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Multicomponent Reactions of Diazoamides: Diastereoselective Synthesis of Mono- and Bis-spirofurooxindoles

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This paper describes the intermolecular generation of carbonyl ylides by dirhodium(II) tetraacetate-catalyzed reaction of 3-diazoindol-2-ones in the presence of aryl aldehydes and heteroaryl aldehydes. These carbonyl ylides were subsequently trapped with dipolarophiles such as dimethyl acetylenedicarboxylate, maleic anhydride, and ethyl acrylate to afford spirofurooxindoles. Consequently, diastereoselective synthesis of spirodihydrofurooxindoles through the multicomponent reactions of cyclic diazoamides was successfully achieved for the first time. The stereochemistry of the spirofurooxindole is unequivocally corroborated by the single-crystal X-ray analysis of the representative product **4o**. Interestingly, these reactions were extended to double multicomponent reactions of bis-cyclic diazoamides to afford the respective complex polycycles in a tandem manner, which led to the construction of four carbon−carbon bonds, two carbon−oxygen bonds, and four chiral centers in a single synthetic step.

Introduction

The discovery of new reactions is a pivotal focal point of research activity in organic chemistry. The continual upsurge in molecular complexity and diversity in the natural product systems urges chemist to increase tools of their arsenal. Tandem[1] and multicomponent reactions are appropriate potential tools for synthetic chemists to increase the efficacy, atom economy, selectivity, and complexity in a particular process. The Strecker synthesis[2] of α-amino cyanides reported in 1850 was generally construed as the first multicomponent reaction (MCR). Multicomponent reactions[3] are highly convergent reactions that display enormous advantages over divergent synthesis in terms of time, yield, and reproducibility. α-Diazo carbonyl compounds find widespread applications in organic chemistry especially in tandem processes and natural product synthesis.[4,5] Metallocarbenoids can be generated from diazo carbonyl compounds that react with a series of functional groups, whereby further subsequent reactions can occur. Curtius synthesized the diazo carbonyl compounds in 1883 for the first time.[6] Despite the century-old invention and its synthetic significance, examples of participation of diazo carbonyl compounds in the MCRs is scarce.[7−11] The intramolecular generation of carbonyl ylides and their subsequent reactions are studied well, which constituted an important method for tetrahydrofuran systems and also applied for the synthesis of many natural products.[5] Contrarily, the intermolecular formation of carbonyl ylides are always considered to be synthetically unsuitable compared to their intramolecular counterparts because of their low selectivity and competitive reactions.[5a] The intermolecular carbonyl ylide formation was first reported[7] by Huisgen and de March in the reaction between diazo

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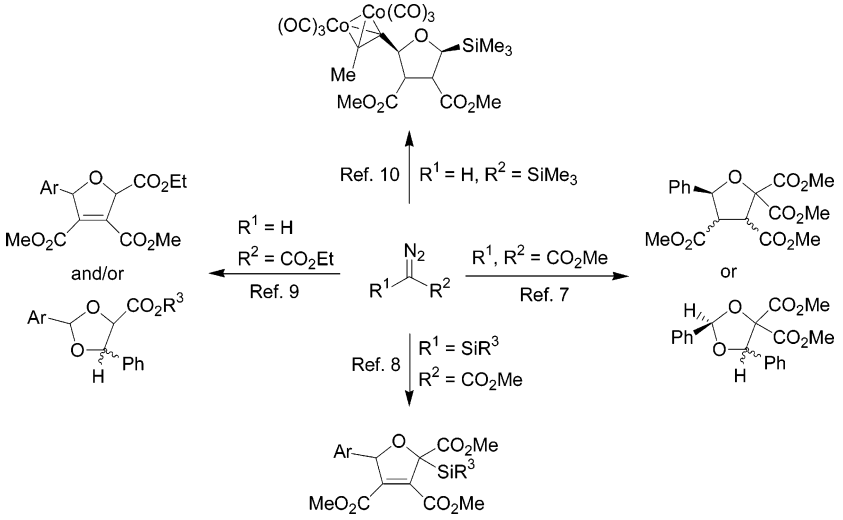
SCHEME 1. Synthesis of Di-/Tetrahydrofurans from Diazo Compounds, Aldehydes, and Dipolarophiles Involving the Intermolecular Formation of Carbonyl Ylides



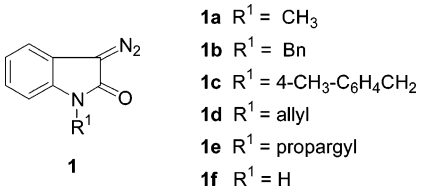


FIGURE 1. Structure of cyclic diazoamides.

compound and benzaldehyde to undergo cycloaddition with another benzaldehyde molecule (to produce dioxolane) or an electron-deficient alkene (to produce a tetrahydrofuran). The reported literature examples[7−10] involving intermolecular formation of carbonyl ylides generated usually from acyclic diazo acetates are illustrated in Scheme 1. In this line, a synthesis of spirodioxolanes and tetrahydrofurans has also recently appeared.[11] Occasionally, these reactions involving intermolecular carbonyl ylide formation are known to yield dioxolane systems, which reduce the scope of this method. The transition-metal-mediated multicomponent synthesis of functionalized heterocyclic systems is rarely encountered.[3b] With a view to unveil the chemistry of diazo carbonyl compounds[12] particularly involving cyclic rhodium carbenoids[13] herein, we delineate the results of the first multicomponent reactions of cyclic diazoamides catalyzed by rhodium(II) acetate in a tandem manner.

