5]-sigmatropic rearrangement occurs with a barrier of 14.7 kcal/mol at 70 °C from intermediate *exo*-**C** (Scheme 1). Interestingly, the [1,3]-sigmatropic rearrangement was found to only take place from the *endo*-diastereomer (i.e., *endo*-**C**) with an associated barrier of 28.8 kcal/mol at the same temperature; in addition, the resulting dihydroindole is 0.7 kcal/mol higher in energy than the starting norcaradiene (Scheme 1, B). Thus, the dihydroindole selectivity can be rationalized based on the conformation of the [4.1.0]-bicycle, which more readily permits an antarafacial interaction in this 8p electron system from intermediate *exo*-**C**.

Alternatively, one can envision a pathway where phthalimido carbene **B** can undergo a formal Friedel-Crafts-type reaction with an arene to give zwitterion **D**, which undergoes ring closure to give dihydroindole **4a** or even cyclopropanes *endo*- and *exo*-**C**. However, this scenario seems unlikely at 70 °C given that zwitterion **D** forms compound **5a** irreversibly.

In conclusion, we report the thermal formal [3+2] cycloaddition reaction of aminotriazoles with neutral arenes. This work is distinctive because it proceeds in an intermolecular fashion and in the absence of a rhodium catalyst, which is in contrast to the works of Murakami, Miura, Lee, and Anbarasan which require dirhodium catalyst, highly reactive acceptor/acceptor rhodium carbenes, very electron-rich anisoles and anilines, are restricted to intramolecular reactions or a low yielding for intermolecular cases on unactivated arenes.

We have found that aminotriazole **1a** undergoes efficient reactions with a variety of substituted arenes to dihydroindoles containing alkyl substitution at the ring fusion position. Furthermore, we showed that these dihydroindoles²⁷ undergo thermal ring-opening to formal C–H functionalization products. This work represents the an additional reactivity mode for phthalimidotriazole **1a** and provides important insight into the nature of donor/acceptor carbenes with heteroatom donor groups and the thermal stability of amine-substituted diazocarbonyl motifs compared to their aryl counterparts.²⁴

EXPERIMENTAL SECTION

GENERAL INFORMATION

All reactions were conducted in oven-dried glassware under an atmosphere of dry argon. All reagents were used as received from commercial suppliers, unless otherwise stated. Dry tetrahydrofuran, diethyl ether, acetonitrile, hexanes, pentanes, toluene, and α,α,α -trifluorotoluene were obtained by passing these previously degassed solvents through activated alumina columns. Dichloromethane (CH_2Cl_2) and chloroform (CHCl_3) were further distilled over calcium hydride before use. Solvents were removed under reduced pressure on a rotatory evaporator. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian-400, Inova-500, or Bruker-600 spectrometer (100, 125, 150 MHz for ^{13}C NMR spectra) in deuterated chloroform (CDCl_3), deuterated benzene (C_6D_6) or deuterated dimethyl sulfoxide (d_6 -DMSO) as indicated. All spectra were taken at 23 °C. Chemical shifts were measured relative to the chemical shift of the residual solvent (^1H NMR CDCl_3 $\delta_{\text{NMR}} = 7.26$ ppm, d_6 -DMSO $\delta = 2.50$ ppm; ^{13}C NMR CDCl_3 $\delta = 77.16$ ppm, C_6D_6 $\delta = 128.06$, d_6 -DMSO $\delta = 39.52$ ppm) as the internal standard, and were reported in parts per million (ppm). For ^{13}C NMR spectra, chemical shifts are reported to one decimal place except. In cases where chemical shift values are the same due to rounding, two decimal places are reported. Abbreviations for signal couplings are as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sex, sextet; sep, septet; and m, multiplet. Coupling constants were taken from the spectra directly and are uncorrected. Infrared (IR) Spectra were collected on a Nicolet Impact Series 10 FT-IR as thin films or pressed solids where stated. Mass spectrometric determinations were carried out on a Thermo Finnigan LTQ-FTMS spectrometer using the ion max source and APCI probe. Analytical thin layer chromatography (TLC) was performed on Millipore-Sigma glass-backed TLC plates (250 μm thickness, 60 Å porosity, F-254 indicator) and visualized using ultraviolet (UV) light or stained with either I_2 , KMnO_4 , ceric ammonium molybdate (Hanessian's stain), or p-anisaldehyde, prepared according to the literature procedure.²⁷ Flash column chromatography was performed with SiliCycle SiliaFlash P60 (60 Å pore diameter, 230 – 400 mesh, 40 – 63 μm particle size) silica gel. X-Ray crystallographic data were visualized using CYLview.²¹ The experimental procedures for collecting X-ray crystallographic data can be found in Section 7. Melting points of recrystallized compounds were obtained using a Mel-Temp® apparatus and are uncorrected. The ratios of products were determined from ^1H NMR analysis of the crude reaction mixtures. The isolated ratios of products are not exactly equal to the crude ratios of products due to changes in the reaction mixture during SiO_2 -gel chromatography and rounding. Of note: Most of the dihydroindole compounds are yellow and can be observed visually during SiO_2 -gel chromatographic separation. The regioselectivity of the transformations were determined by analogy to compounds **4a**, **7a**, **8a** and **7b** for which X-ray crystallographic data was obtained. Triazoles **1a** and **1b** were synthesized according to the literature procedure.¹⁸ Copper 2-thiophenecarboxylate was prepared according to the literature procedure.²⁹ Microwave reactions were performed using a Anton Parr Monowave Extra.

Reaction Optimization (Table 1)—To a flame-dried 4 mL dram vial was added aminotriazole **1a** (146 mg, 0.500 mmol). The solids were then held under vacuum for 15

minutes and the vial was refilled with argon. Solvent (1 mL) and p-xylene (212 mg, 246 μ mol) was then added. The vial was then sealed with a Teflon®-coated screw cap and heated to 70 °C for the amount of time indicated. The entire sample was dissolved in CDCl₃, to which 1,3,5-trimethylbenzene (50 μ L) was added as an internal standard. An aliquot of this solution was then analyzed by ¹H NMR. For Entry 3, the solution was then concentrated again, and the residue purified by column chromatography (see Section 4 for details) to obtain isolated yields of products **4a** and **5a**.

Synthesis of triazole 1b—Solid 2-ethynylisoindoline-1,3-dione (1.00 g, 5.84 mmol) was added to a flame-dried 100 mL 3-neck round-bottomed flask and equipped with two rubber septa, and a L-shaped connector to an Ar inlet. The flask was evacuated and backfilled with Ar (x 3) and toluene (23 mL, 0.25 M) was then added by syringe under an Ar atmosphere. Copper 2-thiophenecarboxylate (56.0 mg, 0.292 mmol) was then added by removing and replacing one septum while under a stream of Ar. p-Toluenesulfonyl azide (1.38 g, 7.01 mmol) in toluene (5 mL) was added dropwise by hand over three minutes at room temperature. The heterogeneous mixture was allowed to stir at room temperature for 12 hours, upon which it was concentrated and filtered through a plug of SiO₂-gel, rinsing with excess ethyl acetate. The homogenous solution was then concentrated, and the resulting off-white solid was then triturated in cold Et₂O and collected by gravity filtration to afford the title compound as an off-white/tan solid. The product is an off-white/tan amorphous solid; mp = 135 – 140 °C decomposes; **Yield**: 1.01 g (47% yield); **R_f** = 0.37 (1:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 9.08 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 2H), 8.02 (dd, *J* = 5.5, 3.0, Hz, 2H), 7.95 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 2.45 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 165.5, 148.4, 136.5, 135.4, 131.5, 131.2, 131.1, 128.7, 124.0, 121.8, 21.3; **IR** (ATIR) 3273, 3169, 2131, 1730, 1352 cm⁻¹; **HRMS** (ESI) *m/z*: [M + H]⁺ Calcd for C₁₇H₁₃O₄N₄S 369.0652; Found 369.0649.

