Palladium-Catalyzed Heteroannulation Leading to Heterocyclic Structures with Two Heteroatoms: A Highly Convenient and Facile Method for a Totally Regio- and Stereoselective Synthesis of (*Z*)-2,3-Dihydro-2-(ylidene)-1,4-benzo- and -naphtho[2,3-*b*]dioxins†

Chinmay Chowdhury,‡ Gopeswar Chaudhuri,‡ Subhadra Guha,§ Alok k. Mukherjee,§ and Nitya G. Kundu*,‡

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta - 700 032, India, and Department of Physics, Jadavpur University, Jadavpur, Calcutta - 700 032, India

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A facile method for the synthesis of (*Z*)-2,3-dihydro-2-(ylidene)-1,4-benzo- and naphthodioxins (**3**) has been developed using palladium−copper catalysis. Aryl halides **2** were found to react with mono-prop-2-ynylated catechol (**1a**) or 2-hydroxy-3-(prop-2-ynyloxy)naphthalene (**1b**) in the presence of $(PPh_3)_2PdCl_2$ (3.5 mol %) and CuI (7 mol %) in triethylamine by stirring at room temperature for 20 h followed by heating at 100 °C for 16 h to give products **3** in good yields. The method is regio- and stereoselective and also amenable to bisheteroannulation. The *Z*-stereochemistry of products **3** was established firmly from ^{1}H NMR, $^3J_{CH}$ values (between vinylic proton and methylenic carbon of the heterocyclic ring), proton NOE measurements, and finally from X-ray analysis. Based on experimental observations and known palladium chemistry, a mechanism has been proposed to explain the regio- and stereoselective product formation. Some of the products **3** were also converted to 1,4-benzodioxan derivatives **6** using hydrogenation procedure. A uracil derivative of possible biological interest, possessing a 1,4-benzodioxinyl functionality at the C-5 position, has been synthesized.

1,4-Benzodioxins and its 2,3-dihydro analogues (1,4-benzodioxans) are versatile organic compounds endowed with rich and fascinating chemistry. Various 2-substituted 1,4-benzodioxans (e.g. piperoxan, pentamoxan, idazoxan, prosympal, WB-4106 and RX 821002) have displayed promising roles in antidepression and antihypertension therapy as α-blocking agents or as *β*-blocking agents.[1] Some of these also exhibit antihyperglycemic properties.[2] Incorporation of 1,4-benzodioxan structural unit in camptothecin, which has potent antitumor and antileukemic properties,[3] overcame a solubility problem in the aqueous system and showed a better pharmacological profile.[4] A recent publication[5] has explored the synthesis and biological evaluation (in vitro and in vivo) of a series of *N*-hydroxyureas based on 1,4-benzodioxan template as inhibitors of 5-lipoxygenase, which is involved in the oxygenation of arachidonic acid to leukotrienes. Thus, compounds that contain the 1,4-benzodioxan structure could form the basis for development of drugs for future therapeutic treatment of asthma and arthritis. Also, the 1,4-benzodioxan nucleus is prevalent in a variety of important natural products (e.g. Silybin and Isosilybin,[6] Eusederins,[7] Purpurenol,[8] and others[9]), some of which exhibit significant biological activity. Moreover, in recent years 1,4-benzodioxin and its 2,3-dihydro analogues attracted considerable interest as intermediates for several important synthetic transformations.[10]

† This paper is dedicated to Professor Jerome A. Berson.

‡ Indian Association for the Cultivation of Science.

§ Jadavpur University.

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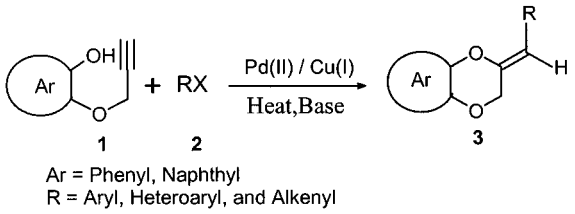
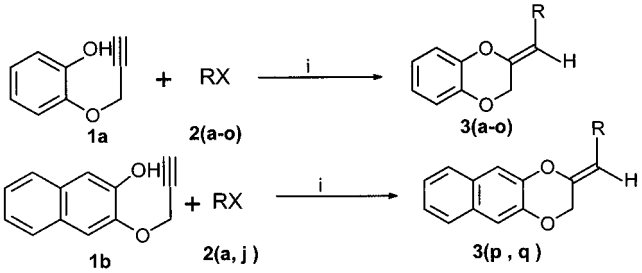
While there are many synthetic routes[11] toward 1,4-benzodioxins, only a handful of synthetic methods for the synthesis of 2,3-dihydro-2-(ylidene)-1,4-benzodioxins are known in the literature.[12] Some of these involve multistep procedures under harsh reaction conditions with attendant poor overall yields, and others lack generality, which considerably diminish their synthetic utility.

Recently, Heck reactions[13] (palladium-catalyzed arylation of olefins) and cross-coupling[14] techniques have emerged as powerful synthetic tools for C−C bond formation. The general application of palladium-catalyzed reactions has provided new avenues to obtain a variety of carbocycles[15] and heterocycles.[16] As a part of our ongoing research to develop heterocyclic structures of potential biological importance,[17] we reported the palladium-catalyzed heteroannulation leading to benzofurans,[18a] phthalides,[18b] quinolines and quinolones[18c] (heterocyclic structures with one heteroatom only). In all these cases, we used an aryl halide which contained a reactive nucleophilic group in the ortho-position and alkynes or acetylenic carbinols as starting materials. Our strategy for the development of heterocyclic ring system relied on (i) C−C bond formation with terminal alkynes under palladium−-copper catalysis[19] and (ii) subsequent nucleophilic attack on the triple bond. With the purpose of developing heterocyclic ring structures with two heteroatoms, we made a suitable modification of the above scheme. We felt that replacing the traditional acetylenic carbinols with mono-prop-2-ynylated catechol or 2-hydroxy-3-(prop-2-ynyloxy)naphthalene and its subsequent reaction with aryl or alkenyl halides under palladium−copper catalysis could result in the formation of 2,3-dihydro-2-(ylidene)-1,4-benzo- or naphthodioxins as shown in Scheme 1.

Scheme 1



Scheme 2[a]



[a] Reaction conditions: (i) 3.5 mol % $(PPh_3)_2PdCl_2$, 7 mol % CuI in Et_3N, stirring at room temperature for 20 h, followed by heating at 100 °C for 16 h.

By choosing appropriate reaction conditions and catalysts, the above route appeared viable. Herein, we wish to report[20] in full details the results we have obtained so far toward this goal.

Results and Discussion

Mono-prop-2-ynylated catechol (**1a**) or 2-hydroxy-3-(prop-2-ynyloxy)naphthalene (**1b**) was found to react with aryl, heteroaryl, or alkenyl halides **2** in the presence of bis(triphenylphosphine)palladium(II) chloride (3.5 mol %) and cuprous iodide (7 mol %) in triethylamine by stirring at room temperature for 20 h followed by heating at 100 °C for 16 h to afford 2,3-dihydro-2-(ylidene)-1,4-benzo- or naphtho[2,3-*b*]dioxins (**3**) in good yields (Scheme 2, Table 1).

