

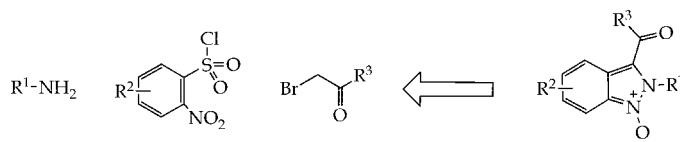
Remarkably Efficient Synthesis of 2*H*-Indazole 1-Oxides and 2*H*-Indazoles via Tandem Carbon–Carbon Followed by Nitrogen–Nitrogen Bond Formation

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Base-catalyzed tandem carbon–carbon followed by nitrogen–nitrogen bond formations quantitatively converted *N*-alkyl-2-nitro-*N*-(2-oxo-2-aryl-ethyl)-benzenesulfonamides to 2*H*-indazoles 1-oxides under mild conditions. Triphenylphosphine or mesyl chloride/triethylamine-mediated deoxygenation afforded 2*H*-indazoles.

Introduction

Synthetic compounds comprising indazole core have recently become an increasingly frequent subject of biological studies as indazole derivatives possess significant potency in a wide range of biological targets. A recently published excellent review article by Cerecetto and colleagues¹ portrayed the diversity of biological activities exhibited by indazoles. Since then, numerous new studies identified indazole-based compounds as potent agents with anti-inflammatory, anticancer,^{2,3} antimicrobial,⁴ antifungal,^{5,6} antiangiogenic,⁷ and cytotoxic⁸ activities.

Indazoles were found to be potent inhibitors of nitric oxide synthetase,^{9,10} factor Xa,¹¹ protein kinases,^{12,13} tubulin,¹⁴ and

TRPV1.^{15,16} It was also shown that they were active as male contraceptives^{17,18} and 5-HT2C receptor agonists.¹⁹

The majority of chemical routes developed for the indazole syntheses were targeted for the preparation of 1,3-derivatized-1*H*-indazoles (reviewed in ref 1), and the synthesis has also been carried out on solid phase.²⁰ Recent reports of 1,3-

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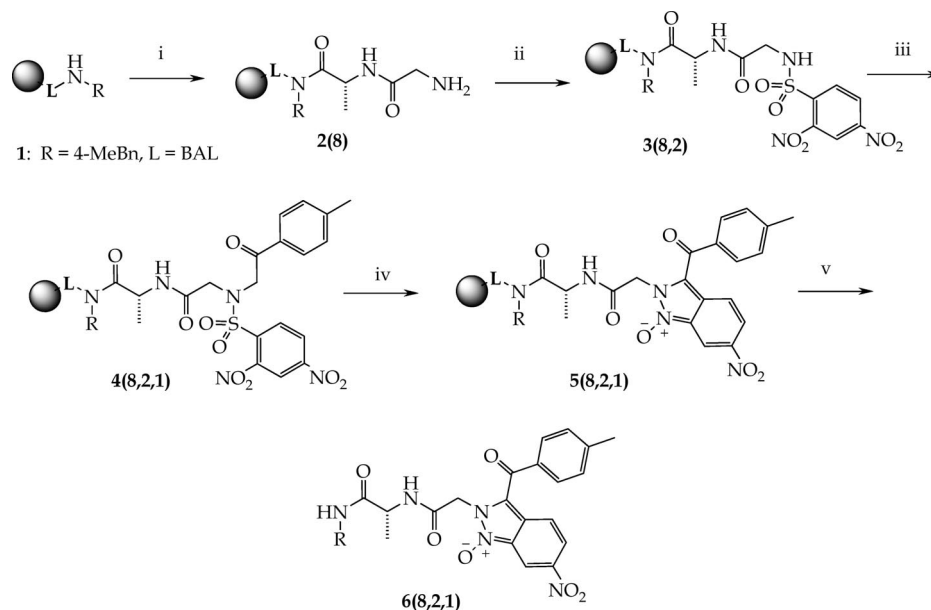
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SCHEME 1. Formation of Indazole Oxides by Tandem Reaction^a

^a Reagents and conditions: (i) traditional Fmoc peptide synthesis; (ii) 2,4-dinitrobenzenesulfonyl chloride, lutidine, DCM, 16 h; (iii) 2-bromo-4'-methylacetophenone, DIEA, DMF, 16 h; (iv) DBU, DMF, 30 min; (v) 50% TFA in DCM, 30 min.