Results and Discussion

We planned in this study to utilize the cyclic diazoamides **1**, which are depicted in Figure 1. Two methods were developed for the preparation of substituted 3-diazo-1,3-dihydro-2*H*-indol-2-ones (**1a**−**e**). The initially adapted method using 10% ethanolic KOH solution (method A, 70−80% yields) was substituted later by NaH/DMF, which gives a better yield (method B, 80−95%). We succeeded in the investigation of the reaction 3-diazo-1-methyl-1,3-dihydro-2*H*-indol-2-one with benzaldehyde and dimethyl acetylenedicarboxylate (DMAD) in the presence of 0.5 mol % of rhodium(II) acetate at room temperature. Diazoamide disappeared in just 30 min and followed by the chromatographic purification of the reaction mixture furnished the compound **4a** in 62% yield as single diastereomer.[14] The FT-IR spectrum of compound **4a** exhibited a characteristic bands at 1663 and 1728 cm^{-1} indicating the presence of amide and ester carbonyl functional groups, respectively. The ^1H NMR spectrum of product **4a** exhibited three characteristic singlets at δ 3.19, 3.61, and 3.68 for methyl groups and a singlet resonance at δ 6.49 for the OCH proton. ^{13}C NMR and DEPT-135 spectral analyses of product **4a** showed peaks for two CH_3 carbons, eight CH carbons, and nine quaternary carbons. The characteristic spectral data obviously confirmed the proposed structure of compound **4a**. The stereochemistry is tentatively assigned on the basis of the X-ray single-crystal analyses of product **4o**. Stimulated by this result, we ventured to explore the reactions of several diazoamides that enabled us to generalize this three-component synthesis of dihydrofurooxindoles **4b**−**k** (Scheme 1). The unsubstituted diazooxindole **1f** exhibits a very slow reaction when compared with substituted diazooxindoles resulting in the product in low yield (entry 6, Table 1). The reason may be the result of poisoning the catalyst by unsubstituted amide functionality.[15,16] The presence of an electron-donating group on aryl aldehydes enhances the yield of spirodihydrofurooxindoles (entries 7−11, Table 1) when compared to the unsubstituted aldehyde (entries 1−6, Table 1). The substitution at the spirodihydrofurooxindoles **4** can widely be varied by employing the range of diazoamides, aldehydes, and dipolarophiles.

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(14) No other isomeric products were detected by ^1H and ^{13}C NMR analyses of the crude reaction mixture.

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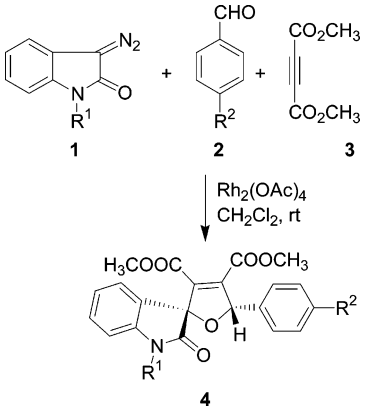
(16) Similar trend was observed in our earlier studies of cyclopropanation and C−H insertion reactions using these cyclic diazoamides. See ref 13.

TABLE 1. Synthesis of Spirofurooxindoles from the Three-Component Reaction of Cyclic Diazoamides, Aldehydes, and DMAD



entry	R^1	R^2	reaction time	product	yield,[a] %
1	CH_3	H	30 min	**4a**	62
2	Bn	H	25 min	**4b**	64
3	*p*-xylenyl	H	20 min	**4c**	50
4	allyl	H	25 min	**4d**	55
5	propargyl	H	25 min	**4e**	58
6	H	H	5 h	**4f**	25
7	CH_3	OCH_3	10 min	**4g**	83
8	Bn	OCH_3	15 min	**4h**	96
9	*p*-xylenyl	OCH_3	10 min	**4i**	87
10	allyl	OCH_3	20 min	**4j**	94
11	propargyl	OCH_3	25 min	**4k**	91

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds.

The scope of this novel multicomponent reaction was further enlarged employing different aromatic aldehydes with multiple functionalities. Insertion with the O−H functionality is a potentially competitive well-known reaction[17] in carbenoid chemistry. Notably, the hydroxy functionality on aromatic aldehydes did not interfere with the generated rhodium(II)-carbenoid intermediate in these reactions. The potential applicability of this novel three-component process is readily seen from the selected examples of compounds **4l**−**q**. The results of this study are described in Table 2.

The stereochemistry at 2- and 5-positions of furan ring system is obviously corroborated by performing the single-crystal X-ray analysis[18] of the representative product **4o** (Figure 2), which confirms the diastereoselectivity. The same stereochemistry is tentatively assigned for all other products. The presence of allyl, propargyl, free amide, and hydroxyl functionalities in the spirofurooxindoles should, in principle, allow us to further functionalize these products by following the standard procedures.