Reaction Conditions. A close look at control reactions (entries 4 and 5, Table 2) indicated that in the absence of CuI or palladium catalysts, no desired 1,4-benzodioxan derivatives **3i** could be obtained. Among various catalysts used, $(PPh_3)_2PdCl_2$ was found to be the most effective. In addition to the palladium catalyst, CuI[21] was needed as an essential cocatalyst. The optimum reaction temperature was found to be 100 °C. On the other hand, when the reactions were carried out at lower temperatures, an acyclic product **4i** was isolated in addition to the cyclized product **3i** (entries 1 and 2, Table 2). The reaction mixture was stirred at room temperature for 20 h before heating.

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Table 1. Results of the Reaction of Mono-prop-2-ynylated Catechol (1a) or 2-Hydroxy-3-(prop-2-ynyloxy)naphthalene (1b) with Halides 2 in Presence of Palladium Catalyst, Copper(I) Iodide and Et_3N[a] (Scheme 2)

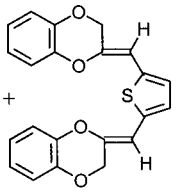
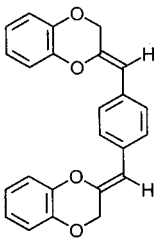
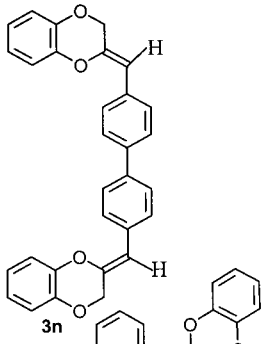
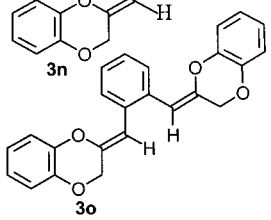
Entry	Mono-prop-2-ynylated catechol **1a** or 2-hydroxy-3-(prop-2-ynyloxy)naphthalene **1b**.	Halides(RX) **2** R	X	Products **3** R	Yields[b] (%)
1	**1a**	C_6H_5- **2a**	I	C_6H_5 **3a**	44
2	**1a**	1-naphthyl **2b**	I	1-naphthyl **3b**	48
3	**1a**	Ph−CH=CH- **2c**	Br	Ph−CH=CH- **3c**	40
4	**1a**	2-thienyl **2d**	I	2-thienyl **3d**	51
5	**1a**	5-formyl-2-thienyl **2e**	Br	5-formyl-2-thienyl **3e**	51
6[c]	**1a**	2,4-dimethoxy-5-pyrimidinyl **2f**	I	2,4-dimethoxy-5-pyrimidinyl **3f**	27
7	**1a**	2-nitro-4-methyl phenyl **2g**	I	2-nitro-4-methyl phenyl **3g**	62
8	**1a**	2-$MeOC_6H_4$- **2h**	I	2-$MeOC_6H_4$- **3h**	42
9	**1a**	3-ClC_6H_4- **2i**	I	3-ClC_6H_4- **3i**	58
10	**1a**	2-$O_2NC_6H_4$- **2j**	I	2-$O_2NC_6H_4$- **3j**	56
11	**1a**	2-$MeOCOC_6H_4$- **2k**	I	2-$MeOCOC_6H_4$- **3k**	48
12[d]	**1a**	5-Iodo-2-thienyl **2l**	I	**3d** +  **3l**	50 (**3d**:**3l**= 1:4)
13[d]	**1a**	4-IC_6H_4- **2m**	I	 **3m**	55

Table 1 (Continued)

Entry	Mono-prop-2-ynylated catechol **1a** or 2-hydroxy-3-(prop-2-ynyloxy)naphthalene **1b**.	Halides(RX) **2** R	X	Products **3** R	Yields[b] (%)
14[d]	**1a**	4'-IC$_6$H$_4$-C$_6$H$_4$- **2n**	I	 **3n**	53
15[d]	**1a**	2-IC$_6$H$_4$- **2o**	I	 **3o**	54
16	**1b**	C$_6$H$_5$- **2a**	I	C$_6$H$_5$- **3p**	57
17	**1b**	2-O$_2$NC$_6$H$_4$- **2j**	I	2-O$_2$NC$_6$H$_4$- **3q**	73

[a] Unless otherwise stated, reactions were carried out at room temperature for 20 h, followed by heating at 100 °C for 16 h using the following molar ratios: **1a** or **1b**:**2**:$(PPh_3)_2PdCl_2$:CuI = 1.3:1:0.035:0.07. [b] Yields refer to chromatographically isolated pure products. [c] Entry 6 was carried out at 120 °C. [d] Stereoselective (*Z*)-bis-heteroannulated products were isolated in each case.

Table 2. Dependence of the Yield of (*Z*)-2,3-Dihydro-2-[(3-chlorophenyl)methylidene]-1,4-benzodioxin (3i) on Catalyst, Temperature, and Base[a]

entry	catalyst	cocatalyst	temp condition	base	product	yield, %[b]
1	$(PPh_3)_2PdCl_2$	CuI	i	Et_3N	**3i** + **4i**	69 (**3i**:**4i** = 1:5)
2	$(PPh_3)_2PdCl_2$	CuI	ii	Et_3N	**3i** + **4i**	63 (**3i**:**4i** = 1:3)
3	$(PPh_3)_2PdCl_2$	CuI	iii	Et_3N	**3i**	58
4	$(PPh_3)_2PdCl_2$	–	iii	Et_3N	**3i**	0
5	–	CuI	iii	Et_3N	**3i**	0
6	$Pd(PPh_3)_4$	CuI	iii	Et_3N	**3i**	51
7	$PdCl_2$	CuI	iii	Et_3N	**3i**	15
8	$Pd(OAc)_2$	PPh_3	iii	Et_3N	**3i**	18
9[c]	$(PPh_3)_2PdCl_2$	CuI	iii	–	**3i**	0

[a] Reaction Conditions: *m*-Chloroiodobenzene (1 mmol), mono-prop-2-ynylated catechol (1.3 mmol), palladium complex (0.035 mmol, except entry 5), CuI (0.07 mmol, except entries 4, 8) in Et_3N (except entry 9) was used in each case employing the following conditions. **Condition i**: Stirred at room temperature (28−30 °C) for 48 h. **Condition ii**: Stirred at room temperature for 20 h followed by heating at 65 °C for 16 h. **Condition iii**: Stirred at room temperature for 20 h followed by heating at 100 °C for 16 h. [b] Yields refer to chromatographically isolated pure products. [c] Entry 9 was carried out in dry acetonitrile instead of Et_3N.

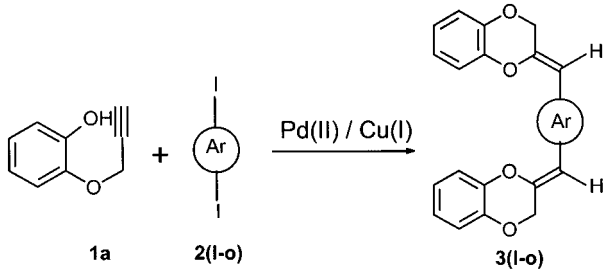
An immediate heating of the reaction mixture after a quick addition of the acetylenic component **1a** or **1b** usually led to considerable amount of polymeric materials and hence to significant reduction in yields. Omission of base yielded no desired 1,4-benzodioxan derivatives **3i**. Among various bases (e.g. diethylamine, triethylamine, piperidine, pyridine, sodium bicarbonate, sodium acetate, K_2CO_3/Bu_4NCl), triethylamine was found to be most effective. The heteroannulation process was also carried out using different types of solvents viz., benzene, acetonitrile, acetonitrile/water (1:1), DME, DMF, and DMSO, with Et_3N (5 equiv) as base in each case. However, cleaner products with optimum yields were obtained in cases where Et_3N was used only. Thus Et_3N was found to be the solvent as well as the base of our choice.