derivatized-*1H*-indazole syntheses include [3 + 2] cycloaddition of diazocompounds with *o*-(trimethylsilyl)aryl triflates,²¹ copper(I)-catalyzed intramolecular amination,²² and from 2-aminobenzoximes via mesyl chloride activation.²³

Reported synthetic procedures for 2,3-derivatized-*2H*-indazoles often required preparation of dedicated intermediates and/or harsh reaction conditions. Substituted-*2H*-indazoles were prepared by thermal decomposition of 2-azidobenzylideneamines,²⁴ by TiCl₄-mediated cyclization of 2-arylazophenylacetic acid derived ketene acetal,²⁵ by cyclization of 2-cyclopropylazobenzene in concentrated sulfuric acid,²⁶ from 2-nitrobenzylamines by electroreduction,²⁷ by reaction of azobenzene with *in situ* prepared isopropylidene carbene,²⁸ and by SnCl₂-mediated cyclization of nitro arenes.²⁹ 2-Acylaminoindazoles were prepared via oxidative cyclization of N-acyl hydrazones of 2-aminoaryl ketones.^{30,31} Polyfused heterocycles containing indazole moiety were prepared by palladium-catalyzed cross-coupling reactions.^{32,33}

Several other synthetic routes were also reported for preparation of *2H*-Indazole 1-oxides. (2-Nitro-benzylidene)-aniline derivatives were reacted with potassium cyanide to produce

2-aryl-3-cyano-*2H*-indazole 1-oxides.^{34–40} Hungarian researchers published several reports for the synthesis of indazole 1-oxides by 1,7-electrocyclization of azomethine ylides.^{41–44}

2-Aryl-*2H*-Indazoles were prepared via SnCl₂-mediated cyclization of 2-nitrobenzylamines.⁴⁵ Indazole moiety has also been introduced as a side-chain of an amino acid.⁴⁶

Our contribution describes a novel and very efficient tandem reaction that provided access to 2,3-substituted-*2H*-indazoles from 2-nitro-*N*-(2-oxo-2-aryl-ethyl)-benzenesulfonamides under mild conditions. These precursors are readily accessible using commercially available building blocks: amines, 2-nitrobenzenesulfonyl chlorides, and bromoketones.

Results

In our ongoing effort to develop new routes for solid-phase syntheses of combinatorial libraries of drug-like molecules of heterocyclic compounds, we were introducing an imidazole ring into a peptide chain. Our reaction sequence involved preparation of 2-nitro-*N*-(2-oxo-2-aryl-ethyl)-benzenesulfonamides **4** on the amino group of resin-bound peptides (Scheme 1). Resin-bound

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TABLE 1. Synthesized Indazole Oxides **6** and Indazoles **8**