After performing the generation of intermolecular carbonyl ylides with diverse aryl aldehydes, we decided to extend this multicomponent reaction to the heteroaryl aldehydes. The 2-furaldehyde was chosen as a benchmark substrate for this study, which led to the concomitant construction of the furofuranyl system, incorporating the spirodihydrofuran ring. Significantly, this becomes the

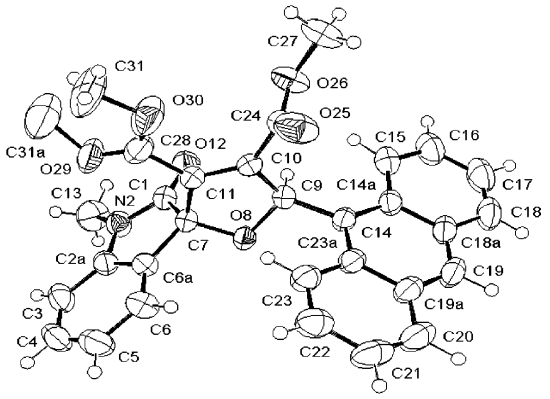


FIGURE 2. ORTEP diagram for the compound **4o**. The ester group methyl had a statistical disorder and was assigned 0.5 occupancy factor and refined. Thermal ellipsoids are drawn at 50% probability.

maiden study that utilizes the heteroaryl aldehyde for the generation of intermolecular carbonyl ylides. The reaction was also stretched to the indole-3-carbaldehyde[19] (entries 5 and 6, Table 3) that led to the synthesis of indole substituted dihydrofuran systems. The results of these studies are illustrated in Table 3. The effort is also invested to examine the course of the reaction with other heterocyclic aldehydes such as 2-thiophenecarbaldehyde and 3-pyridinecarbaldehyde, which failed to produce the dihydrofurans in the presence of DMAD under identical experimental conditions. The aliphatic aldehydes such as *n*-butyraldehyde also failed to participate in this multicomponent process.

The multicomponent reaction of diazoamides can easily be extended using electron deficient alkenes instead of alkyne as dipolarophiles in the above process. Thus, the reaction of diazoamide **1c** and *p*-anisaldehyde in the presence of maleic anhydride underwent [3 + 2]-cycloaddition with the transient intermolecular carbonyl ylide dipoles to furnish the furofuran system **11** as single isomer (Scheme 2). Interestingly, these furofuran systems are present in a number of natural products such as xanthoxylol, epipinoresinol, and epieudesmin, which exhibit broad-ranging biological activities.[20] Similarly, the use of an unsymmetrical dipolarophile was also explored. For example, the presence of ethyl acrylate in this process afforded dihydrofurooxindoles **12** and **13** as a mixture of regioisomers (Table 4). Elucidation of the structure of isomers **12a**,**b** and **13a**,**b** was carried out on the basis of the coupling constants of key proton signals in the ^{1}H NMR spectra.

The rapid generation of molecular complexity in a controlled and predictable manner from simple and readily available starting materials is a contemporary theme in the practice of modern organic synthesis. Complexity and brevity mostly rely on the coupling of individual transformation into one synthetic process. In this line, we speculated the use of appropriate bis-diazoamide or bis-aldehyde would result in the creation of complex molecules by doubling the efficiency the above

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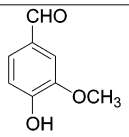
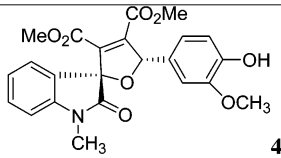
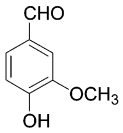
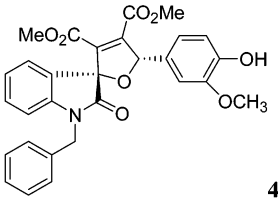
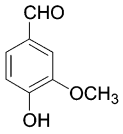
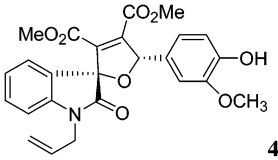
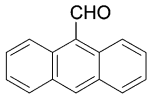
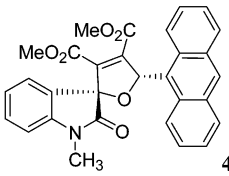
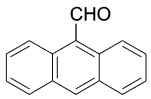
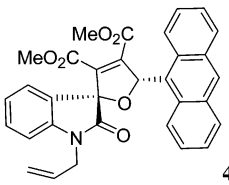
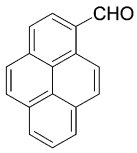
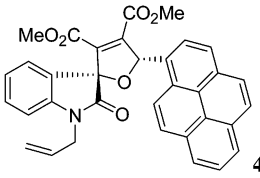
TABLE 2. Three-Component Reaction of Cyclic Diazoamides with Various Aldehydes and DMAD

Entry	Diazoamide	Aldehyde	Product	Yield[a] (%)
1	**1a**		 **4l**	70
2	**1b**		 **4m**	77
3	**1d**		 **4n**	79
4	**1a**		 **4o**	67
5	**1d**		 **4p**	56
6	**1d**		 **4q**	85

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds.

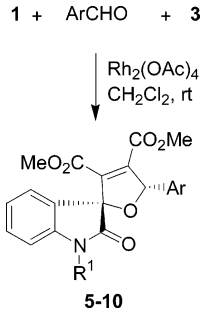
process. The efficiency of this process is further extended to demonstrate the double multicomponent process by utilizing the bis-diazoamide **14** in a tandem manner. The required 1,3-di[(3-diazo-1,3-dihydro-2*H*-indol-2-on-1-yl)-methyl]benzene (**14)** was synthesized by the dialkylation of 1,3-bis(bromomethyl)benzene with 3-diazo-1,3-dihydro-2*H*-indol-2-one (**1f**). The bis-diazoamide **14** was reacted with *p*-anisaldehyde or 1-pyrenecarbaldehyde to furnish the respective interesting bis-spirocyclic system **15**,**16** in the presence of an excess amount of DMAD and 1 mol % of rhodium(II) acetate catalyst (Scheme 3). This reaction efficiently resulted in formation of six chemical bonds and two spiro-dihydrofuran units in a single operation. The complex spiro-polycyclic systems are skillfully and proficiently synthesized from simple, readily available starting materials in brevity.