Mono-prop-2-ynylated catechol (**1a**) required for this investigation was obtained through selective propargylation of catechol. Treatment of catechol (1 equiv) with propargyl bromide (1 equiv) in the presence of potassium carbonate (0.5 equiv) in acetone at 70 °C for 16 h afforded the desired product in 87% yield. Surprisingly, attempts to synthesize 2-hydroxy-3-(prop-2-ynyloxy)naphthalene (**1b**) under similar condition led to the isolation of the dipropargylated product of 2,3-dihydroxynaphthalene. However, changing the base from K_2CO_3 to NaH under room temperature afforded a mixture of mono- (**1b**) and dipropargylated products of 2,3-dihydroxynaphthalene. Aromatic mono- or dihalides were prepared from their corresponding amines using known diazotization procedures.[22]

A wide variety of aryl, heteroaryl, or alkenyl halides possessing different functional groups have been used successfully for the heteroannulation process. Entries 3, 5, 6, 9, 10, and 11 in Table 1 showed the compatibility of the reaction with different functional groups (e.g.,

(22) Vogel, A. I. *A Text Book of Practical Organic Chemistry*, 4th ed.; ELBS, Longman Group Limited: London, 1978, p 695.

Scheme 3



vinyl, formyl, ether, chloro, nitro, and ester). As can be seen from Table 1, electron-withdrawing groups (entries 5, 7, 9, 10, 11, and 17, Table 1) present in aryl halide moieties facilitated the reactions compared to electron-donating groups (entries 6 and 8, Table 1). These results are in conformity with our earlier observations[23] of palladium catalysis. However, when 5-carbomethoxy-2-nitroiodobenzene was used as a coupling partner in this heteroannulation process; no corresponding 1,4-benzodioxan derivative was isolated leading to the recovery of the deiodinated starting material.[24]

The efficacy of this new route leading to the formation of 2,3-dihydro-2-(ylidene)-1,4-benzodioxins (**3**) was also tested by using a variety of aromatic and heteroaromatic diiodides (see entries 12, 13, 14, and 15, Table 1) under palladium−copper-catalyzed condition (Scheme 3).

Interestingly, a totally regio- and stereoselective (*Z*)-(as shown in Scheme 3) bisheteroannulation process, which is an active and rapidly growing area in organic synthesis using palladium catalysis,[25] took place. The *Z*-stereochemistry and structural identifications were made from spectral evidences and finally from X-ray analysis. Thus, this method is amenable to the synthesis of molecules containing polyheteroannulated framework under one pot and operationally simple palladium catalyzed condition.

Identification of Structures. The structures of compounds **3** could be easily assigned from spectral evidences (IR, UV, ^{1}H and ^{13}C NMR, mass spectra) and elemental analyses. In IR spectra, absorption between 1670 and 1680 cm^{-1} confirmed the presence of an exocyclic double bond in products **3**. In ^{1}H NMR, the olefinic proton of the exocyclic double bond generally appeared in the range (δ_H) 5−6 ppm as a sharp singlet. But in some cases lower field shift (δ_H > 6 ppm) was observed due to the deshielding effect of the oxygen present in proximity in electron-withdrawing groups (e.g., CO_2Me, NO_2, etc.) of the aromatic rings of **3**. In addition to it, methylenic protons (O*C*H$_2$) of the heterocyclic rings also appeared as a singlet ranging between (δ_H) 4.56 to 4.75 ppm. Furthermore, ^{13}C NMR, in combination with DEPT analysis provided support in favor of structures **3**. The characteristic carbon signals appeared in the range (δ_c) 64.8 to 66.3 for methylenic carbon (O*C*H$_2$) of the heterocyclic rings and (δ_c) 96.1 to 108.05 ppm for methine carbon (C=*C*H) of the exocyclic double bond of products **3**. Besides NMR spectra, mass spectral data were also very informative. Particularly strong support in favor of the bisheteroannulated products **3l**−**o** which could not be easily distinguished from mono-heteroannulated products by ^{1}H and ^{13}C NMR (due to the same type of regio- and stereoselective cyclization), was obtained from mass spectral data. It should be pointed out here that no *E*-isomers or seven-membered ring compounds were isolated under our reaction conditions.

The heteroannulation process was found to be completely stereoselective since only the *Z*-isomers were obtained. The *Z*-stereochemistry was established on the basis of several evidences. A reasonable working hypothesis[26] is that the olefinic proton signal of the *E*-isomers of products **3** should appear in the lower field region (δ_H > 6 ppm) due to the deshielding effect of oxygen present in 1,4-benzodioxane ring system compared to the corresponding proton of *Z*-isomer. In our case, olefinic proton signals generally appeared in the range of (δ_H) 5−6 ppm indicating the *Z*-stereochemistry. Furthermore, the stereochemistry of the exocyclic double bond of products **3** was determined with the assistance of $^3J_{CH}$ values between the vinylic proton and methylenic carbon (O*C*H$_2$) of the heterocyclic ring. From literature[12a,b] the $^3J_{CH}$ values more than 7 Hz or less than 5 Hz were attributed to *E*- or *Z*-isomers, respectively. In our case, the observed $^3J_{CH}$ values of compounds **3** were always less than 5 Hz, and hence the observed stereochemistry was *Z* in nature. The assignments were also confirmed by carrying out proton NOE experiments: when methylenic protons of the heterocyclic ring (OC*H*$_2$) of compound **3i** were irradiated, a strong enhancement of the vinylic proton signal of the exocyclic double bond was observed and vice versa. This result provided a strong support in favor of the *Z*-stereochemistry. Finally the X-ray diffraction study[27]of 2,5-bis[(*Z*)-2′,3′-dihydro-2′-methylidene-1′,4′-benzodioxinyl]thiophene (**3l**) was also performed which confirmed its structure and the *Z*-stereochemistry. All these observation led us to assign the Z-stereochemistry to compound **3** unambiguously.

Mechanism. Based on our observations and known palladium chemistry, the mechanism of the reaction is suggested to proceed according to Scheme 4.

Transformation of Pd(II) to active catalytic species Pd(0) with the formation of dimers of the acetylenic components is well precedented.[21,28] Oxidative addition of Pd(0) with aryl halides takes place to form σ-aryl palladium(II) complex **B**. Complex **B** undergoes transmetalation[29] by organocopper species **A** to form another intermediate **C**. In the next step, the latter undergoes nucleophilic attack by phenoxide or naphthoxide ion to form the cyclic vinyl palladium species **D** (through path

(23) Pal, M.; Kundu, N. G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 449.

(24) In a parallel experiment, 2-nitro-5-carbomethoxyiodobenzene and phenylacetylene in the presence of $(PPh_3)_2PdCl_2$ (3 mol %) and CuI (7 mol %) in Et_3N, employing the reaction condition of our heteroannulation process resulted in no coupled product. Only the deiodinated product was obtained. This could be explained first by oxidative coupling followed by reduction of the palladated complex by triethylamine. We thank a referee in pointing this out.

(25) Iyoda, M.; Kuwatani, Y.; Ueno, N.; Oda, M. *J. Chem. Soc., Chem. Commun.* **1992**, 158. (b) Tao, W.; Nesbitt, S.; Heck, R. F. *J. Org. Chem.* **1990**, *55*, 63 and see also ref 14d.