compound	-R ¹ -H	R ²	R ³	MS ESI ⁺	purity ^a (%)	isolation	yield ^b (%)
6(1,1,1)	-(CH ₂) ₂ -CONH ₂	H	4-Me-Ph	324	99	B	82
6(1,1,2)	-(CH ₂) ₂ -CONH ₂	H	4-Cl-Ph	344	98	B	63
6(1,1,3)	-(CH ₂) ₂ -CONH ₂	H	4-NH ₂ -3,5-diCl-Ph	393	99	B	52
6(1,1,4)	-(CH ₂) ₂ -CONH ₂	H	3-NO ₂ -Ph	355	77	C	50
6(1,1,5)	-(CH ₂) ₂ -CONH ₂	H	4-OMe-Ph	340	94	A	58
6(1,2,1)	-(CH ₂) ₂ -CONH ₂	4-NO ₂	4-Me-Ph	369	98	B	97
6(1,3,1)	-(CH ₂) ₂ -CONH ₂	4-CF ₃	4-Me-Ph	392	97	B	95
6(1,4,1)	-(CH ₂) ₂ -CONH ₂	4-OMe	4-Me-Ph	354	89	C	59
6(2,1,1)	-CH(CH ₃)-CONH ₂	H	4-Me-Ph	324	89	C	54
6(2,1,5)	-CH(CH ₃)-CONH ₂	H	-OEt	278	88	C	74
6(3,1,1)	-(CH ₂) ₂ -CONH(4-Me-Bn)	H	4-Me-Ph	428	91	C	65
6(4,1,1)	-(CH ₂) ₂ -COOH	H	4-Me-Ph	325	93	C	37
6(5,1,1)	-(CH ₂) ₂ -OH	H	4-Me-Ph	297	93	C	80
6(5,1,5)	-(CH ₂) ₂ -OH	H	-OEt	251	72	C	23
6(6,2,1)	-(CH ₂) ₃ -CONH ₂	4-NO ₂	4-Me-Ph	383	95	C	39
6(6,2,2)	-(CH ₂) ₃ -CONH ₂	4-NO ₂	4-Cl-Ph	403	90	C	17
6(6,2,3)	-(CH ₂) ₃ -CONH ₂	4-NO ₂	4-NH ₂ -3,5-diCl-Ph	452	91	C	23
6(6,2,5)	-(CH ₂) ₃ -CONH ₂	4-NO ₂	4-OMe-Ph	399	95	C	29
6(6,3,1)	-(CH ₂) ₃ -CONH ₂	4-CF ₃	4-Me-Ph	406	99	A	30
6(6,3,2)	-(CH ₂) ₃ -CONH ₂	4-CF ₃	4-Cl-Ph	426	84	C	28
6(6,3,3)	-(CH ₂) ₃ -CONH ₂	4-CF ₃	4-NH ₂ -3,5-diCl-Ph	475	98	B	64
6(6,3,5)	-(CH ₂) ₃ -CONH ₂	4-CF ₃	4-OMe-Ph	422	99	A	69
6(6,4,1)	-(CH ₂) ₃ -CONH ₂	4-OMe	4-Me-Ph	368	81	C	21
6(7,1,3)	-(CH ₂) ₃ -NH ₂	H	4-NH ₂ -3,5-diCl-Ph	379	98	A	81
6(7,2,1)	-(CH ₂) ₃ -NH ₂	4-NO ₂	4-Me-Ph	355	92	A	93
6(7,2,3)	-(CH ₂) ₃ -NH ₂	4-NO ₂	4-NH ₂ -3,5-diCl-Ph	424	97	A	99
6(7,2,5)	-(CH ₂) ₃ -NH ₂	4-NO ₂	4-OMe-Ph	371	90	A	92
6(7,3,1)	-(CH ₂) ₃ -NH ₂	4-CF ₃	4-Me-Ph	378	99	A	85
6(7,3,2)	-(CH ₂) ₃ -NH ₂	4-CF ₃	4-Cl-Ph	398	94	A	90
6(7,3,3)	-(CH ₂) ₃ -NH ₂	4-CF ₃	4-NH ₂ -3,5-diCl-Ph	447	99	A	84
6(7,3,5)	-(CH ₂) ₃ -NH ₂	4-CF ₃	4-OMe-Ph	394	97	B	99
8(1,3,1)	-(CH ₂) ₂ -CONH ₂	4-CF ₃	4-Me-Ph	376	87	C	48
8(1,5,1)	-(CH ₂) ₂ -CONH ₂	4-NH ₂	4-Me-Ph	323	72	C	23

^a Purity of crude product before purification. ^b Yield after purification.

dipeptide Fmoc-Ala-Gly-NH-(4-Me)Bn **2(8)** was synthesized on 4-(4-methylbenzyl)aminomethyl-3-methoxy-phenoxy)-butyric acid resin **1** (BAL resin). The Fmoc group was cleaved and resin-bound primary amines were reacted with 2,4-dinitrobenzenesulfonyl chloride to access sulfonamide **3**. Alkylation with bromoketones afforded polymer-supported *N*-(2-oxo-2-aryl-ethyl)-2,4-dinitrobenzenesulfonamides **4(8,2,1)** (for R-groups numbering refer to Table 1). Short exposure (30 min) to a base (DBU) in DMF led to transformation to 2*H*-indazoles 1-oxides **6(8,2,1)**.

The structure of **6(8,2,1)** was determined by analysis of 1D and 2D ¹H and ¹³C NMR spectra. Proton connectivities were derived by examination of the DQF-COSY spectrum. Signals of all carbons with directly attached protons were assigned using the gHSQC spectrum. Finally, the gHMBC spectrum was used to assign quaternary carbons and to check the correctness of the connectivities established by the interpretation of the other spectra.