The bis-diazoamide **17** with alkyl spacer was also synthesized by the alkylation of 3-diazo-1,3-dihydroindol-2-one with 1,3-dibromopropane in K_2CO_3/DMF. 1,3-Di(3-diazo-1,3-dihydro-2*H*-indol-2-on-1-yl)propane (**17**) was subjected to the double multicomponent reaction with 1-allyl indol-3-carbaldehyde in the presence of DMAD to afford the corresponding bis-spirofurooxindole **18** in 57% yield (Scheme 4).

After exploring the double multicomponent reaction of bis-diazoamides, we were interested in exploring the use of bis-aryl aldehydes in this process. For this purpose, bis-aldehydes **19a**,**b** with alkyl spacers were synthesized from the reaction of corresponding dihaloalkanes with 4-hydroxybenzaldehyde. The reaction of bis-aldehydes with an excess of diazoamide and DMAD in the presence of a catalytic amount of $Rh_2(OAc)_4$ afforded the bis-spirooxindoles **20**−**23** in good yields (Table 5). These processes demonstrated prime examples for the multistep, one-pot operation of cyclic diazoamides and in turn are equivalent to a five-component[21] reaction.

In this operationally simple three-component process, mechanistically, the rhodium(II) acetate catalyst reacted

TABLE 3. Multicomponent Reactions of Cyclic Diazoamides with Heteroaryl Aldehydes and DMAD

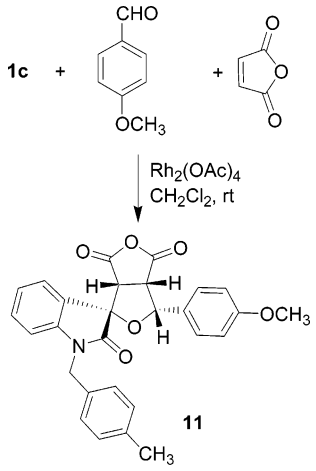


5-10

entry	diazoamide	R^1	Ar	product	yield,[a] %
1	**1a**	CH_3	furan-2-yl	**5**	68
2	**1b**	Bn	furan-2-yl	**6**	81
3	**1d**	allyl	furan-2-yl	**7**	80
4	**1e**	propargyl	furan-2-yl	**8**	57
5	**1a**	CH_3	1-allylindol-3-yl	**9**	68
6	**1d**	allyl	1-allylindol-3-yl	**10**	75

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds.

SCHEME 2. Multicomponent Reactions of 1c with Aldehyde and Maleic Anhydride



with cyclic diazoamides to produce the respective cyclic rhodium carbenoids, which underwent the intermolecular reaction with an appropriate aldehyde to produce the respective carbonyl ylide intermediates. From the observed stereochemistry of the products, we propose the selective formation of carbonyl ylide **24a** rather than **24b** (Figure 3). The symbiotic steric interactions between the amide oxygen and Ar group may shun the formation of **24b**. Further, the rotamer (180° rotation around indolyl carbon/carbonyl oxygen bond of aldehyde) that can arise from the ylide **24a** experiences the electrostatic repulsion between the 4H-proton (indole numbering) of indole moiety and aldehyde proton. Similarly, the rotamer of the ylide **24b** suffers from Ar−Ar steric hindrance. Thus, the most favorable transient intermediate **24a** stereoselectively underwent 1,3-dipolar cycloaddition reactions with alkyne or alkenes to furnish the spiro-furooxindoles in a diasteroselective manner. Moreover, similar types of cyclic metallo-carbenoid intermediates always have a propensity to undergo 1,3-dipolar cycloaddition reactions,[22,23] cyclopropanation,[13a] and C−H insertion[13b,c] reactions. No formation of dioxolane compounds was noticed in the above reactions with an excess amount of aldehyde. Interestingly, these cyclic diazoamides have recently been discovered[24] to afford stereoselective epoxide ring formation. Thus, the clean reaction obtained is remarkable. To the best of our knowledge, this represents the first paradigm in which the cyclic rhodium carbenoid generates the carbonyl ylides in an intermolecular fashion.

Conclusion

In conclusion, the three-component reactions of cyclic diazoamides involving rhodium(II) acetate catalyst are described for the spirofuran synthesis incorporating the oxindole unit. This method constitutes a distinct example in which the cyclic diazoamides participate in the multicomponent reactions. The processes involving bis-diazoamides and bis-aldehydes lead to the simultaneous creation of four carbon−carbon bonds, two carbon−oxygen bonds, and four chiral centers in a single synthetic step. The operational simplicity and high yields with diastereoselectivity are salient features of this multistep, one-pot process to synthesize the novel functionalized heterocyclic compounds.

Experimental Section

Due to a very long relaxation time, the resonance for the carbon atom adjacent to the diazo functional group was usually not detected in the ^{13}C NMR analysis for the diazo compounds prepared in this study.