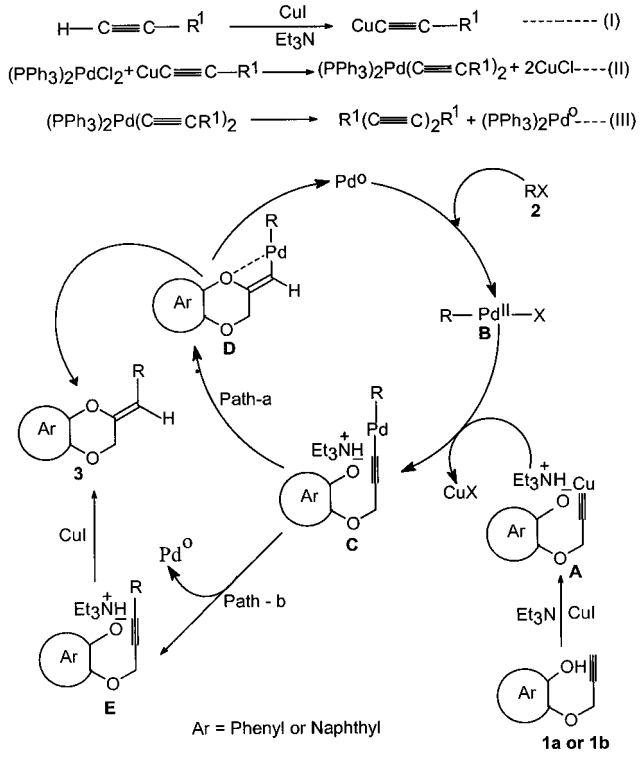
(26) In case of (*E*)- and (*Z*)-isomers, different chemical shift values of vinylic proton of exocyclic double bond due to the deshielding effect of oxygen of some heterocyclic rings have been invoked to account for the results: (a) Jager, V.; Gunther, H. J. *Tetrahedron Lett.* **1977**, 2543. (b) Yamamoto, M. *J. Chem. Soc., Chem. Commun.* **1978**, 649. (c) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. R. *J. Org. Chem.* **1992**, *57*, 976.

(27) X-ray data of compound **3l** has been deposited at Cambridge Cystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

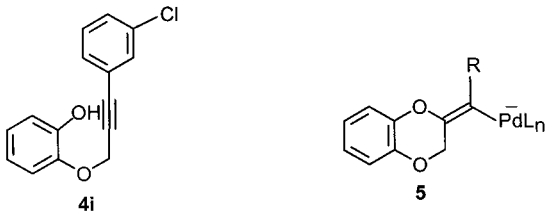
(28) Kundu, N. G.; Pal, M.; Chowdhury, C. *J. Chem. Res.* **1993**, 432.

(29) Nakamura, E.; Isaka, M.; Matsuzawa, S. *J. Am. Chem. Soc.* **1988**, *110*, 1297.

Scheme 4

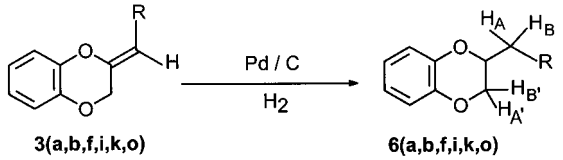


a) where Pd(II) is stabilized by coordination with oxygen.[30] Finally, elimination of Pd(0) from **D** furnishes the 1,4-benzodioxan derivative **3** ensuring the *Z*-stereochemistry. On the other hand, intermediate **C** undergoes (path b) reductive elimination to afford the acyclic intermediate **E**. The acyclic intermediate **E** would be cyclized in a stereoselective way with the assistance of CuI and Et_3N leading to the products **3**. Our stereochemical outcome (*Z*) rules out the possibility of mechanistic pathway proposed by Luo et al.,[16b] and also addition of RPdX on the triple bond is less probable due to the requirement of CuI as a cocatalyst. Furthermore, cyclization of the acyclic intermediate **E** driven by Pd(0) is less likely due to the involvement of a negative palladium(0) species **5** which is an unfavorable process from energy consideration.[16c] The feasibility of Pd(0) and Pd(II)[31] catalyzed cyclization was also discarded on the



basis of control experiments.[32] To understand the role of CuI and base toward cyclization, in two separate

Scheme 5



experiments the acyclic intermediate **4i** was heated at 100 °C for 16 h in Et_3N only, and with 7 mol % CuI in Et_3N, respectively. The corresponding cyclized 1,4-benzodioxan derivative **3i** was obtained in 30% yield in the former case, while the latter experiment (in the presence of CuI) afforded the product **3i** in 75% yield. These observations revealed that cooperative assistance of CuI[33] and Et_3N could have prompted the stereoselective cyclization of the acyclic intermediate **E**. Hence, it can be concluded that this stereoselective heteroannulation might be propagated either by path a or path b through the acyclic intermediates.[34,35]

Scope of the Reaction. To further extend the scope of the described method, we have investigated the feasibility of applying this method for the preparation of the saturated analogues of compounds **3** using hydrogenation procedure. This will provide the 1,4-benzodioxan derivatives **6** which display the key structural features of many naturally occurring[6−9] and biologically active compounds.[1] The hydrogenation was accomplished using Pd/C as catalyst in excellent yields (Scheme 5, Table 3).

The saturated 1,4-benzodioxan derivatives **6** were characterized by spectral evidence and elemental analyses. Thus our method provides us with an efficient and facile route for the construction of 1,4-benzodioxan ring structure.

Moreover, the structure−activity relationship and pharmacological profile of 2-methylene-1,4-benzodioxan and 3-substituted-2-methylene-1,4-benzodioxans is well established in the literature.[36] Thus a facile and efficient method for the synthesis of 2-methylene-1,4-benzodioxan (**7**) and its analogues was highly desirable. In the past,[11d,36] 2-methylene-1,4-benzodioxan has been synthesized through multistep procedures with poor overall yield starting from catechol. We have accomplished the synthesis of compound **7** in two steps with an overall yield of 65% as shown in Scheme 6.

Recently, we have also synthesized a number of uracil derivatives substituted at the C-5 position leading to 5-acylethynyl uracils[17a] (5-AEUs), 5-acylvinyl uracils (5-AVUs),[17b] or at the C-6 position leading to 6-acylvinyl uracils[17c] (6-AVUs) and other 6-substituted uracil compounds.[17d] Some of these compounds were found to act

(30) The coordination between palladium and oxygen or other heteroatom is well precedented in the literature: (a) Jeffery, T. *Tetrahedron Lett.* **1993**, *34*, 1133. (b) Kang, S.-K.; Jung, K.-Y.; Park, C.-H.; Namkoong, E.-Y.; Kim, T.-H. *Tetrahedron Lett.* **1995**, *36*, 6287. (c) Bernocchi, E.; Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1992**, *33*, 3073. (d) Chiusoli, G. P.; Costa, M.; Pergreffi, P.; Reverberi, S.; Salerno, G. Giazz. *Chim. Ital.* **1985**, *115*, 691.

(31) Lambert, C.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 5323.

(32) In two separate experiments, the acylic intermediate **4i** (240 mg, 1 mmol) was heated at 100 °C for 16 h in Et_3N in the presence of $(PPh_3)_2PdCl_2$ (20 mg, 0.035 mmol) or $Pd(PPh_3)_4$ (40 mg, 0.035 mmol), no cyclized product **3i** was obtained.