Reaction Scope and Product Characterization Disubstituted Arenes (Figure 2)

Representative procedure: To a flame-dried 4 mL dram vial was added aminotriazole **1a** (146 mg, 0.500 mmol). The solids were then held under vacuum for 15 minutes and the vial was refilled with argon. Solvent (1 mL) and arene (2.00 mmol, 4.0 equiv) was then added under argon. The vial was then sealed with a Teflon®-coated screw cap and heated to 70 °C for the amount of time indicated. The entire sample was dissolved in CDCl₃, to which 1,3,5-trimethylbenzene (50 μ L) was added as an internal standard. An aliquot of this solution was then analyzed by ¹H NMR. The solution was then concentrated again, and the residue purified by column chromatography to obtain products **4** as an orange amorphous solid and C–H insertion product **5** as a yellow amorphous foam.

Reaction of 1a with p-xylene: The combined isolated yield of both isomers **4a** and **5a** is 152 mg (82% yield) using 146 mg (0.500 mmol) triazole **1a**. The ratio by crude ¹H NMR analysis of **4a** to **5a** is 2.7:1.

2-(5,7a-dimethyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4a): An analytical sample of **4a** was obtained by recrystallization from a saturated solution in refluxing ethanol to give the product as orange needles. X-ray quality crystals

were grown by slow evaporation of diethyl ether from a saturated solution of **4a**. **Yield:** 102 mg (55% yield); **R_f** = 0.20 (3:1 hexanes:ethyl acetate); **mp** = 92 – 95 °C; **¹H NMR** (500 MHz, CDCl₃) δ 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.78 (dd, *J* = 5.4, 3.1, 2H), 6.92 (d, *J* = 1.7 Hz, 1H), 6.09 (d, *J* = 9.9 Hz, 1H), 5.96 (d, *J* = 10.4 Hz, 1H), 5.30 – 5.25 (m, 1H), 4.29 – 4.24 (m, 1H), 2.93 (s, 3H), 1.73 (t, *J* = 1.9 Hz, 3H) 1.67 (s, 3H); **¹³C NMR** (125 MHz, CDCl₃) δ 166.9, 134.8, 131.8, 129.4, 128.3, 125.3, 123.9, 123.6, 119.1, 116.7, 64.9, 50.2, 41.2, 30.9, 21.6; **IR** (ATIR) 3105, 3129, 3072, 3025, 2928, 2852, 1714, 1372, 1153, 717 cm⁻¹; **HRMS** (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₁₉O₄N₂S 371.1060; Found 371.1056.

(E)-N-(2-(2,5-dimethylphenyl)-2-(1,3-dioxoisindolin-2-yl)vinyl)methanesulfonamide (5a): The product is an amorphous yellow foam; **Yield:** 50.6 mg (27% yield); **R_f** = 0.10 (3:1 hexanes:ethyl acetate); **¹H NMR** (500 MHz, CDCl₃) δ 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.1, 2H), 7.20 – 7.02 (m, 3H), 6.68 (d, *J* = 11.8 Hz, 1H), 6.20 (d, *J* = 11.8 Hz, 1H), 3.11 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H); **¹³C NMR** (125 MHz, CDCl₃) δ 167.5, 136.4, 134.5, 134.4, 131.7, 131.2, 131.1, 130.6, 130.4, 125.7, 123.8, 113.6, 41.6, 21.0, 19.2; **IR** (ATIR) 3248, 2019, 2927, 2866, 1711.41, 1374, 1339, 1156, 746 cm⁻¹; **HRMS** (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₁₉O₄N₂S 371.1060; Found 371.1062.

Reaction of 1b with p-xylene: The combined isolated yield of both isomers **4b** and **5b** is: 39.7 mg (52% yield) using 63.0 mg (0.171 mmol) **1b** and 286 mg (61% yield) using 368.4 (1.0 mmol) **1b**. The ratio by crude ¹H NMR analysis of **4b** to **5b** 2.8:1; Note: The compounds do not separate completely by SiO₂-gel chromatography and the remaining mass balance is accounted for in mixed fractions.

2-(5,7a-dimethyl-1-tosyl-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4b): **Column chromatography:** (4:1:1 hexanes:ethyl acetate:toluene); The product is an orange amorphous solid; **Yield** 162 mg (35% yield) using 1.00 mmol **1b**; **R_f** = 0.24 (4:1:1 hexanes:ethyl acetate:toluene); **¹H NMR** (600 MHz, CDCl₃) δ 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.77 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.71 (d, *J* = 8.3 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 1.7 Hz, 1H), 5.90 (d, *J* = 9.8 Hz, 1H), 5.49 (d, *J* = 9.1 Hz, 1H), 5.03 (dt, *J* = 2.7, 1.3 Hz, 1H), 4.11 – 4.08 (m, 1H), 2.36 (s, 3H), 1.63 (s, 3H), 1.34 – 1.33 (m, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 166.8, 143.0, 138.3, 134.7, 131.8, 129.5, 129.0, 128.4, 127.3, 124.9, 124.3, 123.8, 118.5, 117.2, 64.6, 49.8, 30.4, 21.6, 21.0; **IR** (ATIR) 3031, 2971, 2923, 1720, 1383, 1181 cm⁻¹; **HRMS** (ESI) *m/z*: [M + H]⁺ Calcd for C₂₅H₂₃O₄N₂S 447.1373; Found 447.1378.

(E)-N-(2-(2,5-dimethylphenyl)-2-(1,3-dioxoisindolin-2-yl)vinyl)-4-methylbenzenesulfonamide (5b): An analytical sample of the ring-opened isomer **5b** was obtained during recrystallization of the chromatographed product **4b** in refluxing methanol. The product is a white solid; **Yield:** 33.8 mg, (7% yield) using 1.00 mmol **1b** obtained as pure compound; **R_f** = 0.08 (4:1:1 hexanes:ethyl acetate:toluene); **¹H NMR** (600 MHz, CDCl₃) δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.3d (d, *J* = 7.9 Hz, 1H), 7.08 – 7.03 (m, 2H), 6.91 (apparent s, 1H), 6.78 (d, *J* = 11.9 Hz, 1H), 6.21 (d, *J* = 11.8 Hz, 1H), 2.48 (s, 3H), 2.24 (s, 3H), 2.90 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 167.4, 144.4, 136.8, 136.1, 134.5, 134.4, 131.7, 131.0, 130.9, 130.7, 130.4,

130.1, 127.0, 125.9, 123.7, 114.5, 21.8, 21.0, 18.8; **IR** (ATIR) 3251, 2922, 2865, 1716, 1376, 1167 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₅H₂₂O₄N₂NaS 469.1193; Found 469.1192.

Reaction of 1a with 1,4-diethylbenzene: The combined isolated yield of both isomers **4c** and **5c** is 41.3 mg (60% yield) using 50.0 mg (0.171 mmol) of **1a**; the ratio of **4c** to **5c** by crude ¹H NMR analysis is 3.6:1.