Dimethyl 1′-Methyl-5-phenyl-2′-oxo-1′,2′-dihydro-5*H*-spiro(furan-2,3′-indole)-3,4-dicarboxylate (4a). To a dry CH_2Cl_2 (20 mL) solution of 3-diazo-1-methyl-1,3-dihydro-2*H*-indol-2-one (**1a**, 250 mg, 1.45 mmol), benzaldehyde (306 mg, 2.89 mmol), and dimethyl acetylenedicarboxylate (246 mg, 1.73 mmol) was added rhodium(II) acetate dimer (3.2 mg, 0.5 mol %) catalyst. The reaction mixture was stirred for 30 min, and the chromatographic purification (hexane/EtOAc, 65:35) of the residue afforded 352 mg (62%) of **4a** as a yellow solid: mp 140−142 °C (hexane/EtOAc); IR (KBr) 3057, 2956, 1728, 1663, 1615, 1494, 1471, 1438, 1265, 1159, 1090, 1024, 738 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.19 (s, 3H), 3.57 (s, 3H), 3.68 (s, 3H), 6.49 (s, 1H), 6.82 (d, 1H, $J = 7.7$ Hz), 7.08 (t, 1H, $J = 7.5$ Hz), 7.30−7.48 (m, 7H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 26.9 (CH_3), 53.0 (CH_3), 89.2 (*C*H), 90.6 (*quat-C*), 109.2 (*C*H), 123.7 (*C*H), 125.5 (*C*H), 127.2 (*quat-C*), 128.0 (*C*H), 129.3 (*C*H), 129.8 (*C*H), 131.6 (*C*H), 134.7 (*quat-C*), 137.8 (*quat-C*), 145.1 (*quat-C*), 145.5 (*quat-C*), 161.6 (*quat-C*), 163.1 (*quat-C*), 174.0 (*quat-C*); EIMS *m/z* 393 (M^+, 36), 361 (53), 334 (38), 290 (16), 275 (23), 246 (16), 121 (18), 105 (100), 77 (30). Anal. Calcd for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87; N, 3.56. Found: C, 67.36; H, 4.79; N, 3.49.

Compound 11. A mixture of 3-diazo-1-(4-methylbenzyl)-1,3-dihydro-2*H*-indol-2-one (**1c**, 200 mg, 0.76 mmol), 4-methoxybenzaldehyde (124 mg, 0.91 mmol), and maleic anhydride (97 mg, 0.99 mmol) was allowed to react with rhodium(II)

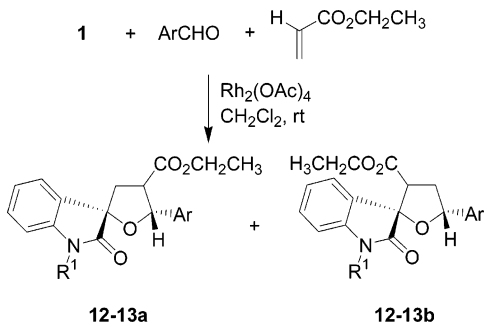
(21) For other five-components reactions, see: (a) Janvier, P.; Bienaymé, H.; Zhu, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4291−4294. (b) Ugi, I.; Steinbrückner, C. *Chem. Ber.* **1961**, *94*, 2802−2814.

(22) Pirrung, M. C.; Blume, F. *J. Org. Chem.* **1999**, *64*, 3642−3649.

(23) (a) Pirrung, M. C.; Lee, Y. R. *J. Am. Chem. Soc.* **1995**, *117*, 4814−4821. (b) Pirrung, M. C.; Lee, Y. R. *J. Chem. Soc., Chem. Commun.* **1995**, 673−674. (c) Pirrung, M. C.; Lackey, K.; Zhang, J.; Sternbach, D. D.; Brown, F. *J. Org. Chem.* **1995**, *60*, 2112−2124.

(24) Muthusamy, S.; Gunanathan, C.; Nethaji, M. *Synlett* **2004**, 639−642.

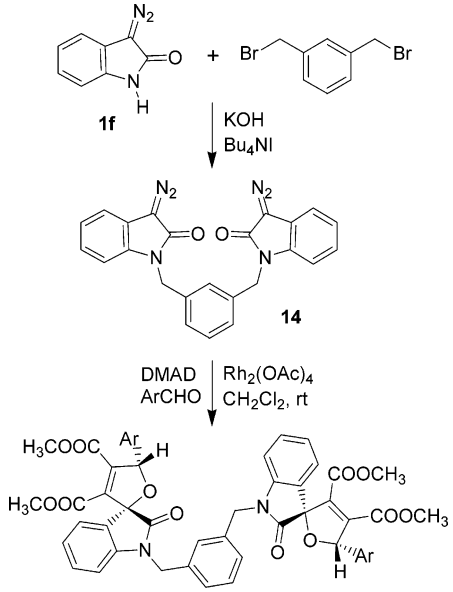
TABLE 4. Multicomponent Reactions of 1 with Aldehydes and Ethyl Acrylate



entry	diazoamide	aldehyde	R^1	product	yield,[a] %	ratio,[b] % **a**/**b**
1	**1c**	2-furaldehyde	*p*-xylenyl	**12**	33	51:49
2	**1e**	4-$CH_3OC_6H_4CHO$	propargyl	**13**	67	59:41

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds. [b] Determined from ^{1}H NMR spectrum of the crude reaction mixture.