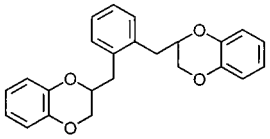
(33) See other CuI-catalyzed heteroannulation: Ezquerra, J.; Pedregal, C.; Lamas, C. *J. Org. Chem.* **1996**, *61*, 5804.

(34) Although a referee suggested that path b is the most probable path for the formation of the products **3**, we, however, do not preclude path a in the stereoselective formation of the products **3**.

(35) To shed some light on the mechanistic rationale in favor of *Z*-stereochemistry, we also performed molecular mechanics calculations (MMX) on two representative molecules (**3a, 3p**) which show that *Z*-isomers are slightly more stable than *E*-isomers from energy considerations [**3a**(*Z*): MMX energy $\epsilon_{(Z)\text{-}\mathbf{3a}}$ =24.84 kcal mol^{-1}; **3a**(*E*): $\epsilon_{(E)-\mathbf{3a}}$ = 25.27 kcal mol^{-1} and **3p**(*Z*): $\epsilon_{(Z)-\mathbf{3p}}$ = 32.35 kcal mol^{-1}; $\epsilon_{(E)-\mathbf{3p}}$ = 32.79 kcal mol^{-1}].

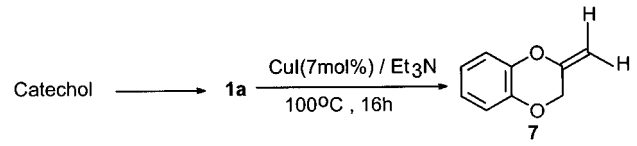
(36) Augstein, J.; Green, S. M.; Monro, A. M.; Potter, G. W. H.; Worthing, C. R.; Wrigley, T. I. *J. Med. Chem.* **1965**, *8*, 446.

Table 3. Hydrogenation of 2-Arylidene-1,4-benzodioxan Derivatives 3a,b,f,i,k,o[a] (Scheme 5)

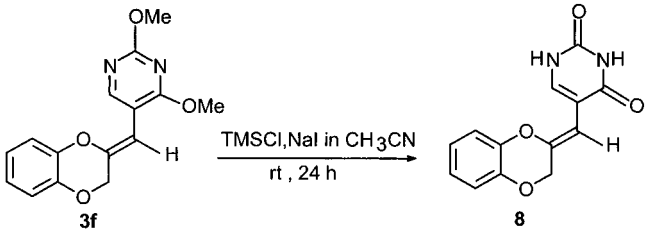
Entry	Starting Materials 3	Products (6) R	Yields[b] (%)
1	3a	C_6H_5 6a	88
2	3b	1-Naphthyl 6b	85
3	3f	2,4-dimethoxypyrimidin-5-yl 6f	89
4	3i	3-ClC_6H_4- 6i	95
5	3k	2-$MeOCOC_6H_4$- 6k	92
6	3o	 6o	93

[a] Hydrogenation was carried out by treatment of compound **3** (0.05 mmol) in dry ethanol (8 mL) with hydrogen at room temperature under atmospheric pressure with Pd/C (10%) as catalyst. [b] Yields refer to chromatographically isolated pure products.

Scheme 6



Scheme 7



as inhibitors of thymidylate synthase (TS), a crucial enzyme required for cellular multiplication processes. They were also active against CCRF-CEM human lymphoblastoid cells, HT-29 colon carcinoma cells, and L1210/0 mouse leukemia cells. In view of these promising results, we have synthesized the novel 5-substituted uracil derivative **8** with a 1,4-benzodioxinyl functional group at the C-5 position of the uracil ring (Scheme 7).

Compound **3f** was synthesized using our synthetic protocol. Demethylation of compound **3f** under neutral condition[37] afforded the uracil derivative **8**. The structure of product **8** was assigned from spectral evidences. Thus we have enlarged the scope of our synthetic protocol by the synthesis of novel uracil derivatives of possible biological significance.[38]

Conclusion

We have described for the first time, a successful palladium-catalyzed procedure for the synthesis of 2,3-dihydro-2-(ylidene)-1,4-benzo- and naphtho[2,3-*b*]dioxins. The most attractive features of the synthesis are that readily available, inexpensive reagents are used under easily attainable experimental conditions. The excellent regio- and stereoselectivity exhibited by this procedure makes it all the more attractive. A variety of functional groups can be accommodated in the structures without affecting the main heteroannulation process. The method is also amenable for the (*Z*)-stereoselective bisheteroannulation process. The possible biological significance of the compounds, which can be synthesized through this procedure, makes it all the more attractive to both organic and medicinal chemists.

Experimental Section

Melting points are uncorrected. Reactions were performed under argon atmosphere. All catalysts and cocatalyst used were commercially available. Solvents and reagents were purified by conventional methods. The petroleum ether used is the fraction boiling at 60−80 °C. Ether refers to diethyl ether. Silica gel TLC was performed on 60F-254 precoated sheets. Aryl iodides (**2b**, **2g**, **2i**, **2j**, **2m**, **2n**, and **20**) were prepared according to the procedure given in ref 22 for the synthesis of iodobenzene (**2a**) and are also commercially avialable. *β*-Bromostyrene,[39] 2-iodothiophene,[40] 2,5-diiodothiophene,[40] 5-iodo-2,4-dimethoxypyrimidine,[41] and methyl-2-iodobenzoate[42] were synthesized according to known procedures. 2-Bromo-5-formylthiophene (**2e**) and 2-iodoanisole (**2h**) were purchased from a commercial source.

^{1}H NMR in $CDCl_3$ solutions were recorded at 100, 200, or 300 MHz and that of CCl_4 solutions at 60 MHz. ^{13}C NMR spectra were recorded at 50 or 75 MHz. $^3J_{CH}$ values were obtained performing ^{13}C NMR experiments under proton-coupled mode.

Mono-prop-2-ynylated Catechol (1a). A mixture of pyrocatechol (20 g, 181.63 mmol) and anhydrous K_2CO_3 (12.54 g, 90.81 mmol) in dry acetone was stirred for 1 h at room temparature. Propargyl bromide (21.6 g, 181.63 mmol) in 15 mL of dry acetone was then added very carefully during 1 h. The whole mixture was then heated under reflux for 16 h with constant stirring. Acetone was removed from the mixture, and the residue was poured in 500 mL of water and extracted with chloroform (3 × 150 mL). The combined organic layer was washed with water and dried over anhydrous Na_2SO_4. After removal of solvent, the residue was purified through sublimation (120 °C, at 0.25 mmHg press). A colorless white solid (23.4 g, 87%) was obtained; mp 46−47 °C; IR 3510 (br), 3300, 1600 cm^{-1}. UV (EtOH) λ_{max}/nm 204.4 (log ϵ 4.10), 276.8 (3.39); ^{1}H NMR (60 MHz, CCl_4) δ 2.49 (t, J = 2 Hz, 1H), 4.59 (d, J = 2 Hz, 2H), 5.89 (br, 1H), 6.59−7.06 (m, 4H). Anal. Calcd for $C_9H_8O_2$: C, 72.95; H, 5.44. Found: C, 72.81; H, 5.86.