2-(5,7a-diethyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4c): Column chromatography: 4:1 (hexane:ethyl acetate) to 3:1 (hexanes:ethyl acetate); **Yield:** 31.6 mg (46% yield); **R_f** = 0.19 (3:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.88 (d, *J* = 1.8 Hz, 1H), 6.10 – 6.05 (m, 2H), 5.25 (dt, *J* = 2.8, 1.3 Hz, 1H), 4.41 (dt, *J* = 3.3, 2.0 Hz, 1H), 2.92 (s, 3H), 2.03 (tdt, *J* = 9.2, 5.3, 1.9 Hz, 2H), 1.98 (dq, *J* = 7.4, 4.5 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.5 Hz, 3H). **¹³C NMR** (150 MHz, CDCl₃) δ 166.8, 134.7, 133.9, 131.8, 129.4, 124.2, 124.0, 123.8, 117.5, 117.2, 68.8, 46.6, 40.6, 35.9, 28.5, 12.8, 7.7. **IR** (ATIR) 2966, 2933, 2878, 1719, 1384, 1349 1155 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₁H₂₃O₄N₂S 399.1373; Found 399.1365.

(E)-N-(2-(2,5-diethylphenyl)-2-(1,3-dioxoisoindolin-2-yl)vinyl)methanesulfonamide (5c) 11.6:1 mixture of *E*- and *Z*- isomers. Data for major isomer reported. **Yield:** 9.70 mg (14% yield); **R_f** = 0.10 (3:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.25 – 7.23 (m, 1H), 7.21 – 7.18 (m, 2H), 6.70 (d, *J* = 11.8 Hz, 1H), 6.17 (d, *J* = 11.8 Hz, 1H), 3.10 (s, 3H), 2.67 – 2.59 (m, 4H), 1.23 (t, *J* = 7.6 Hz, 3H), 1.19 (t, *J* = 7.5 Hz, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 167.5, 142.7, 140.6, 134.5, 131.8, 130.4, 129.94, 129.64, 129.3, 125.9, 123.4, 113.9, 41.6, 28.4, 25.1, 15.6, 15.2. **IR** (ATIR) 3261, 2966, 2931, 1716, 1377, 1150 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₁H₂₃O₄N₂S 399.1373; Found 399.1371.

Reaction of 1a with 1,4-diisopropylbenzene: The combined isolated yield of both isomers **4d** and **5d** is 24.3 mg (33% yield) using 50.0 mg (0.171 mmol) triazole **1a** the ratio of **4d** to **5d** by crude ¹H NMR analysis is 3.6:1.

2-(5,7a-diisopropyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3dione (4d): Column chromatography: 5:1 (hexanes:ethyl acetate) to 3:1 (hexanes:ethyl acetate); **Yield:** 17.5 mg (24% yield); **R_f** = 0.23 (3:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.90 (d, *J* = 5.4, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.83 (d, *J* = 1.9 Hz, 1H), 6.14 (dd, *J* = 10.2, 1.2 Hz, 1H), 6.09 (d, *J* = 10.2 Hz, 1H), 5.24 – 5.21 (m, 1H), 4.48 (apparent s, 1H), 2.94 (s, 3H), 2.32 (sep, *J* = 6.8 Hz, 1H), 2.24 (sep, *J* = 6.9 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 2.6 Hz, 3H), 0.95 (d, *J* = 2.5 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 166.8, 138.1, 134.7, 131.8, 128.0, 124.4, 124.3, 123.9, 118.0, 116.0, 72.4, 42.8, 40.2, 38.4, 33.3, 21.4, 21.1, 16.9, 15.4; **IR** (ATIR) 2961, 2929, 2873, 1723, 1385, 1347, 1158 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₃H₂₇O₄N₂S 427.1686; Found 427.1676.

(E)-N-(2-(2,5-diisopropylphenyl)-2-(1,3-dioxoisindolin-2-yl)vinyl)methanesulfonamide (5d): Yield: 6.8 mg (9% yield). 1.2:1 mixture of *E*- and *Z*- isomers. Data for major isomer reported Compound decomposes neat at -20°C over two days. $R_f = 0.13$ (3:1 hexanes/ethyl acetate); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.85 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.74 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.31 (d, $J = 8.1$ Hz, 1H), 7.27 – 7.24 (m, 2H), 7.24 (d, $J = 2.0$ Hz, 1H), 6.72 (s, 1H), 3.23 (sep, $J = 6.8$ Hz, 1H), 3.10 (s, 3H) 2.80 (sep, $J = 7.1$ Hz, 1H, 1.27 (d, $J = 5.3$ Hz, 3H), 1.24 (apparent d, 6H), 1.10 (d, $J = 6.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) 18 carbon atoms found; δ 167.5, 147.3, 145.8, 134.6, 131.7, 129.6, 128.9, 128.4, 126.7, 126.2, 123.8, 114.2, 41.6, 33.7, 29.6, 24.8, 24.4, 24.1; **IR** (ATIR) 3265, 2961, 2928, 2870, 1717, 1375, 1160 cm^{-1} **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{26}\text{O}_4\text{N}_2\text{NaS}$ 449.1506 Found 449.1504.

Reaction of 1a with p-cymene: The combined isolated yield of isomers **4e**, **4e'**, **5e** and **5e'** is 45.1 mg, (66% yield) using 50.0 mg (0.171 mmol) triazole **1a**. The dihydroindoles **4e** and **4e'** were obtained in 4.5:1 rr in the crude reaction mixture.

2-(5-isopropyl-7a-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4e) and 2-(7a-isopropyl-5-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4e'): Yield: 37.7 mg (55% yield); (5:1) Mixture of two regioisomers upon isolation; $R_f = 0.18$ (3:1 hexanes:ethyl acetate); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.90 (dd, $J = 5.5, 3.1$ Hz, 2H); 7.78 (dd, $J = 5.5, 3.1$ Hz, 2H), 6.96 (d, $J = 1.6$ Hz, 1H), 6.10 (s, 1H), 6.09 (s, 1H), 5.24 (dq, $J = 3.9$ Hz, 1.1 Hz), 4.24 (dt, $J = 4.4, 1.5$ Hz, 1H), 2.90 (s, 3H), 2.27 (apparent sept, $J = 6.9$ Hz, 1H), 1.66 (s, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 166.8, 138.1, 134.7, 131.8, 127.5, 125.5, 123.9, 123.6, 116.9, 116.6, 64.9, 49.8, 40.7, 33.3, 30.7, 21.4, 21.1; **IR** (ATIR) cm^{-1} 2961, 2930, 2871, 1775, 1716, 1379, 1339, 1153, 718; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{23}\text{O}_4\text{N}_2\text{S}$ 399.1373; Found 399.1372.

(E)-N-(2-(1,3-dioxoisindolin-2-yl)-2-(2-isopropyl-5-methylphenyl)vinyl)methanesulfonamide (5e) and (E)-N-(2-(1,3-dioxoisindolin-2-yl)-2-(5-isopropyl-2-methylphenyl)vinyl)methanesulfonamide (5e'): Yield: 7.40 mg (11%, yield); $R_f = 0.11$ (3:1 hexanes:ethyl acetate); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (major isomer) 7.85 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.74 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.21 – 7.13 (m, 3H), 6.68 (d, $J = 11.8$ Hz, 1H), 6.23 (d, $J = 11.8$ Hz, 1H), 3.09 (s, 3H), 2.85 (sep, $J = 6.9$ Hz, 1H), 2.37 (s, 3H), 1.21 (d, $J = 6.9$ Hz, 6H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 167.5; 147.4, 134.7, 134.5, 131.7, 131.2, 131.09, 128.3, 127.7, 126.1, 123.8, 113.7, 41.6, 33.6, 24.1, 19.2; (Minor isomer) 167.5, 145.5, 136.2, 134.5, 131.6, 131.2, 131.0, 129.6, 126.7, 126.1, 123.7, 113.6, 41.5, 29.5, 24.1 21.0; **IR** (ATIR) 3255, 2960, 2927, 2870, 1713, 1670, 1374; 1340, 1150 cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{23}\text{O}_4\text{N}_2\text{S}$ 399.1373; Found 399.1377.