SCHEME 3. Synthesis of Bis-spiropolycyclic Systems via Double Three-Component Reaction



acetate dimer (1.7 mg, 0.5 mol %) in dry CH_2Cl_2 for 30 min under an argon atmosphere. Chromatographic purification (hexane/EtOAc, 70:30) of the residue afforded 132 mg (37%) of yellow solid: mp 172−174 °C (hexane/EtOAc); IR (KBr) 2940, 1782, 1704, 1615, 1516, 1490, 1468, 1375, 1255, 1176, 1045, 943, 914, 759 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.82 (s, 3H), 3.90 (d, 1H, J = 8.6 Hz), 4.28 (t, 1H, J = 8.5 Hz), 4.78 (d, B part of AB system, 1H, J = 15.6 Hz), 4.91 (d, A part of AB system, 1H, J = 15.6 Hz), 6.29 (d, 1H, J = 8.1 Hz), 6.79 (d, 1H, J = 8.4 Hz), 6.93 (d, 2H, J = 8.7 Hz), 7.10−7.20 (m, 5H), 7.28−7.36 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 21.7 (*C*H$_3$), 44.3 (*C*H$_2$), 52.9 (*C*H), 55.9 (*C*H$_3$), 82.0 (*C*H), 84.7 (*quat-C*), 110.6 (*C*H), 114.8 (*C*H), 122.8 (*quat-C*), 124.1 (*C*H), 127.2 (*C*H), 127.9 (*C*H), 128.2 (*C*H), 130.4 (*C*H), 130.9 (*quat-C*), 132.2 (*C*H), 132.4 (*quat-C*), 138.5 (*quat-C*), 144.1 (*quat-C*), 160.8 (*quat-C*), 168.5 (*quat-C*), 168.9 (*quat-C*), 175.4 (*quat-C*); MS (EI) *m*/*z* 470 (M+1, 4), 469 (M$^+$, 11), 451 (11), 233 (19), 146 (21), 135 (100); HRMS (FAB) calcd for $C_{28}H_{24}NO_6$ (MH$^+$) 470.1604, found 470.1611.

Synthesis of compounds 12a and 12b. A mixture of 3-diazo-1-(4-methylbenzyl)-1,3-dihydro-2*H*-indol-2-one (**1c**, 150 mg, 0.57 mmol), 2-furaldehyde (109 mg, 1.14 mmol) and ethyl acrylate (89 mg, 0.85 mmol) was allowed to react with rhodium(II) acetate dimer (1.3 mg, 0.5 mol %) in dry CH_2Cl_2 for 45 min under an argon atmosphere. After removal of solvent, the residue was purified by column chromatography (hexane/EtOAc, 80:20) to give 42 mg (17%) of **12a** and 39 mg (16%) of **12b**.

SCHEME 4. Double Three-Component Reaction of Bis-diazoamide

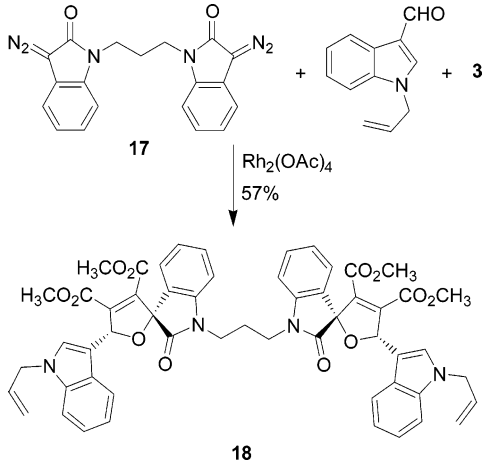
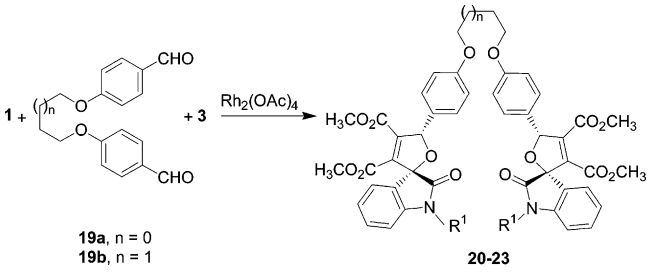


TABLE 5. Double Three-Component Reactions Using Bis-Aldehydes



entry	diazoamide	R^1	*n*	product	yield, %
1	**1b**	Bn	0	**20**	72
2	**1d**	allyl	0	**21**	83
3	**1c**	*p*-xylenyl	1	**22**	76
4	**1d**	allyl	1	**23**	75

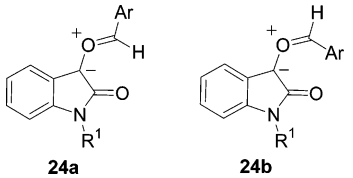


FIGURE 3. Intermolecularly generated possible carbonyl ylide intermediates.

Ethyl 1′-(4-methylbenzyl)-5-(furan-2-yl)-2′-oxo-1′,2′-dihydro-5*H*-spiro(3,4-dihydrofuran-2,3′-indole)-4-carboxylate (12a): yellow solid; mp 58−60 °C (hexane/$CHCl_3$); IR (KBr) 2927, 1727, 1615, 1468, 1372, 1265, 1174, 908, 734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.06 (t, 3H, J = 7.1 Hz), 2.30 (s, 3H), 2.60 (1H, X part of ABX system, dd, J = 13.2, 7.6 Hz), 3.05 (1H, B part of ABX system, dd, J = 13.2, 10.4 Hz), 3.96 (q, 2H, J = 7.2 Hz), 4.26−4.32 (m, 1H), 4.81 (s, 2H), 5.82 (d, 1H, J = 8.9 Hz), 6.33−6.43 (m, 2H), 6.56−6.68 (m, 2H), 6.83−6.91 (m, 1H), 7.01−7.25 (m, 4H), 7.45−7.69 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 14.7 (*C*H_3), 21.8 (*C*H_3), 37.7 (*C*H_2), 44.0 (*C*H_2), 48.4 (*C*H), 61.6 (*C*H_2), 76.8 (*C*H), 83.9 (*quat-C*), 109.7 (*C*H), 110.0 (*C*H), 111.0 (*C*H), 124.0 (*C*H), 125.6 (*C*H), 127.3 (*C*H), 127.8 (*C*H), 128.1 (*quat-C*), 130.0 (*C*H), 130.2 (*C*H), 130.7 (*C*H), 133.1 (*quat-C*), 138.1 (*quat-C*), 143.4 (*C*H), 152.8 (*quat-C*), 171.4 (*quat-C*), 178.2 (*quat-C*); HRMS (FAB) calcd for $C_{26}H_{26}NO_5$ (MH^+) 432.1811, found 432.1819.