Two amide protons H-2 and H-5 (Figure 1) resonated at δ 8.39 and 8.84, respectively. Their corresponding signals showed as triplet and doublet. The amide H-5 signal exhibited a cross-peak with a signal (doublet of quartet) at δ 4.31 in the DQF-COSY spectrum. This signal simultaneously showed a cross-peak to the doublet at δ 1.27. These two resonances were, therefore, assigned to the methine CH-4 and methyl CH₃-4_a protons, respectively. The amide H-2 signal displayed a cross-peak to two protons doublet at δ 4.24 belonging to the methylene CH₂-1 protons. The methylene CH₂-7 protons resonated as two one proton doublets at δ 5.53 and 5.60, respectively. The doublets (²*J* = 16.4 Hz) exhibited only a mutual cross-peak in

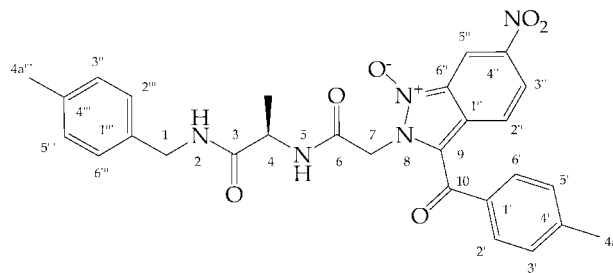
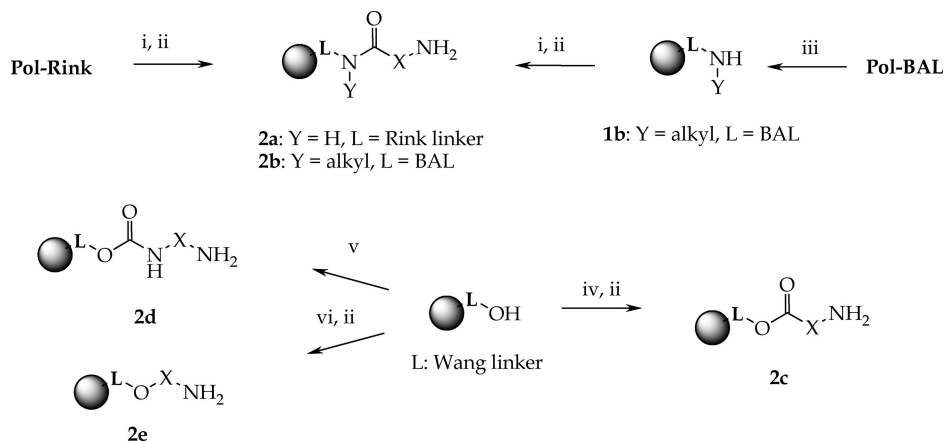


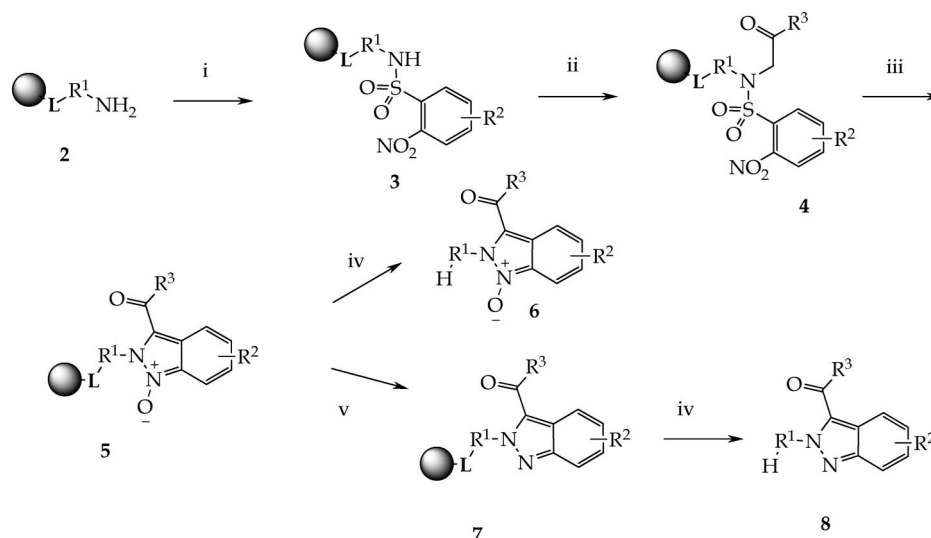
FIGURE 1. Atom numbering of compound **6(8,2,1)**.