Reaction of 1b with p-cymene: The combined isolate yield of isomers is 232.2 mg (49% yield) using 363 mg triazole (1.00 mmol) **1b**; Note: The dihydroindoles **4f** and **4f'** and C–H insertion products **5f** and **5f'** do not completely separate by SiO_2 -gel chromatography.

2-(5-isopropyl-7a-methyl-1-tosyl-*cis*-3a,7a-dihydro-1*H*-indol-3-yl)isoindoline-1,3-dione (4f) and 2-(7a-isopropyl-5-methyl-1-tosyl-*cis*-3a,7a-dihydro-1*H*-indol-3-yl)isoindoline-1,3-dione (4f’): Column chromatography: (6:1:1 hexanes:ethyl acetate:toluene); The pure compound was obtained in 185.8 mg (39% yield) and the regioselective ratio of **4f:4f’** is 4.5:1 by crude ^1H NMR analysis; $R_f = 0.28$ (4:1:1 hexanes:ethyl acetate:toluene); ^1H NMR (600 MHz, CDCl_3) δ 7.89 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.77 (dd, $J = 5.4, 3.1$ Hz, 2H), 7.69 (d, $J = 8.3$ Hz, 2H), 7.23 – 7.16 (m, 3H), 5.94 (d, $J = 10.0$ Hz, 1H), 5.60 (d, $J = 10.0$ Hz, 1H), 5.03 – 4.93 (m, 1H), 4.20 – 4.10 (m, 1H), 2.33 (s, 3H), 1.87 (sept, $J = 6.6$ Hz, 1H), 1.65 (s, 3H), 0.69 (d, $J = 6.8$ Hz, 3H), 0.68 (d, $J = 6.8$ Hz, 1H); (minor isomer) 7.75 (d, $J = 8.3$ Hz, 0.4H), 7.22 – 7.20 (m, 0.4H), 7.11 (d, $J = 1.8$ Hz, 0.4H), 5.84 (d, $J = 10.0$ Hz, 0.2H), 5.45 (d, $J = 10.1$ Hz, 0.2H), 5.02 – 4.98 (m, 0.2H), 4.38 – 4.31 (m, 0.2H), 2.39 – 2.32 (m, 0.8H), 1.32 – 1.31 (m, 0.6H), 1.05 (d, $J = 6.8$ Hz, 0.6H), 0.93 (d, $J = 6.9$ Hz, 0.6H), (phthalimide protons not found); ^{13}C NMR (150 MHz, CDCl_3) δ (major) 166.7, 142.9, 138.2, 138.0, 134.5, 131.7, 129.0, 127.4, 127.2; 124.5; 124.2, 123.7, 116.5, 115.6, 64.9, 49.7, 32.9, 30.7, 21.4, 20.9, 20.8; (minor) 166.7, 142.7, 138.1, 134.5, 130.0, 128.7, 125.7, 122.7, 118.1, 118.0, 71.6, 42.7, 38.2, 21.4, 21.0, 16.9, 15.5. (17 carbons found); IR (ATIR) 3030.1, 2962, 2925, 2871, 1719, 1382, 1348, 1184, 1161 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{27}\text{O}_4\text{N}_2\text{S}$ 475.1686; Found 475.1692.

(*E*)-*N*-(2-(1,3-dioxoisindolin-2-yl)-2-(2-isopropyl-5-methylphenyl)vinyl)-4-methylbenzenesulfonamide (5f) and (*E*)-*N*-(2-(1,3-dioxoisindolin-2-yl)-2-(5-isopropyl-2-methylphenyl)vinyl)-4-methylbenzenesulfonamide Yield: 40.6 mg (9% yield) of the pure compound was obtained. $R_f = 0.17$ (4:1:1 hexanes:ethyl acetate:toluene); ^1H NMR (600 MHz, CDCl_3) δ (major isomer reported) 7.83 (d, $J = 5.5, 3.0$ Hz, 2H), 7.77 (d, $J = 8.3$ Hz, 2H), 7.72 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.36 (d, $J = 7.9$ Hz, 2H), 7.10 – 7.08 (m, 2H), 6.97 (s, 1H), 6.77 (d, $J = 9.6$ Hz, 1H), 6.19 (d, $J = 10.4$ Hz, 1H), 2.76 (sept, $J = 6.9$ Hz, 1H), 2.45 (s, 3H), 2.08 (s, 3H), 1.15 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ (major reported) 167.4, 147.2, 144.4, 136.8, 134.8, 134.4, 131.8, 131.0, 130.96, 130.07, 128.6, 127.6, 127.0, 126.1, 123.7, 114.5, 33.6, 24.0, 21.8, 18.8; IR (ATIR) 3255, 2960, 2926, 2870, 1714, 1374, 1166, 1089 cm^{-1} ; HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{27}\text{O}_4\text{N}_2\text{S}$ 475.1686; Found 475.1691.

Reaction of 1a with 4-ethyltoluene: The combined isolated yield of all isomers **4g**, **4g’**, **5g** and **5g’** is (68% yield) using 50.0 mg (0.171 mmol) triazole **1a**; The product is a yellow oil. The dihydroindoles **4g** and **4g’** is isolated as a mixture of inseparable regioisomers in 1.6:1 rr by crude ^1H NMR analysis.

2-(5-ethyl-7a-methyl-1-(methylsulfonyl)-*cis*-3a,7a-dihydro-1*H*-indol-3-yl)isoindoline-1,3-dione (4g) 2-(7a-ethyl-5-methyl-1-(methylsulfonyl)-*cis*-3a,7a-dihydro-1*H*-indol-3-yl)isoindoline-1,3-dione (4g’): Column chromatography: 4:1 (hexanes:ethyl acetate); Yield: 24.7 mg (37% yield); $R_f = 0.21$ (4:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, C_6D_6) mixture of regioisomers (1.5:1 after isolation), *denotes minor regioisomer δ 7.39 – 7.35* (m, 4.5H), 7.16 – 7.13 (m, 1.5H), 7.08* (d, $J = 1.9$ Hz, 1 H), 6.88 – 6.83 (m, 4.5H), 6.13 (d, $J = 10.0$ Hz, 1.5H), 6.11* (d, $J = 10.1$ Hz, 1H), 5.63 – 5.54* (m, 2.5H), 5.31 (dq, $J = 2.7, 1.3$ Hz, 1.5H), 5.28* (dq, $J = 2.9, 1.4$ Hz, 1H); 4.61 – 4.57* (m,

1H), 4.39 – 4.35 (m, 1.5H), 2.44* (s, 3H), 2.42 (s, 4.5H), 2.01* (dddd, $J = 21.1, 13.7, 7.4, 6.4$ Hz, 2H), 1.71 (dddt, $J = 9.1, 7.4, 5.3, 1.7$ Hz, 3H), 1.61 (s, 4.5H), 1.38 – 1.37* (apparent t, $J = 6$ Hz, 3H), 0.95* (t, $J = 7.4$ Hz, 3H), 0.72 (t, $J = 7.5$ Hz, 4.5H); **¹³C NMR** (150 MHz, C₆D₆) δ 166.51, 166.46, 134.05, 134.02, 132.1, 129.6, 128.4, 126.0, 124.8, 124.6, 124.3, 123.3, 119.2, 118.0, 116.4, 116.2, 68.6, 64.9, 50.4, 47.1, 40.6, 40.4, 36.3, 30.6, 28.6, 21.3, 12.8, 7.5 (28 of 32 carbons found); **IR** (ATIR) 2967, 2931, 1718, 1381, 1345, 1153 cm⁻¹; **HRMS** (ESI) m/z : [M + H]⁺ Calcd for C₂₀H₂₁O₄N₂S 385.1217; Found 385.1220.