Ethyl 1′-(4-methylbenzyl)-5-(furan-2-yl)-2′-oxo-1′,2′-dihydro-5*H*-spiro(3,4-dihydrofuran-2,3′-indole)-3-carboxylate (12b): yellow solid; mp 74−76 °C (hexane/CH_2Cl_2); IR (KBr) 2926, 1728, 1615, 1469, 1374, 1264, 1181, 1015, 909, 733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.53 (t, 3H, J = 7.1 Hz), 2.30 (s, 3H), 2.57−2.69 (m, 1H), 3.10 (dd, 1H, J = 24.1, 12.5 Hz), 3.59−3.79 (m, 2H), 3.93 (dd, 1H, J = 12.5, 7.3 Hz), 4.70 (B part of AB system, 1H, J = 15.5 Hz), 5.01 (A part of AB system, 1H, J = 15.5 Hz), 5.54 (dd, 1H, J = 11.0, 4.9 Hz), 6.35 (dd, 1H, J = 3.2, 1.8 Hz), 6.45 (d, 1H, J = 2.9 Hz), 6.64 (d, 1H, J = 7.6 Hz), 6.98−7.39 (m, 6H), 7.40−7.45 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 13.9 (*C*H_3), 21.7 (*C*H_3), 33.9 (*C*H_2), 44.5 (*C*H_2), 53.2 (*C*H), 61.4 (*C*H_2), 76.1 (*C*H), 83.9 (*quat-C*), 109.8 (*C*H), 111.0 (*C*H), 123.7 (*C*H), 125.7 (*C*H), 128.0 (*C*H), 128.2 (*quat-C*), 130.0 (*C*H), 130.4 (*quat-C*), 130.7 (*C*H), 133.1 (*quat-C*), 138.0 (*quat-C*), 143.8 (*C*H), 152.3 (*quat-C*), 170.1 (*quat-C*), 177.3 (*quat-C*); HRMS (FAB) calcd for $C_{26}H_{26}NO_5$ (MH^+) 432.1811, found 432.1816.

1,3-Di[(3-diazo-1,3-dihydro-2*H*-indol-2-on-1-yl)methyl]-benzene (14). To a 10% ethanolic KOH solution (20 mL) was added 3-diazo-1,3-dihydro-2*H*-indol-2-one (1 g, 6.28 mmol) and the resulting mixture stirred for 1 h. Then 1,3-bis(bromomethyl)benzene (0.83 g, 3.14 mmol) was added to the above reaction mixture at 0 °C. The reaction mixture was slowly brought to the room temperature, a catalytic amount of tetrabutylammonium iodide was added, and the mixture was allowed to stir for 3 days. After that, the solvent was removed under reduced pressure and the resulting residue poured into ice−water. The aqueous solution was extracted with dichloromethane (3 × 30 mL). The combined organic layer was washed with brine and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure and the emerging residue chromatographed using silica gel column to yield 0.924 g (35%) of red solid: mp 146−148 °C; IR (KBr) 2924, 2096, 1683, 1610, 1468, 1400, 1343, 1174, 1102, 747 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 4.96 (s, 4H), 6.68−6.72 (m, 2H), 7.01−7.08 (m, 4H), 7.15−7.25 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 44.6 (*C*H_2), 110.1 (*C*H), 117.2 (*quat-C*), 118.8 (*C*H), 122.7 (*C*H), 126.0 (*C*H), 126.6 (*C*H), 127.1 (*C*H), 129.9 (*C*H), 134.0 (*quat-C*), 137.2 (*quat-C*), 167.4 (*quat-C*). Anal. Calcd for $C_{24}H_{16}N_6O_2$: C, 68.56; H, 3.84; N, 19.99. Found: C, 68.77; H, 3.91; N, 20.16.