the DQF-COSY spectrum. In the gHMBC spectrum, the resonance of the methylene CH₂-1 protons showed a cross-peak with the carbon signal at δ 126.96 corresponding to the C-2''' and C-6''' carbons of the methyl benzyl moiety. Signals of the remaining carbons and protons of this moiety were then assigned by analyzing the gHSQC, DQF-COSY, and gHMBC spectra. The methylene CH₂-7 proton signals displayed cross-peaks in the gHMBC spectrum only with the carbon signals at δ 163.64 and 118.23 corresponding to the carbonyl C-6 and olefinic C-9 carbons, respectively. Simultaneously, the C-9 carbon signal showed a cross-peak to the H-2'' proton signal of the nitro aryl moiety and the carbonyl C-6 signal exhibited a cross-peak to the amide H-5 proton signal. Resonances of the other protons and carbons of this moiety as well as the 4-methyl phenyl moiety were finally allocated by examining the DQF-COSY, gHSQC, and gHMBC spectra. These facts unambiguously prove the structure of the **6(8,2,1)**.

Very efficient formation of indazole oxides from easily accessible precursors prompted us to evaluate the scope and

SCHEME 2. Preparation of Five Types of Resin-Bound Amines^a

^a Reagents and conditions: (i) Fmoc-amino acid, DIC, HOBT, DMF/DCM, 16 h; (ii) 50% piperidine, DMF, 15 min; (iii) amine, 10% AcOH, DMF, 16 h, then NaBH(OAc)₃, 5 h; (iv) Fmoc-amino acid, PPh₃, DIAD, 3 h; (v) CDI, pyridine, DCM, 2 h, then diamine, DCM, 2 h; (vi) trichloroacetonitrile, DBU, DCM, 2 h, then Fmoc-amino alcohol, BF₃•Et₂O, 1 h.

SCHEME 3. Indazoles Synthesis^a

^a Reagents and conditions: (i) 2-nitrobenzenesulfonyl chloride, lutidine, DCM, 16 h; (ii) bromoketone or bromoacetate, DIEA, DMF, 16 h; (iii) DBU, DMF, 30 min; (iv) 50% TFA in DCM, 30 min; (v) mesyl chloride, TEA, DCM, 16 h.

limitations of this transformation. Three reaction components used in the synthesis included primary amines, 2-nitrobenzenesulfonyl chlorides, and bromoketones. For solid-phase synthesis, we have chosen to immobilize amines. To access target compounds with diversity of functional groups at R¹ position of target indazoles, we prepared five types of resin-bound amines (Scheme 2). (i) Immobilization using carboxyl group of amino acids provided polymer-supported amines **2a** by acylation of Rink amide resin.⁴⁷ (ii) Secondary amides were prepared from backbone amide linker (BAL)⁴⁸ via reductive amination with primary amines (resin **1b**), followed by acylation with Fmoc-amino acids (**2b**). (iii) Free acids were accessed from resin **2c**, obtained by esterification⁴⁹ of Wang resin⁵⁰ with Fmoc-amino acids. (iv) Diamines (unprotected) were attached to CDI-treated

Wang resin^{51,52} to form resin **2d**. (v) Fmoc-amino alcohols were linked to Wang resin *via* trichloroacetimidate intermediate⁵³ and yielded resin **2e**.

Immobilization of amine via bifunctional building blocks does not provide a traceless solid-phase synthesis of indazoles. Five types of resin-bound amines allowed synthesis of target compounds with an amide, secondary amide, acid, amine, and alcohol in the R¹ side-chain of the target indazoles.