(E)-N-(2-(1,3-dioxoisindolin-2-yl)-2-(2-ethyl-5-

methylphenyl)vinyl)methanesulfonamide (5g) and (E)-N-(2-(1,3-dioxoisindolin-2-

yl)-2-(5-ethyl-2-methylphenyl)vinyl)methanesulfonamide (5g'): The products are a yellow oil. The enamines **5g'** and **5g** is isolated as a mixture of inseparable regioisomers. **Yield**: 20.1 mg (31% yield); **R_f** = 0.13 (4:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) mixture of regioisomers (1.7:1 after isolation) *denotes minor regioisomer; (53.2 of 53.4 hydrogens found) δ 7.41 – 7.32 (m, 7.6H), 7.02* (d, $J = 7.9$ Hz, 1H), 6.96 (d, $J = 7.8$ Hz, 1.7H), 6.91 – 6.81 (m, 8.9H), 6.79* (d, $J = 11.9$ Hz, 1H), 6.77 (d, $J = 11.8$ Hz, 1.6H), 6.09 – 6.01 (m, 2.5H), 2.43 (s, 5.2H), 2.39 – 2.24 (m, 4.6H), 2.20 (s, 3.1H), 2.17 (s, 5.0H), 1.99 (s, 3H), 1.19 (t, $J = 7.5$ Hz, 3H), 0.99 (t, $J = 7.6$ Hz, 5H). **¹³C NMR** (150 MHz, CDCl₃) δ 166.9, 166.8, 142.5, 140.3, 136.0, 134.7, 133.44, 133.41, 132.0, 131.8, 131.13, 131.11, 130.7, 130.4, 129.2, 129.1, 128.8, 128.0, 127.8, 126.4, 126.3, 122.98, 122.96, 40.3, 40.29, 40.25, 28.1, 25.0, 20.4, 19.0, 15.3, 15.0 (32 of 32 carbons found); **IR** (ATIR) 3259, 2965, 3929, 1715, 1377 1158 cm⁻¹; **HRMS** (ESI) m/z : [M + H]⁺ Calcd for C₂₀H₂₁O₄N₂S 385.1217; Found 385.1223.

Reaction of 1a with 4-*t*-butyltoluene: The combined yield of both isomers **4h** and **5h** is 42 mg (59% yield) using 50.0 mg (0.171 mmol) triazole **1a**; the ratio of **4h** to **5h** by crude ¹H NMR analysis is 3.7:1; the regioselectivity for formation of dihydroindole **4h** is > 20:1 rr.

2-(5-(tert-butyl)-7a-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-

yl)isindoline-1,3-dione (4h): Column chromatography: 4:1 hexanes:ethyl acetate; **Yield**: 32.5 mg (46% yield) **R_f** = 0.34 (2:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.90 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.78 (dd, $J = 5.5, 3.0$ Hz, 2H), 6.94 (d, $J = 1.5$ Hz, 1H), 6.28 (dd, $J = 10.2, 1.2$ Hz, 1H), 6.10 (dt, $J = 10.2, 1.0$ Hz, 1H), 5.29 (dt, $J = 2.6, 1.3$ Hz, 1H), 4.24 – 4.16 (m, 1H), 2.88 (s, 3H), 1.65 (s, 3H), 1.00 (s, 9H); **¹³C NMR** (150 MHz, CDCl₃) δ 166.9, 140.3, 134.7, 131.8, 126.7, 125.2, 123.92, 123.86, 116.9, 115.4, 64.4, 50.0, 40.7, 34.1, 30.5, 28.6; **IR** (ATIR) cm⁻¹; **HRMS** (APCI) m/z : [M – H]⁻ Calcd for C₂₂H₂₃O₄N₂S 411.1373; Found 411.1385; No minor regioisomers were detected by ¹H NMR.

(E)-N-(2-(5-(tert-butyl)-2-methylphenyl)-2-(1,3-dioxoisindolin-2-

yl)vinyl)methanesulfonamide (5h): **Yield**: 9.50 mg (13% yield); 5.9:1 mixture of *E*- and *Z*-isomers. Data for major isomer reported. **R_f** = 0.24 (2:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.85 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.74 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.39 (d, $J = 2.2$ Hz, 1H), 7.32 (dd, $J = 8.1, 2.2$ Hz, 1H), 7.19 (d, $J = 8.1$ Hz, 1H), 6.69 (d, $J = 11.7$ Hz, 1H), 6.17 (d, $J = 11.7$ Hz, 1H), 3.11 (s, 3H), 2.37 (s, 3H), 1.29 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 167.4, 149.7, 134.4, 131.6, 130.8, 127.0, 126.8, 125.8, 123.7, 114.1, 41.5,

34.4, 31.3, 18.9; **IR** (ATIR) cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{25}\text{O}_4\text{N}_2\text{S}$ 413.1530; Found 413.1533.

Reaction of 1a with ethyl 4-methylbenzoate: No ring opened isomers or other regioisomers were detected by ^1H NMR. **Yield** 25.1 mg (34% yield) using 50.0 mg (0.171 mmol) triazole **1a**.

ethyl 3-(1,3-dioxoisindolin-2-yl)-7a-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indole-5-carboxylate (4i): **Column chromatography:** 3:1 (hexanes:ethyl acetate); the product is a yellow oil; **Yield:** 25.1 mg, (34% yield) $R_f = 0.13$ (3:1 hexanes:ethyl acetate); **^1H NMR** (600 MHz, CDCl_3) δ 7.91 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.80 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.02 (d, $J = 1.9$ Hz, 1H), 6.66 (dt, $J = 3.1, 1.1$ Hz, 1H), 6.64 – 6.62 (m, 1H), 6.23 (dt, $J = 10.1, 1.1$ Hz, 1H), 4.52 – 4.50 (m, 1H), 4.25 – 4.16 (m, 2H), 2.93 (s, 3H), 1.72 (s, 3H), 1.27 (t, $J = 7.1$ Hz, 3H); **^{13}C NMR** (150 MHz, CDCl_3) δ 166.7, 165.0, 134.9, 133.1, 131.7, 126.0, 125.5, 124.2, 124.0, 123.2, 113.6; 64.4, 61.3, 50.3, 41.6, 30.8, 14.3 **IR** (ATIR) 2981, 2930, 1718, 1383, 1155 cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{21}\text{O}_6\text{N}_2\text{S}$ 429.1115; Found 429.1128.

Reaction of 1a with 4-bromotoluene: No ring opened isomers or other regioisomers were detected by ^1H NMR. **Yield** 15.3 mg (14% yield) using 50.0 mg (0.171 mmol) triazole **1a**.