2-Hydroxy-3-(prop-2-ynyloxy)naphthalene (1b). A 1.09 g (27.5 mmol) amount of sodium hydride (60% suspension in mineral oil) was placed in a 500 mL round-bottom flask fitted with an anhydrous calcium chloride guard tube. After washing the sodium hydride with dry benzene (3 × 10 mL) and flushing with argon, dry THF (100 mL) was added. To this mixture, 2,3-dihydroxynaphthalene (4.22 g, 26.4 mmol) in dry THF (50 mL) dropwise during 90 min. After stirring for 6 h at room temperature, propargyl bromide (2.4 g, 20 mmol) was added to the mixture, and it was stirred again for another 20 h. The reaction mixture was then poured into ice−water, acidified with dilute HCl, and extracted with ether. The ether layer was washed with brine, dried over anhydrous Na_2SO_4, and

(37) Morita, T.; Okamoto, Y.; Sakurai, H. J. *Chem. Soc., Chem. Commun.* **1978**, 874.
(38) The biological activity of compound **12** is under study and will be reported elsewhere.
(39) A. I. Vogel, *A Text Book of Practical Organic Chemistry*; 4th ed.; ELBS, Longman Group Limited: London, **1978**; p 349.
(40) Barker, J. M.; Huddleston, P. R.; Wood, M. L. *Synth. Commun.* **1975**, *5*, 59.
(41) Das, B.; Kundu, N. G. *Synth. Commun.* **1988**, 855.
(42) Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218.

concentrated. The residue showed two spots on TLC plate, and they were separated by column chromatography over neutral alumina. 2,3-Bis(prop-2-ynyloxy)naphthalene (970 mg, 20%) was collected first with benzene as eluent. 2-Hydroxy-3-(prop-2-ynyloxy)naphthalene (**1b**) (2.08 g, 40%) was eluted later with ethyl acetate/benzene (5/95, v/v); mp 94−96 °C; IR 3515 (br), 3300, 1600 cm^{-1}; UV (EtOH) λ_{max}/nm 210.5 (log ϵ 3.12), 280.4 (4.1); ^1H NMR (60 MHz, CCl_4) δ 2.49 (t, J = 2 Hz, 1H), 4.83 (d, J = 2 Hz, 2H), 5.73 (br, 1H), 7.09−7.76 (m, 6H). Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.76; H, 5.08. Found: C, 78.52; H, 5.21.

Typical Procedure for the Synthesis of (*Z*)-2,3-Dihydro-2-benzylidene-1,4-benzodioxins (3a). A mixture of iodobenzene **2a** (410 mg, 2 mmol), $(PPh_3)_2PdCl_2$ (50 mg, 0.07 mmol), and CuI (26 mg, 0.14 mmol) in triethylamine (8 mL) was stirred under argon atmosphere for 15 min. Then mono-prop-2-ynylated catechol **4** (390 mg, 2.63 mmol) was added very slowly with great care. The resulting solution was further stirred at room temperature for 20 h and then heated at 100 °C for 16 h. After removal of triethylamine, the reaction mixture was poured in 150 mL of water and extracted with ether (3 × 75 mL). The ether extracts were washed with water, dried over anhydrous Na_2SO_4, and concentrated. The residue was chromatographed over neutral alumina eluting with petroleum ether/chloroform (70/30, v/v), affording compound **3a** (200 mg, 44%) as a colorless oil: IR (liquid film) 1680, 1600, 1580 cm^{-1}; UV (EtOH) λ_{max}/nm 339.2 (log ϵ 3.51), 262.2 (4.16); ^1H NMR (200 MHz, $CDCl_3$) δ 4.60 (s, 2H), 5.56 (s, 1H), 6.92−6.99 (m, 2H), 7.10−7.38 (m, 5H), 7.67 (d, J = 8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.94 ($^3J_{CH}$ = 4.83 Hz), 106.91, 116.67, 117.35, 122.16, 122.50, 126.81, 128.28, 128.80, 134.19, 142.42, 143.38, 144.08. Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.33; H, 5.39. Found: C, 80.67; H, 5.41.

Similar reaction conditions were employed for **3b**−**q**. The only difference was that in case of **3f** a temp of 120 °C was used instead of 100 °C. The yields of the products from the reactions are listed in Table 1. The important spectral data of some of the compounds **3** are listed below and others (**3b**, **3c**, **3d**, **3g**, **3h**, **3j**, **3q**) have been incorporated in Supporting Information.

(*Z*)-2,3-Dihydro-2-[(5-formylthienyl)methylidene]-1,4-benzodioxin (3e): mp 107−109 °C; IR 1675, 1650, 1600, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 207.2 (log ϵ 4.4), 278.8 (3.85), 356.6 (4.42); ^1H NMR (200 MHz, $CDCl_3$) δ 4.60 (s, 2H), 5.92 (s, 1H), 6.92−7.01 (m, 3H), 7.11 (d, J = 4 Hz, 1H), 7.18−7.25 (m, 1H), 7.62 (d, J = 4 Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 64.81 ($^3J_{CH}$ = 4.4 Hz), 100.66, 116.89, 117.39, 122.59, 123.34, 127.18, 136.14, 141.88, 142.56, 143.57, 145.51, 146.39, 182.93. Anal. Calcd for $C_{14}H_{10}O_3S$: C, 65.11; H, 3.90. Found: C, 65.04; H, 3.98.

(*Z*)-2,3-Dihydro-2-[(2,4-dimethoxypyrimidin-5-yl)methylidene]-1,4-benzodioxin (3f): mp 100−103 °C; IR 1685, 1600, 1570, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 206.4 (log ϵ 4.27), 270.4 (4.30); ^1H NMR (200 MHz, $CDCl_3$) δ 4.0 (s, 6H), 4.65 (s, 2H), 5.7 (s, 1H), 6.85−7.0 (m, 3H), 7.05−7.20 (m, 1H), 9.05 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 54.07, 54.76, 65.76, 96.12, 116.70, 117.45, 122.37, 122.78, 127.63, 129.21, 142.27, 144.0, 144.13, 157.69; MS *m/e* (rel inten) 286 (M^+, 100), 177 (37), 163 (51), 148 (20), 133 (33). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.92; H, 4.92; N, 9.78. Found: C, 62.52; H, 5.04; N, 9.64.

(*Z*)-2,3-Dihydro-2-[(3-chlorophenyl)methylidene)]-1,4-benzodioxin (3i): mp 65−67 °C; IR 1680, 1590, 1495 cm^{-1}; UV (EtOH) λ_{max}/nm 209.8 (log ϵ 4.47), 280.0 (4.30); ^1H NMR (200 MHz, $CDCl_3$) δ 4.60 (s, 2H), 5.52 (s, 1H), 6.96−6.98 (m, 3H), 7.13−7.32 (m, 3H), 7.51−7.55 (m, 1H), 7.72−7.74 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.85, 105.52, 116.70, 117.39, 122.31, 122.78, 126.76, 126.83, 128.61, 129.44, 134.13, 135.95, 142.20, 144.01, 144.51. Anal. Calcd for $C_{15}H_{11}O_2Cl$: C, 69.65; H, 4.28. Found: C, 69.62; H, 4.36.

(*Z*)-2,3-Dihydro-2-[(2-carbomethoxyphenyl)methylidene]-1,4-benzodioxin (3k): colorless oil; IR (liquid film) 1720, 1675, 1600 cm^{-1}; UV (EtOH) λ_{max}/nm 279.8 (log ϵ 4.04), 235.8 (4.11); ^1H NMR (200 MHz, $CDCl_3$) δ 3.86 (s, 3H), 4.65 (s, 2H), 6.48 (s, 1H), 6.74−7.07 (m, 4H), 7.29 (t, J = 8 Hz, 1H), 7.51 (t, J = 8 Hz, 1H), 7.93 (dd, J = 7.8, 1.4 Hz, 1H), 8.03 (d, J = 8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.78, 65.95 ($^3J_{CH}$ = 4.95 Hz), 104.46, 116.55, 117.24, 122.06, 122.47, 126.41, 128.72, 130.26, 130.69, 131.46, 134.50, 142.23, 143.84, 144.06, 167.77. Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.32; H, 4.99. Found: C, 72.24; H, 5.11.