Synthesis of indazoles from five types of polymer-supported amines is portrayed in Scheme 3. Resin-bound primary amines **2** (L represents any linker described in Scheme 2), were reacted with 2-nitrobenzenesulfonyl chlorides to access sulfonamides **3**. Alkylation with bromoketones cleanly afforded polymer-supported *N*-alkyl-2-nitro-*N*-(2-oxo-2-aryl-ethyl)-benzenesulfonamides **4**. Short exposure to a base (DBU) mediated formation of indazole 1-oxides **5** by tandem of carbon–carbon followed

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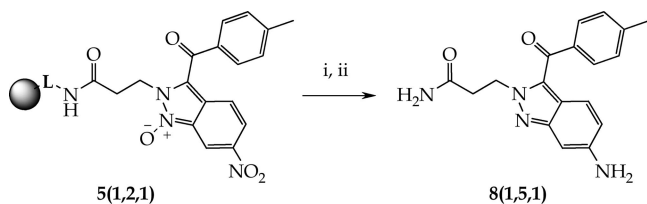
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SCHEME 4. Tin(II) Chloride Reduction of Compound 5(1,2,1)^a

^a Reagents and conditions: (i) SnCl₂·2H₂O, DIEA, DMF, 2 h; (ii) 50% TFA, DCM, 1 h.

by nitrogen–nitrogen bond-forming reactions. Cleavage of indazole oxides from the resin was accomplished by TFA solution in DCM to yield products **6**. The TFA solution was evaporated and isolation and purification of indazole oxides **6** was carried out by three different methods depending on the purity of crude preparations: precipitation using diethyl ether (method A), passing through a C18 cartridge (method B), or HPLC purification (method C).

We synthesized a set of indazole oxides using four 2-nitrobenzenesulfonyl chlorides and four bromoketones with various electron-withdrawing as well as electron-donating substituents (Table 1). Five different linkers were used, which provided access to amides, *N*-alkyl amides, acids, amines, and alcohols, respectively.

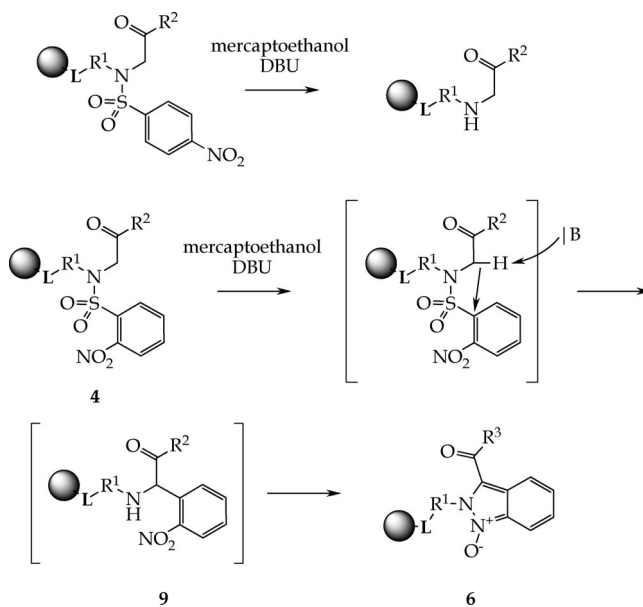
The synthetic route is amenable to combinatorial synthesis. We prepared a combinatorial array of indazole oxides using two resin-bound amines prepared from β-Ala and 1,3-diaminopropane, two 2-nitrobenzenesulfonyl chlorides, and four bromoketones by using the split–split method.

To access the parent heterocycle, we evaluated several deoxygenation methods and reduced the resin-bound indazole oxides **5** to indazoles **7**. Attempts to deoxygenate the resin-bound indazole oxides using InCl₃^{54,55} was not successful; overnight reaction at elevated temperature (100 °C) yielded indazoles only in single-digit percentage points. Reduction with SmI₂ yielded a mixture of products. Deoxygenation using PPh₃⁴⁰ provided clean indazoles, but required lengthy (2 days) exposure at elevated temperature (100 °C). Mesityl chloride in the presence of triethylamine⁵⁶ at ambient temperature turned to be the reagent of choice for mild (ambient temperature) deoxygenation of indazole oxides to indazoles. We have not tested the “explosive” hexamethyldisilane method.⁵⁷

Interestingly, treatment of the resin-bound indazole oxide **5(1,2,1)** with tin(II) chloride afforded not only reduction of the nitro group but deoxygenation of the product **8(1,5,1)** as well (Scheme 4). Reduction of nitro group in compound **5(1,1,4)** yielded mixture of products, nitro group reduced, but not deoxygenated, compound being the major component.