2-(5-bromo-7a-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (4j): **Column chromatography:** 4:1 (hexanes:ethyl acetate); **Yield:** 15.3 mg (67% purity, 14% yield) $R_f = 0.10$ (3:1 hexanes:ethyl acetate); **^1H NMR** (600 MHz, CDCl_3) δ 7.90 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.79 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.02 (d, $J = 1.7, 1.1$ Hz, 1H), 5.92 – 5.89 (m, 1H), 4.42 – 4.35 (m, 1H), 2.98 (s, 2H), 1.70 (s, 1H); Phthalimide byproduct 7.87 (dd, $J = 5.5, 3.0$ Hz, 1H), 7.76 (dd, $J = 5.5, 3.0$ Hz, 1H); **^{13}C NMR** (150 MHz, CDCl_3) δ 166.6, 134.9, 131.6, 129.32, 127.6, 124.2, 124.0, 123.9, 115.1, 114.8; 63.7, 52.3, 41.6, 30.4. Phthalimide byproduct 167.9, 134.5, 132.8, 123.8, **IR** (ATIR) 3203, 3063, 2973, 1719, 1383 cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_4\text{N}_2\text{BrS}$ 435.0022; Found 435.0018; No ring opened isomers were detected by ^1H NMR.

Reaction of 1a with m-xylene: The combined yield of all isomers is 47.1 mg (74% yield) using 50.0 mg (0.171 mmol) triazole **1a**; the ratio by crude ^1H NMR analysis of **4k** to **5k** is 1:12; the product is a pale yellow amorphous solid upon concentration from benzene. The dihydroindole **4k** could not be isolated by SiO_2 -column chromatography but is observed in the crude reaction mixture.

(E)-N-(2-(2,4-dimethylphenyl)-2-(1,3-dioxoisindolin-2-yl)vinyl)methanesulfonamide (5k): **Column chromatography:** 2:1 (hexanes:ethyl acetate); **Yield** 47.1 mg, (74% yield); $R_f = 0.17$ (2:1 hexanes:ethyl acetate); **^1H NMR** (600 MHz, CDCl_3) δ 7.83 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.74 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.22 (d, $J = 7.8$ Hz, 1H), 7.07 (apparent s, 1H), 7.05 – 7.00 (m, 1H), 3.10 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H). **^{13}C NMR** (150 MHz, CDCl_3) δ 167.5, 139.7, 137.4, 134.5, 132.0, 131.7, 130.1, 128.3, 127.6, 125.7, 123.8, 113.7, 41.6, 21.3, 19.5;

IR (ATIR) 3261, 3024, 2927, 1713, 1377, 1159 cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{19}\text{O}_4\text{N}_2\text{S}$ 371.1060; Found 371.1057.

Reaction Scope and Product Characterization Monosubstituted Arenes (Figure 3)

Representative procedure: To a flamed dried 10 mL round-bottom flask was added freshly prepared aminotriazole **1a** (292 mg, 1.00 mmol, 1.0 equiv). The flask was then fitted with a rubber septum and placed under vacuum for 15 min. The flask was then refilled with Ar and 1,2-DCE (2.0 mL) and toluene (425 μL , 4.0 mmol, 4.0 equiv) were added. The white heterogeneous mixture was then lowered into an oil bath pre-heated to 65 $^{\circ}\text{C}$ and stirred for 290 min. The flask was removed from the heat, and the solvent was removed under reduced pressure. The resulting brown/orange oil was then purified by column chromatography to afford dihydroindole **7a** as an orange amorphous solid. The solids from the lower R_f spot (a mixture of compounds **8a** and **9a**) was then triturated in ethanol, and the solids were collected using a Hirsch funnel to afford dihydroindole **8a** as an amorphous yellow solid and C–H insertion product **9a** as a yellow foam.

Reaction of 1a with toluene: The **combined isolated yield** of all isomers: 151 mg, (42% yield) using 292 mg (1.00 mmol) of triazole **1a**. The ratio of **7a** to **8a** to **9a** by crude ^1H NMR is 1.3:1.2:1.0

2-(7a-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (7a): An analytical sample was obtained by recrystallization from a saturated solution in refluxing ethanol to give the product as shiny orange flakes. X-ray quality crystals were grown by vapor diffusion of pentanes into a solution of **7a** in dichloromethane. **Yield:** 54.3 mg (15% yield); R_f = 0.28 (2:1 hexanes:ethyl acetate); **mp** = 131 – 132 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.89 (dd, J = 5.5, 3.0 Hz, 2H), 7.78 (dd, J = 5.5, 3.0 Hz, 1H), 6.97 (d, J = 1.8 Hz, 1H), 6.15 – 6.07 (m, 2H), 5.90 (dddd, J = 9.8, 4.4, 2.5, 1.8 Hz, 1H), 5.62 (ddt, J = 9.8, 3.0, 1.0 Hz, 1H), 4.31 – 4.24 (m, 1H), 2.95 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.8, 134.8, 131.7, 125.2, 124.9, 124.9, 124.5, 123.9, 120.7, 115.7, 65.0, 49.8, 41.2, 31.0; **IR** (ATIR) 3112, 3048, 2970, 2929, 1784, 1720, 1385, 1344, 1151, 716 cm^{-1} ; **HRMS** (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{17}\text{O}_4\text{N}_2\text{S}$ 357.0904; Found 357.08998.

The **combined yield** of dihydroindole **8a** and C–H insertion product **9a** is 96.7 mg (27% yield) after column chromatography.

2-(6-methyl-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (8a): An analytical sample of dihydroindole **8a** was obtained by heating in ethanol, cooling, and filtering the precipitate to give the product **8a** as an amorphous off-white solid. X-ray quality crystals were grown by vapor diffusion of pentanes into a solution of **8a** in dichloromethane. R_f = 0.15 (2:1 hexanes:ethyl acetate); **mp** = 165 – 168 $^{\circ}\text{C}$; ^1H -NMR (400 MHz, CDCl_3) δ 7.90 (dd, J = 5.5, 3.0 Hz, 2H), 7.78 (dd, J = 5.5, 3.0 Hz, 2H), 6.96 (d, J = 2.0 Hz, 1H), 5.79 (ddd, J = 9.8, 2.4, 1.3 Hz, 1H), 5.73 (ddt, J = 4.0, 2.6, 1.2 Hz, 1H), 5.51 (apparent ddd, J = 9.7, 3.1, 0.5 Hz, 1H) 4.91 (apparent dq, J = 5.0, 1.1 Hz, 1H), 4.71 (apparent dq, J = 13.4, 2.6 Hz, 1H), 2.96 (s, 3H); 1.83 (t, J = 1.3 Hz, 3H). ^{13}C NMR (100

MHz, CDCl₃) δ 166.5, 134.8, 134.1, 131.7, 126.3, 124.7, 123.9, 123.1, 117.6, 116.0, 58.1, 40.7, 38.7, 22.1; **IR** (ATIR) 3104, 3019, 2929, 1786, 1710, 1386, 1333, 1188, 715 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₁₈H₁₇O₄N₂S 357.0904; Found 357.0905.