2,5-Bis[(*Z*)-2′,3′-dihydro-2′-methylidene-1′,4′-benzodioxinyl]thiophene (3l): mp 146−148 °C; IR 1680, 1600, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 361.4 (log ϵ 4.37), 344.2 (4.46), 288.2 (3.85), 205.4 (4.44); ^1H NMR (300 MHz, $CDCl_3$) δ 4.63 (s, 4H), 5.91 (s, 2H), 6.95−7.03 (m, 6H), 7.04 (s, 2H), 7.23 (t, J = 6 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 65.21 ($^3J_{CH}$ = 4.36 Hz), 101.97, 116.72, 117.50, 122.28, 122.68, 126.45, 136.97, 141.38, 142.54, 143.90; MS *m/e* (rel inten) 376 (M^+, 100), 268 (21), 256 (21), 160 (30), 148 (21), 115 (16). Anal. Calcd for $C_{22}H_{16}O_4S$: C, 70.19; H, 4.28. Found: C, 70.42; H, 4.50.

1,4-Bis[(*Z*)-2′,3′-dihydro-2′-methylidene-1′,4′-benzodioxinyl]benzene (3m): mp 210−212 °C; IR 1680, 1600, 1495 cm^{-1}; UV ($CHCl_3$) λ_{max}/nm 241.8 (log ϵ 4.08), 321.4 (4.64), 336 (4.54); ^1H NMR (300 MHz, $CDCl_3$) δ 4.63 (s, 4H), 5.60 (s, 2H), 6.95−7.01 (m, 6H), 7.17−7.20 (m, 2H), 7.71 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 66.06 ($^3J_{CH}$ = 4.48 Hz), 106.80, 116.72, 117.38, 122.20, 122.53, 128.81, 132.82, 142.46, 143.47, 144.09; MS *m/e* (rel intensity) 370 (M^+, 100), 261 (25), 152 (88), 147 (20), 141 (24), 115 (48). Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.89. Found: C, 77.94; H, 4.97.

4,4′-Bis[(*Z*)-2′,3′-dihydro-2′-methylidene-1′,4′-benzodioxinyl]biphenyl (3n): mp 204−206 °C, IR 1680, 1600, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 270.4 (log ϵ 4.02), 314.4 (4.33); ^1H NMR (300 MHz, $CDCl_3$) δ 4.64 (s, 4H), 5.63 (s, 2H), 6.95−7.01 (m, 6H), 7.15−7.19 (m, 2H), 7.63 (d, J = 8 Hz, 4H), 7.75 (d, J = 8 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 66.10 ($^3J_{CH}$ = 4.34 Hz), 106.62, 116.76, 117.44, 122.28, 122.61, 126.77, 129.28, 133.33, 139.01, 142.49, 143.65, 144.13; MS *m/e* (rel inten) 446 (M^+, 46), 328 (10), 230 (15), 216 (100), 160 (62), 154 (30). Anal. Calcd for $C_{30}H_{22}O_4$: C, 80.71; H, 4.96. Found: C, 80.62; H, 4.78.

1,2-Bis[(*Z*)-2′,3′-dihydro-2′-methylidene-1′,4′-benzodioxinyl]benzene (3o): mp 116−118 °C; IR 1680, 1600, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 209 (log ϵ 4.66), 289.4 (4.46); ^1H NMR (200 MHz, $CDCl_3$) δ 4.58 (s, 4H), 5.72 (s, 2H), 6.86−6.93 (m, 6H), 6.97−7.04 (m, 2H), 7.18−7.28 (m, 2H), 7.81−7.86 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 65.93 ($^3J_{CH}$ = 4.81 Hz), 104.78, 116.80, 117.28, 122.22, 122.44, 126.85, 129.68, 131.96, 142.40, 143.55, 144.04; MS *m/e* (rel inten) 370 (M^+, 7), 261 (100), 153 (30), 141 (10), 128 (31). Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.89. Found: C, 77.60; H, 4.94.

(*Z*)-2,3-Dihydro-2-benzylidene-1,4-naphtho[2,3-*b*]dioxin (3p): mp 131−133 °C; IR 1680, 1600, 1510 cm^{-1}; UV (EtOH) λ_{max}/nm 331.4 (log ϵ 3.72), 274.8 (4.58), 224.2 (4.66); ^1H NMR (300 MHz, $CDCl_3$) δ 4.71 (s, 2H), 5.66 (s, 1H), 7.25−7.43 (m, 6H), 7.57 (s, 1H), 7.70−7.77 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 66.26, 107.03, 112.42, 112.99, 124.67, 124.81, 126.62, 126.69, 126.94, 128.37, 128.85, 129.78, 129.86, 134.07, 142.41, 143.50, 144.20. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.18; H, 5.14. Found: C, 83.41; H, 5.19.

Synthesis of Mono-3-(3-chlorophenyl)prop-2-ynylated Catechol (4i) and (*Z*)-2,3-Dihydro-2-[(3-chlorophenyl)-methylidene]1,4-benzodioxin (3i) under Condition i. To a magnetically stirred solution of 3-chlorophenyl iodide **2i** (715 mg, 3 mmol) in triethylamine was added a mixture of $(PPh_3)_2$-$PdCl_2$ (73 mg, 0.10 mmol) and CuI (40 mg, 0.21 mmol) under oxygen free argon atmosphere, and the resulting solution was further stirred for another 30 min. Mono-prop-2-ynylated catechol **1a** (580 mg, 3.91 mmol) was added carefully, and the whole mixture was further stirred at room temperature for another 48 h. After usual workup, the crude product obtained was purified by column chromatography over neutral alumina. The cyclized product **3i** (95 mg, 12%) was obtained in earlier fractions by elution with $CHCl_3$/petroleum ether (30/70, v/v). On the other hand, the acyclic product **4i** (450 mg, 57%) was isolated with $CHCl_3$ as eluent. The spectral data for compound **3i** has been reported earlier. Compound **4i**: colorless oil; IR (liquid film) 2240, 3450 (br), 1600 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 4.93 (s, 2H), 7.04−7.49 (m, 9H, OH, and aromatic).

Anal. Calcd for $C_{15}H_{11}O_2Cl$: C, 69.63; H, 4.28. Found: C, 69.78; H, 4.16.

Synthesis of Mono-3-(3-chlorophenyl)prop-2-ynylated Catechol (4i) and (*Z*)-2,3-Dihydro-2-[(3-chlorophenyl)-methylidene]-1,4-benzodioxin (3i) under Condition ii. To a magnetically stirred solution of 3-chlorophenyl iodide **2i** (715 mg, 3 mmol) in trimethylamine (8 mL) was added a mixture of $(PPh_3)_2PdCl_2$ (73 mg, 0.10 mmol) and CuI (40 mg, 0.21 mmol) under oxygen free argon atmosphere, and the whole mixture was stirred for 30 min at room temperature. Then mono-prop-2-ynylated catechol **1a** (580 mg, 3.91 mmol) was added carefully, and the stirring was continued for another 20 h. It was then heated at 65 °C for 16 h. After removal of triethylamine, workup and chromatography over neutral alumina as usual, the mixture of products **3i** and **4i** were separated as described in the previous experiment. Yields of compounds **3i** and **4i** were 120 mg (16%) and 370 mg (47%), respectively. The spectral data of compound **3i** and **4i** were given earlier.