Discussion

Tandem reaction of 2-nitrobenzenesulfonylated α-aminoketones **4** leading to indazole oxides **6** involved two consecutive transformations, C–C bond formation followed by N–N bond

SCHEME 5. Different Reactivities of 2- and 4-Nitrobenzenesulfonyl Derivatives

formation. Unlike 4-nitrobenzenesulfonyl derivatives, treatment of the 2-nitroderivatives **4** with mercaptoethanol and DBU does not cleave the 2-Nos group by the thiol (Scheme 5). Instead, the 2-Nos group is cleaved by an internal C-nucleophile generated by DBU from the α-ketosulfonamide. This transformation can be regarded as a variation of S–C Smiles rearrangement involving an internal C-nucleophile. The precedent for analogous carbon–carbon bond formation can be found in base-catalyzed formation of methyl-[9-(4-nitro-phenyl)-9H-fluoren-9-yl]-amine from *N*-(9H-fluoren-9-yl)-*N*-methyl-4-nitrobenzenesulfonamide.⁵⁸

The 2-nitrobenzylamine intermediate **9** underwent spontaneous cyclative dehydration to form indazole oxides **6**. This second step in the tandem reaction, formation of nitrogen–nitrogen bond, has been known for years and it was employed, for example, in the synthesis of 3,4-fused cinnolines^{59,60} and indazole oxides.^{39,40,42,44}

A distant analogy to the tandem synthesis of indazole oxides can be also found in the synthesis of 1-oxy-benzo[1,2,4]triazin-3-ylamine **11** (Scheme 6), reported more than 60 years ago.⁶¹ 2-Nitrobenzenesulfonyl guanidine **10** was converted to 3-aminobenzo[e][1,2,4]triazine 1-oxide *via* intramolecular cleavage of the Nos group by an internal *N*-nucleophile followed by cyclative dehydration involving N–N bond formation.

Conclusion

Tandem reaction involving C–C and N–N bond formations quantitatively converted polymer-supported *N*-alkyl-2-nitro-*N*-(2-oxo-2-aryl-ethyl)-benzenesulfonamides to 2*H*-indazoles 1-oxides under mild conditions without any noticeable side-reaction. The transformation tolerated a range of substituents and was insensitive to electronic properties of R groups. Synthesis did not require preparation of dedicated building blocks and it was

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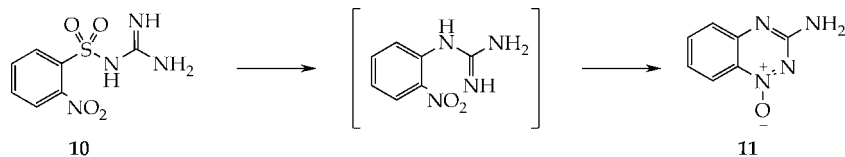
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SCHEME 6. Synthesis of 1-Oxy-benzo[1,2,4]triazin-3-ylamine and 3-Phenylindazole



carried out using commercially available compounds. Triphenylphosphine or mesyl chloride/TEA-mediated deoxygenation yielded 2*H*-indazoles.

Experimental Section

Reaction with 2-Nos-Cl (Resins 3). Resins 2, ~1 g, were washed with DCM, a solution of 2-Nos-Cl (3 mmol) and lutidine (3.3 mmol, 382 μ L) in 10 mL DCM was added to the resin and slurry was shaken overnight at ambient temperature. The resin was washed 3 \times with DMF and 3 \times with DCM.

Reaction with Bromoketones (Resins 4). Resins 3, ~250 mg, were washed 3 \times with DCM and 5 \times with DMF. A solution of 0.5 M bromoketone (1.5 mmol) and 1 M DIEA (3 mmol, 522 μ L) in 3 mL DMF was added. The slurry was shaken overnight at ambient temperature. The resin was washed 3 \times with DMF and 5 \times with DCM.

Cyclization to Indazole Oxides (Resins 5). Resins 4, ~250 mg, were washed 5 \times with DMF. A solution of 0.2 M DBU (1 mmol, 150 μ L) in 5 mL DMF was added, and the resin slurry was shaken at ambient temperature for 30 min. Resins were washed 3 \times with DMF, 5 \times with DCM, and 3 \times with MeOH, and dried.