(E)-N-(2-(1,3-dioxisoindolin-2-yl)-2-(o-tolyl)vinyl)methanesulfonamide (9a): The product is an amorphous yellow foam obtained from the concentrated ethanol layer described above. **R_f** = 0.15 (2:1 hexanes:ethyl acetate); 5:1 mixture of isomers **¹H-NMR** (400 MHz, CDCl₃) δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.36 – 7.21 (m, 4H), 6.71 (d, *J* = 12.0 Hz, 1H), 6.14 (d, *J* = 12.0 Hz, 1H) 3.12 (s, 3H), 2.41 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 167.3, 137.5, 134.6, 134.4, 131.5, 131.1, 130.0, 129.6, 126.6, 127.8, 123.7, 113.2, 41.5, 19.5; **IR** (ATIR) 3259, 2928, 2854, 1714, 1377, 1338, 717 cm⁻¹; **HRMS** (ESI) m/z: [M + Na]⁺ Calcd for C₁₈H₁₆O₄N₂NaS 379.0723; Found 379.0719.

Reaction of 1a with t-butylbenzene: The combined isolated yield of all isomers is 148 mg (37% yield). The ratio of **7b** to **8b** to **9b** is 1.0:4.0:0.0 by crude NMR analysis using 292 mg (1.00 mmol) triazole **1a**.

2-(7a-(tert-butyl)-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (7b): An analytical sample was obtained by recrystallization from a saturated solution of **7b** in refluxing ethanol to give the product as yellow flat needles. The pure dihydroindole **7b** was obtained in 19.7 mg, (5% yield); **R_f** = 0.29 (3:1 hexanes:ethyl acetate); **¹H NMR** (500 MHz, CDCl₃) δ 7.90 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.6, 3.0 Hz, 2H), 6.85 (d, *J* = 2.0 Hz, 1H), 6.47 – 6.24 (m, 1H); 6.19 (dd, *J* = 10.3, 5.6 Hz, 1H), 5.87 (dddd, *J* = 9.7, 5.6, 2.7, 0.5 Hz, 1H), 5.64 (ddt, *J* = 9.7, 3.2, 1.0 Hz, 1H), 4.67 – 4.63 (m, 1H), 2.91 (s, 3H), 1.05 (s, 9H); **¹³C NMR** (125 MHz, CDCl₃) δ 166.7, 134.8, 131.7, 126.4, 126.0, 124.9, 123.9, 122.1, 120.4, 120.1, 74.0, 44.0, 40.8, 38.4, 24.6; **IR** (ATIR) 3111, 3043, 2966, 2910, 1722, 1384, 1346, 1158 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₁H₂₃O₄N₂S 399.1369; Found 399.1373.

2-(6-(tert-butyl)-1-(methylsulfonyl)-cis-3a,7a-dihydro-1H-indol-3-yl)isoindoline-1,3-dione (8b): The product elutes from SiO₂-gel column containing phthalimide hydrolysis byproducts. The products are purified by precipitation from cold ethanol, and collection on a Hirsch funnel. Contains 9% of an unidentified dihydroindole impurity. The products are a yellow amorphous solid. The combined yield of both isomers is 128 mg (32% yield); **R_f** = 0.18 (3:1 hexanes:ethyl acetate); **¹H NMR** (400 MHz, CDCl₃) δ 7.90 (dd, *J* = 5.3, 3.2 Hz, 2H), 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 6.99 (d, *J* = 1.9 Hz, 1H), 6.07 (ddd, *J* = 10.1, 2.4, 1.6 Hz, 1H), 5.79 – 5.73 (m, 1H); 5.53 (ddd, *J* = 10.1, 3.1, 1.0 Hz, 1H), 4.92 (dd, *J* = 13.2, 5.1 Hz, 1H), 4.66 (ddtd, *J* = 13.2, 3.2, 2.1, 1.0 Hz, 1H), 2.96 (s, 3H), 1.09 (s, 9H); **¹³C NMR** (100 MHz, CDCl₃) δ; 166.4, 145.9, 134.6, 131.5, 124.6, 123.7, 123.0, 123.0, 117.3, 112.0, 58.1, 40.4, 39.1, 34.4, 28.4. **IR** (ATIR) 2964, 2909, 4872, 1720, 1381, 1349, 1156, 717 cm⁻¹; **HRMS** (ESI) m/z: [M + H]⁺ Calcd for C₂₁H₂₃O₄N₂S 399.1373; Found 399.1369.

Reaction of 1a with biphenyl—The combined isolated yield of all isomers is 37.3 mg (52% yield) using 50 mg (0.171 mmol) triazole **1a**. The ratio of **7c** to **8c** to **9c** is 0:2.3:1.0 by crude NMR analysis using 50 mg (0.684 mmol) triazole **1a**.

2-(1-(methylsulfonyl)-6-phenyl-*cis*-3a,7a-dihydro-1*H*-indol-3-yl)isoindoline-1,3-dione

(8c): An analytical sample was obtained by recrystallization from refluxing methanol. The product is a yellow amorphous solid. **mp** = 137 – 142 °C; **R_f** = 0.12 (2:1 hexanes:ethyl acetate); **¹H NMR** (600 MHz, CDCl₃) δ 7.91 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.47 – 7.40 m, 2H), 7.42 – 7.29 (m, 3H), 7.04 (d, *J* = 2.0 Hz, 1H), 6.33 (ddd, *J* = 10.0, 2.5, 1.4 Hz, 1H), 6.23 – 6.21 (m, 1H), 5.71 (ddd, *J* = 10.0, 3.2, 1.0 Hz, 1H), 5.10 (dd, *J* = 13.4, 5.1 Hz, 1H), 4.88 – 4.79 (m, 1H), 2.99 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 166.6; 139.5; 137.5; 134.8, 131.7, 128.8; 128.3; 126.1; 124.8; 124.5; 124.3; 124.0; 117.5; 117.4; 58.1; 40.9; 39.0; **IR** (ATIR) 3105, 3058, 29828, 1717, 1379, 1347, 1154 cm⁻¹; **HRMS** (ESI) *m/z*: [M – H]⁻ Calcd for C₂₃H₁₇O₄N₂S 417.0915; Found 417.0915.

(*E*)-*N*-(2-([1,1'-biphenyl]-2-yl)-2-(1,3-dioxisoindolin-2-yl)vinyl)methanesulfonamide

(9c): **R_f** = 0.08 (2:1 hexanes:ethyl acetate:toluene); **¹H NMR** (400 MHz, CDCl₃) δ 7.75 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.71 (dd, *J* = 5.3, 3.2 Hz, 2H), 7.58 – 7.55 (m, 2H), 7.45 – 7.41 (m, 1H), 7.45 – 7.41 (m, 2H), 7.37 – 7.35 (m, 1H), 7.28 – 7.24 (m, 2H), 7.22 – 7.18 (m, 1H), 6.52 (d, *J* = 12.0 Hz, 1H), 6.39 (d, *J* = 12.0 Hz, 1H), 2.77 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 167.3; 140.7, 140.5, 134.4, 131.6, 131.5, 130.5, 129.6, 129.5, 128.86, 128.67, 128.4, 127.8, 124.2, 123.5, 112.7, 40.1; **IR** (ATIR) 3266, 3060, 2926, 1715, 1375, 1144 cm⁻¹; **HRMS** (APCI) *m/z*: [M – H]⁻ Calcd for C₂₃H₁₇O₄N₂S 417.0915; Found 417.0915.

Reaction of 1a with anisole: The combined yield of both isomers is 251.1 mg, (56% yield using 292 mg (1.00 mmol) triazole **1a**; The ratio of *para*-**9d** to *ortho*-**9d** is 1.0:1.0 by ¹H NMR analysis of the crude reaction mixture. Note: *ortho*-**9d** and *para*-**9d** are not completely separable by SiO₂-gel column chromatography and the remaining mass balance is accounted for in the mixed fractions.