Typical Procedure for the Synthesis of 2,3-Dihydro-2-benzyl-1,4-benzodioxin (6a) via Hydrogenation Procedure. Compound **3a** (110 mg, 0.5 mmol) was hydrogenated in the presence of 10% Pd/C catalyst (20 mg) in dry ethanol (8 mL) under atmospheric pressure. After 16 h, the catalyst was removed by filtration and washed with ethanol (5 mL). The combined filtrate was evaporated to dryness to give a gummy material which was purified by column chromatography over neutral alumina with chloroform as eluent. This afforded **6a** as a colorless oil (100 mg, 88%): IR (liquid film) 1600, 1490, 1450 cm^{-1}; UV (EtOH) λ_{max}/nm 279.2 (log ϵ 3.46), 308.2 (4.31); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.89 (dd, J_{AB} = 13.8 Hz, J_{AX} = 7.4 Hz, $1H_A$), 3.12 (dd, J_{AB} = 13.8 Hz, J_{BX} = 6.2 Hz, $1H_B$), 3.89 (dd, $J_{A'B'}$ = 11.2 Hz, $J_{A'X}$ = 6.9 Hz, $1H_{A'}$), 4.16 (dd, $J_{A'B'}$ = 11.2 Hz, $J_{B'X}$ = 2.2 Hz, $1H_{B'}$), 4.29−4.40 (m, 1H), 6.76−6.88 (m, 4H, aromatic), 7.18−7.36 (m, 5H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.47, 66.89, 73.60, 116.97, 117.32, 121.18, 121.48, 126.76, 128.54, 129.29, 136.38, 143.20. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.23. Found: C, 79.30; H, 6.29.

Similarly, compounds **6b**,**f**,**i**,**k**,**o**) were synthesized through hydrogenation of the corresponding unsaturated analogues **3b**,**f**,**i**,**k**,**o**. Yields have been reported under Table 3. The important spectral data of some of the compounds (**6i**,**k**) are listed below and others (**6b**,**f**,**o**) have been incorporated in Supporting Information.

2,3-Dihydro-2-[(3-chlorophenyl)methyl]-1,4-benzodioxin (6i): colorless oil; IR (liquid film) 1600, 1490 cm^{-1}; UV (EtOH) λ_{max}/nm 207.4 (log ϵ 4.41), 279.4 (3.52); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.89 (dd, J_{AB} = 13.8 Hz, J_{AX} = 7.5 Hz, $1H_A$), 3.12 (dd, J_{AB} = 13.8 Hz, J_{BX} = 6.3 Hz, $1H_B$), 3.90 (dd, $J_{A'B'}$ = 11.4 Hz, $J_{A'X}$ = 7.2 Hz, $1H_{A'}$), 4.17 (dd, $J_{A'B'}$ = 11.4 Hz, $J_{B'X}$ = 2 Hz, $1H_{B'}$), 4.34−4.41 (m, 1H), 6.79−6.91 (m, 3H, aromatic), 7.22−7.38 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.69, 66.90, 73.70, 96.25, 117.11, 117.45, 121.29, 121.57, 126.90, 128.68, 129.41, 136.49, 143.23, 143.33. Anal. Calcd for $C_{15}H_{13}O_2Cl$: C, 69.10; H, 5.02. Found: C, 69.18; H, 5.11.

2,3-Dihydro-2-[(2-carbomethoxyphenyl)methyl]-1,4-benzodioxin (6k): mp 72−74 °C; IR 1715, 1600, 1490 cm^{-1}; UV (EtOH) λ_{max}/nm 207.8 (log ϵ 4.43), 224.4 (4.18), 279.8 (3.69); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.26 (dd, J_{AB} = 13.3 Hz, J_{AX} = 7.5 Hz, $1H_A$), 3.41 (dd, J_{AB} = 13.3 Hz, J_{BX} = 5.2 Hz, $1H_B$), 3.89 (s, 3H), 3.98 (dd, $J_{A'B'}$ = 11.2 Hz, $J_{A'X}$ = 6.5 Hz, $1H_{A'}$), 4.24 (dd, $J_{A'B'}$ = 11.2 Hz, $J_{B'X}$ = 2 Hz, $1H_{B'}$), 4.43−4.46 (m, 1H), 6.75−6.87 (m, 4H, aromatic), 7.32 (t, J = 6.9 Hz, 2H, aromatic), 7.45 (t, J = 8 Hz, 1H, aromatic), 7.96 (d, J = 8 Hz, 1H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.95, 51.94, 67.23, 73.51, 96.24, 116.65, 117.49, 121.46, 122.01, 126.89, 129.62, 130.92, 131.93, 132.64, 139.15, 143.15, 167.43. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.81; H, 5.67. Found: C, 71.61; H, 5.84.

2,3-Dihydro-2-methylene-1,4-benzodioxin (7). To a well stirred solution of mono-prop-2-ynylated catechol **1a** (444 mg, 3 mmol) in Et_3N was added CuI (40 mg, 0.21 mmol), and the whole mixture was allowed to stir at room temperature for 30 min. Then it was heated at 100 °C for 16 h. After removal of solvent, it was diluted with water and extracted with Et_2O. The ether extracts were washed with water, dried (anhydrous Na_2SO_4), and concentrated. The residue was chromatographed over neutral alumina, eluting with chloroform in petroleum ether (10/90, v/v) to afford 330 mg (74%) of **7** as colorless oil:[11d] IR 1670, 1600, 1500 cm^{-1}; UV (EtOH) λ_{max}/nm 212 (log ϵ 4.29), 234.8 (3.0), 278 (3.32); ^{1}H NMR (60 MHz, CCl_4) δ 4.4 (s, 2H), 4.26 (d, J_{AB} = 2 Hz, $1H_A$), 4.66 (d, J_{AB} = 2 Hz, $1H_B$), 6.86−7.03 (m, 4H).

***(Z)*-2,3-Dihydro-2-[(2′,4′-dioxo-1′,2′,3′,4′-tetrahydropyrimidin-5-yl)methylidene]-1,4-benzodioxin (8).** To a magnetically stirred solution of compound **3f** (143 mg, 0.5 mmol) in dry acetonitrile (8 mL) under argon atmosphere were added anhydrous sodium iodide (250 mg, 1.67 mmol) and chlorotrimethylsilane (0.2 mL, 1.58 mmol). The resulting mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure, and the residue was treated with a few drops of sodium metabisulfite solution and then water, filtered and dried to yield compound **8** as pale yellow solid (93 mg, 72%): mp >275 °C; IR 1710, 1680, 1600 cm^{-1}; UV (EtOH) λ_{max}/nm 205.2 (log ϵ 4.11), 253 (4.32), 312.2 (3.21); ^{1}H NMR (100 MHz, DMSO d_6) δ 4.64 (s, 2H), 5.68 (s, 1H), 6.96−7.2 (m, 4H), 8.0 (s, 1H), 10.48 (br, 1H), 11.36 (br, 1H). Anal. Calcd for $C_{13}H_{10}O_4N_2$: C, 60.48; H, 3.90; N, 10.85. Found: C, 60.34; H, 4.10; N, 10.98.

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Supporting Information Available: Spectroscopic data for compounds **3b**−**d**,**g**,**h**,**j**,**q**, **6b**,**f**,**o** and experimental details of the X-ray diffraction study for compound **3l** with ORTEP diagram (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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