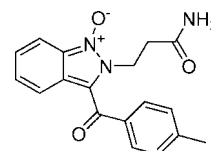
Cleavage and Isolation (6). Indazole oxides 6 were obtained after cleavage with 50% TFA in DCM for 1 h. TFA solution was collected, resin was washed 3 \times with 50% TFA, combined extracts were evaporated by a stream of nitrogen, and oily product was triturated with ether. Three isolation and purification methods were used depending on the purity of crude product. Compounds that precipitated after being triturated with ether were collected and the precipitate was dried (method A). Compounds that did not precipitate after ether trituration were dissolved in minimum quantity of methanol (~0.5 mL), diluted with 20 mL 10 mM aqueous ammonium acetate buffer, and passed through a C18 cartridge. The cartridge was washed by ammonium acetate buffer and compounds eluted by 66% MeCN in ammonium acetate buffer. The solution was evaporated and the residue lyophilized overnight (method B). Alternatively, compounds were purified by semi-preparative reverse phase HPLC (method C). Samples were analyzed by LCMS.

Deoxygenation (Resins 7). Resins 5, ~250 mg, were washed 5 \times with DCM. A solution of 2.5 mL of 0.7 M TEA (245 μ L) in DCM was added. The syringe was connected with the second syringe containing 2.5 mL 0.5 M mesyl chloride (96 μ L). Connected syringes were left in a freezer for 30 min and the mesyl chloride solution was drawn into the syringe with the resin. The resin slurry was shaken at ambient temperature for 16 h. Resins were washed 5 \times with DCM and 3 \times with MeOH and dried. Cleavage from the resin and purification was carried out as described for compounds 6.

Deoxygenation and Reduction of the Nitro Group (Resin 7(1,5,1)). Resin 5(1,2,1), 250 mg, was washed 3 \times with DMF, and 2 mL of a solution of 1 M tin chloride dihydrate and 1 M

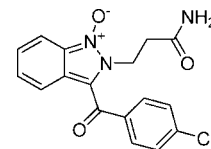
DIEA, prepared under nitrogen bubbling, was added to the resin, and the resin slurry was shaken overnight. The resin was washed very thoroughly 7 \times with DMF and 3 \times with DCM. Cleavage from the resin and purification was carried out as described for compounds 6.

Analytical Data of Individual Compounds. 2-(3-Amino-3-oxopropyl)-3-(4-methylbenzoyl)-2*H*-indazole 1-oxide 6(1,1,1). Yield 32 mg (82%). ESI-MS m/z = 324, [M + H]⁺. ¹H NMR (300



MHz, DMSO-*d*₆) δ : 7.76 (d, J = 8.56 Hz, 1 H) 7.68 (d, J = 8.01 Hz, 2 H) 7.44 (br. s., 1 H) 7.40 (d, J = 8.01 Hz, 2 H) 7.31–7.38 (m, 1 H) 7.19–7.29 (m, 1 H) 6.93 (br. s., 1 H) 6.85 (d, J = 8.84 Hz, 1 H) 4.94 (t, J = 7.18 Hz, 2 H) 2.73 (t, J = 7.32 Hz, 2 H) 2.45 (s, 3 H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ : 181.6, 170.9, 143.1, 136.5, 129.3, 129.2, 128.5, 127.5, 126.3, 120.1, 119.6, 117.4, 113.3, 42.1, 32.6, 21.3. HRMS (FAB) m/z calcd for C₁₈H₁₈N₃O₃ [M + H]⁺ 324.1348, found 324.1353.

2-(3-Amino-3-oxopropyl)-3-(4-chlorobenzoyl)-2*H*-indazole 1-oxide 6(1,1,2). Yield 26 mg (63%). ESI-MS m/z = 344, [M + H]⁺.



¹H NMR (300 MHz, DMSO-*d*₆) δ : 7.73–7.83 (m, 3 H) 7.68 (d, J = 8.56 Hz, 2 H) 7.45 (br. s., 1 H) 7.33–7.42 (m, 1 H) 7.19–7.33 (m, 1 H) 6.94 (br. s., 1 H) 6.84 (d, J = 8.56 Hz, 1 H) 4.95 (t, J = 7.18 Hz, 2 H) 2.73 (t, J = 7.32 Hz, 2 H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ : 180.5, 170.9, 137.9, 137.5, 131.0, 128.9, 128.6, 128.0, 126.4, 120.0, 119.9, 117.0, 113.4, 42.1, 32.4. HRMS (FAB) m/z calcd for C₁₇H₁₅N₃O₃Cl [M + H]⁺ 344.0802, found 344.0783.

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Supporting Information Available: Details of experimental procedures, spectroscopic data for synthesized compounds, and copies of NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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