(*E*)-*N*-(2-(1,3-dioxisoindolin-2-yl)-2-(4-methoxyphenyl)vinyl)methanesulfonamide

(para-9d): Chromatography: 2:1 (hexanes:ethyl acetate) to 1:1 (hexanes:ethyl acetate). **Yield:** 107 mg (24% yield) **R_f** = 0.28 (1:1 hexanes:ethyl acetate); **¹H NMR** (400 MHz, CDCl₃) δ 7.91 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.80 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.19 – 7.13 (m, 2H), 6.94 (d, *J* = 10.8 Hz, 1H), 6.86 – 6.80 (m, 2H), 3.78 (s, 3H), 3.03 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 167.0, 159.8, 134.8, 132.0, 126.7, 126.1, 124.1, 121.6, 114.7, 114.5, 55.5, 41.6; **IR** (ATIR) 3256, 2075, 2934, 2838, 1718, 1401, 1148, 721 cm⁻¹; **HRMS** (APCI) *m/z*: [M – H]⁻ Calcd for C₁₈H₁₅O₅N₂S 371.0696; Found 371.0712.

(*E*)-*N*-(2-(1,3-dioxisoindolin-2-yl)-2-(2-methoxyphenyl)vinyl)methanesulfonamide

(ortho-9d): Yield: 11.7 mg, (3% yield); (**R_f** = 0.21 (1:1 hexanes:ethyl acetate); **¹H NMR** (400 MHz, CDCl₃) δ 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0, 2H), 7.34 (ddd, *J* = 8.4, 7.5, 1.7 Hz, 1H), 7.23 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.02 – 6.95 (m, 2H), 6.92 (d, *J* = 11.8 Hz, 1H), 6.66 (d, *J* = 11.3 Hz, 1H), 3.87 (s, 3H), 3.10 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃) δ 167.6, 156.3, 134.5, 131.8, 130.6, 129.6, 126.3, 123.8, 121.9, 121.8, 113.0, 110.8, 56.7, 41.7; **IR** (ATIR) 3270, 3076, 3025, 2933, 2839, 1716, 1379, 1160, 721 cm⁻¹; **HRMS** (APCI) *m/z*: [M – H]⁻ Calcd for C₁₈H₁₅O₅N₂S 371.0696; Found 371.0709.

Studies on the ring-opening of compound 4a (Figure 4)—For the reaction in CDCl_3 , ethylene carbonate (5.6 mg) was dissolved in 5.6 mL CDCl_3 , and 0.70 mL of this solution was added to an oven-dried NMR tube containing solid cycloadduct **4a** (6.5 mg, 17.5 μmol). The homogenous solution was then heated to 70 °C and was analyzed by ^1H NMR at the indicated time points.

For the reaction in C_6D_6 , ethylene carbonate (6.4 mg) was dissolved in 6.4 mL C_6D_6 , and 0.70 mL of this solution was added to an oven-dried NMR tube containing solid cycloadduct **4a** (6.5 mg, 17.5 μmol). The homogenous solution was then heated to 70 °C and was analyzed by ^1H NMR at the indicated time points.

For the reaction in CD_3CN , ethylene carbonate (10.0 mg) was dissolved in 10.0 mL CD_3CN , and 0.70 mL of this solution was added to an oven-dried NMR tube containing solid cycloadduct **4a** (6.5 mg, 17.5 μmol). The homogenous solution was then heated to 70 °C and was analyzed by ^1H NMR at the indicated time points.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Murakami and Miura, 2017 (Ref. 16c)

D. Davies, 2012 (Ref. 18)

E. This work

Figure 1.

Representative examples of *N*-sulfonyltriazoles participating in dearomatization reactions. *N*-phthalimidetriazole (**1**) undergoes thermal cyclopropanation reactions (Davies, 2012) and dearomatization reactions (this work).

Figure 2:

a) Products are obtained as a separable mixture of the [3+2] cycloadduct **4** and C–H insertion products **5** favoring the isomer indicated unless otherwise stated. The isolated yield of only the dihydroindole product(s) given. The ^1H NMR yield of cycloadduct **4** determined from the crude reaction mixture is given in parenthesis. See the Supporting Information for combined isolated amounts of both **4** and **5** b) Conditions 50.0 mg (0.171 mmol) triazole **1a**, 4 equiv arene **3**, 0.50 M at 70°C in CHCl_3 for 90 min. c) Mixtures of dihydroindole regioisomers are inseparable by column chromatography d) Performed with 1.00 mmol triazole **1b** e) No ring-opened isomers (**5**) were detected by ^1H NMR analysis.

Figure 3:

^a Products are obtained as a mixture of the [3+2]-cycloadducts **7** and **8** and C–H insertion products **9** favoring the compound indicated. Combined isolated yield in parenthesis. 1,2-DCE = 1,2-dichloroethane. See the Supporting Information for details.

Figure 4. Conversion of dihydroindole **4a** to arene **5a** thermally in CD₃CN (green), in C₆D₆ (blue) and CDCl₃ (red). The reaction in C₆D₆ is markedly slower.

Scheme 1.

Proposed mechanism for the synthesis of dihydroindoles from triazole **1a** and rationalization of dihydroindole regioselectivity from sigmatropic rearrangements. Energetically preferred pathway shown in blue. Transition state energies are calculated relative to *endo*-C and are given in parenthesis as G/ H at 343 K. See the supporting information for details. RXN = reaction, RAR = rearrangement, Rot = rotation, TS = transition state.

Table 1.

Formal [3+2]-Cycloaddition Reaction Optimization.

entry	solvent	4a:5a	combined ¹ H NMR yield ^a
1	1,2-DCE	2.5:1	77%
2	CH ₂ Cl ₂	1.4:1	72%
3	CHCl ₃	2.7:1	82% (82%)
4	TCE	5.1:1	4%
5 ^b	TCE	1:3.2	47%
6 ^c	THF	-	-
7	MeCN	1:2.2	22%
8	TFT	4.7:1	52%
9 ^d	hexanes	-	-
10 ^c	acetone	-	-
11 ^e	ethanol	-	-
12 ^f	water	-	-
13 ^f	CHCl ₃	3.8:1	57%
14 ^g	CHCl ₃	5.5:1	55%
15	EtOAc	3.4:1	31%
16	dioxane	2.0:1	64%
17 ^h	CHCl ₃ :hexane (1:1)	11.5:1	23%

^a) Products are obtained as a mixture of the [3+2] cycloadduct **4a** and C-H insertion products **5a** favoring the isomer indicated. Combined isolated yield in parenthesis. Reaction conditions 146.2 mg (0.50 mmol) triazole **1a**, 247 mL (2.00 mmol) p-xylene, 1.0 mL CH₂Cl₂, 70 °C, 1.5 h

^b) Reaction time 18 h

^c) Triazole **1a** is completely consumed, but produces non-specific decomposition.

^d) No reaction, triazole **1a** is not consumed.

^e) O-H insertion product obtained, see the Supporting Information for details.

^f) Microwave heating at 60 °C

^g) microwave heating at 70 °C, 0.5 h, 0.09 M

^h) 7% triazole **1a** remaining. 1,2-DCE = 1,2-dichloroethane. TFT = α,α,α-trifluorotoluene.

TCE = trichloroethylene, THF = tetrahydrofuran. Hex = hexanes.