1,3-Di[(5-(4-methoxyphenyl)-2′-oxo-1′,2′-dihydro-5*H*-spiro(furan-2,3′-indole)-3,4-dicarboxylic acid dimethyl ester)-1′-ylmethyl]benzene (15). To a dry CH_2Cl_2 (20 mL) solution of bis-diazoamide (**14**, 100 mg, 0.14 mmol), 4-methoxybenzaldehyde (130 mg, 0.95 mmol), and dimethyl acetylenedicarboxylate (81 mg, 0.57 mmol) was added rhodium(II) acetate dimer (1.1 mg, 1.0 mmol) catalyst. The reaction mixture was stirred for 35 min, and the column chromatographic (hexane/EtOAc, 50:50) purification of the residue afforded 136 mg (62%) of **15** as an orange solid: mp 106−108 °C (hexane/$CHCl_3$); IR (KBr) 3056, 2957, 1729, 1663, 1614, 1514, 1489, 1467, 1438, 1265, 1179, 1026, 906, 739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.53 (s, 6H), 3.72 (s, 6H), 3.81 (s, 6H), 4.68 (d, 1H, B part of AB system, J = 15.7 Hz), 4.72 (d, 1H, B part of AB system, J = 15.7 Hz), 5.06 (d, 1H, A part of AB system, J = 15.7 Hz), 5.10 (d, 1H, A part of AB system, J = 15.7 Hz), 6.48 (s, 2H), 6.58 (t, 2H, J = 7.0 Hz), 6.91−7.14 (m, 6H), 7.26−7.47 (m, 12H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 44.5 (*C*H_2), 53.1 (*C*H_3), 53.2 (*C*H_3), 55.9 (*C*H_3), 89.0 (*C*H), 90.4 (*quat-C*), 110.4 (*C*H), 114.8 (*C*H), 123.9 (*C*H), 125.7 (*C*H), 127.3 (*C*H), 127.5 (*quat-C*), 129.7 (*C*H), 130.0 (*C*H), 130.3 (*C*H), 131.6 (*C*H), 134.5 (*quat-C*), 136.6 (*quat-C*), 138.9 (*quat-C*), 144.2 (*quat-C*), 146.0 (*quat-C*), 161.1 (*quat-C*), 161.8 (*quat-C*), 163.3 (*quat-C*), 174.4 (*quat-C*); HRMS (FAB) calcd for $C_{52}H_{45}N_2O_{14}$ (MH^+) 921.2871, found 921.2859.

1,3-Di[(5-(1-allylindol-3-yl)-2′-oxo-1′,2′-dihydro-5*H*-spiro-(furan-2,3′-indole)-3,4-dicarboxylic acid dimethyl ester)-1′-yl]propane (18): brown solid; mp 102−104 °C (hexane/$CHCl_3$); IR (KBr) 3057, 2955, 1726, 1615, 1550, 1466, 1438, 1266, 1018, 738 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.13 (t, 2H, J = 6.8 Hz), 3.62 (s, 6H, *C*H_3), 3.68 (s, 6H, *C*H_3), 3.74−3.81 (overlapping m, 4H), 4.72 (d, 4H, J = 5.3 Hz), 5.04−5.24 (m, 4H), 5.92−6.06 (m, 2H), 6.85 (s, 2H), 6.87 (s, 2H), 6.97 (t, 2H, J = 7.3 Hz), 7.13−7.34 (m, 12H), 7.81 (dd, 2H, J = 6.4, 1.9 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 25.8 (*C*H_2), 38.9 (*C*H_2), 49.5 (*C*H_2), 53.2 (*C*H_3), 83.2 (*C*H), 90.0 (*quat-C*), 109.4 (*C*H), 110.6 (*C*H), 112.5 (*quat-C*), 118.2 (*C*H_2), 120.1 (*C*H), 120.7 (*C*H), 122.9 (*C*H), 123.7 (*C*H), 125.9 (*C*H), 127.4 (*quat-C*), 128.0 (*quat-C*), 128.6 (*C*H), 131.5 (*C*H), 133.7 (*C*H), 134.2 (*quat-C*), 137.4 (*quat-C*), 144.2 (*quat-C*), 146.3 (*quat-C*), 161.8 (*quat-C*), 163.8 (*quat-C*), 174.6 (*quat-C*); HRMS (FAB) calcd for $C_{55}H_{49}N_4O_{12}$ (MH^+) 957.3347, found 957.3357.

1,3-Di[4-(3,4-dimethyl 1′-benzyl-2′-oxo-1′,2′-dihydro-5*H*-spiro(furan-2,3′-indole)-3,4-dicarboxylate)-5-phenyloxy]-propane (20): brown solid; mp 116−118 °C (hexane/$CHCl_3$); IR (KBr) 2953, 1728, 1613, 1512, 1490, 1467, 1436, 1248, 1176, 1020, 752 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.26 (t, 2H, J = 5.9 Hz), 3.52 (s, 6H), 3.71 (s, 6H), 4.16 (t, 4H, J = 5.9 Hz), 4.75 (d, B part of AB system, 2H, J = 15.7 Hz), 5.05 (d, A part of AB system, 2H, J = 15.7 Hz), 6.48 (s, 2H), 6.69 (d, 2H, J = 7.7 Hz), 6.94 (d, 4H, J = 8.5 Hz), 7.04 (t, 2H, J = 7.5 Hz), 7.18−7.43 (m, 18H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 29.9 (*C*H_2), 44.7 (*C*H_2), 53.1 (*C*H_3), 53.2 (*C*H_3), 65.2 (*C*H_2), 89.0 (*C*H), 90.4 (*quat-C*), 110.3 (*C*H), 115.4 (*C*H), 123.9 (*C*H), 125.8 (*C*H), 127.6 (*quat-C*), 128.0 (*C*H), 128.3 (*C*H), 129.4 (*C*H), 129.8 (*C*H), 130.2 (*quat-C*), 131.6 (*C*H), 134.7 (*quat-C*), 136.1 (*quat-C*), 144.4 (*quat-C*), 146.1 (*quat-C*), 160.3 (*quat-C*), 161.7 (*quat-C*), 163.3 (*quat-C*), 174.4 (*quat-C*); HRMS (FAB) calcd for $C_{59}H_{51}N_2O_{14}$ (MH^+) 1011.3340, found 1011.3356.

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Supporting Information Available: General information, experimental procedures, and spectral data for all new compounds. ^1H, ^{13}C, and DEPT-135 spectra of **4a**−**q**, **5**−**13**, **15**, **16**, **18**, and **20**−**23**, and X-ray structural data of compound **4o** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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