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Intramolecular cyclization of phenol derivatives with C=C double bond in a side chain

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Abstract

Intramolecular cyclization of phenol derivatives with C=C double bond on a side chain was examined using copper and silver catalyst. For example, 2-allylphenol (**1a**) was converted to 2,3-dihydro-2-methylbenzofuran (**2a**) in 70% yield using $Cu(OTf)_2$ or in 90% yield using $AgClO_4$. This catalysis was applied to cyclization of 2-allylphenol derivatives, 2-(3-butenyl)phenol, benzoic acids with C=C double bond, 2-allyl-*N*-tosylaniline, and 2-(3-butenyloxy)phenol. Furthermore, allyl phenyl ether was converted to **2a** via Claisen rearrangement and cyclization.

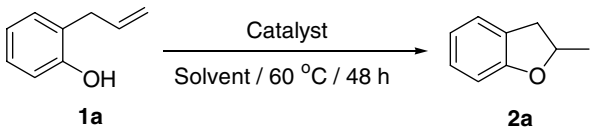
Keywords: Intramolecular addition; Copper; Silver; 2,3-Dihydrobenzofuran; 3,4-Dihydro-2H-1-benzopyrane; 3,4-Dihydro-2H-1,5-benzodioxepin

1. Introduction

As oxygen containing heterocyclic compounds, such as 2,3-dihydrobenzofuran [1], 3,4-dihydro-2*H*-1-benozopyrane [2], 3,4-dihydro-2*H*-1,5-benzodioxepin [3], are found as a moiety of some biologically active materials, syntheses of these compounds under neutral conditions have been focused on [4–6]. We have already found the intramolecular cyclization of 2-allylphenol and related compounds using ruthenium catalysts [7,8]. Although this reaction gave cyclic products in good to excellent yields, ruthenium compounds are relatively expensive, and the TON was not satisfactory. In the course of this research, we found that the copper and silver compounds also catalyze this cyclization efficiently and described the results here [9].

2. Results and discussion

At first, catalytically active metal species were searched for cyclization of 2-allylphenol (**1a**). Among various metal species tested, $Cu(OTf)_2$, $Cu(ClO_4)_2 \cdot 6H_2O$, $CuOTf \cdot C_6H_6$, AgOTf, $AgClO_4$, $AlCl_3$, and $FeCl_3$ showed some catalytic activities under standard conditions (in $CHCl_3$, 60 °C, 48 h). Interestingly, for copper and silver complexes, triflates and perchlorates showed catalytic activity, while tetrafluoroborates did not work as a catalyst. Other metal triflates ($Zn(OTf)_2$, NaOTf, $Bu_4N(OTf)$, $Sn(OTf)_2$, $Yb(OTf)_3$, $La(OTf)_3$) and other metal halides ($CuCl_2$, $CuBr_2$, AgCl, $ZnCl_2$, LiCl, $PbCl_2$, $SnCl_2 \cdot 2H_2O$) showed no catalytic activity (see Table 1).



1a **2a**

2.1. Copper catalyst

Solvent effect was examined using $Cu(OTf)_2$, and representative results are listed in Table 2. Using nonpolar or less polar solvent promoted the reaction well, while polar

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Table 1
Effect of various metal species on intramolecular cyclization of 2-allylphenol[a]

Entry	Catalyst	Yield[b] (%)
1	$Cu(OTf)_2$	70
2	$Cu(ClO_4)_2 \cdot 6H_2O$	51
3	$Cu(BF_4)_2 \cdot 6H_2O$	0
4[c]	$CuOTf \cdot C_6H_6$	42
5	AgOTf	7
6	$AgClO_4$	58
7	$AgBF_4$	0
8	$AlCl_3$	29
9	$FeCl_3$	7

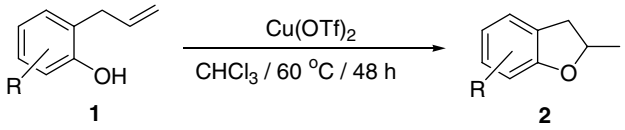
[a] Reaction conditions: **1a** (1.0 mmol), catalyst (10 mol%), $CHCl_3$ (1.5 mL), 60 °C, 48 h, under Ar.
[b] Yield was determined by ^1H NMR using internal standard (dibenzyl ether) method.
[c] 20 mol% of catalyst was used.

Table 2
Effect of solvent on intramolecular cyclization of **1a** with $Cu(OTf)_2$[a]

Entry	Solvent (mL)	Yield[b] (%)
1	$CHCl_3$ (1.5)	70
2[c]	CH_2Cl_2 (1.5)	33
3	*n*-hexane (1.5)	33
4	Benzene (1.5)	55
5	Toluene (1.5)	59
6	Cyclohexane (1.5)	53

[a] Reaction conditions: **1a** (1.0 mmol), $Cu(OTf)_2$ (10 mol%), 60 °C, 48 h, under Ar.
[b] Yield was determined by ^1H NMR using internal standard (dibenzyl ether) method.
[c] At reflux temperature.

solvent (THF, DMSO, CH_3CN, DMF, CH_3OH, and C_2H_5OH) retarded the reaction to give no product at all. Especially, substrate**1a** was converted to **2a** in chloroform in 70% yield.



Effect of substituent on phenyl ring of 2-allylphenol was then examined (Table 3). Substrates **1b** and **1c**, having methyl or methoxy at 6-position, smoothly reacted to give 2,3-dihydrobenzofuran derivatives in 89% and 76% yield, respectively. On the other hand, 2-allyl-4-methoxyphenol (**1d**) was converted to **2d** in 55% yield. In case of substrates **1e** and **1f**, which have chloride or nitro group at 6-position, reactions were sluggish to give products in far low yields. These results suggest that the reaction is mainly controlled by nucleophilic attack by hydroxy group of phenol because the substrates with electron-donating group showed higher reactivity than the substrates with electron-withdrawing group. At the same time, substituents at 6-position were

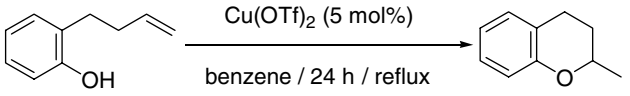
Table 3
Intramolecular cyclization of 2-allylphenol derivatives with $Cu(OTf)_2$[a]

Entry	Substrate		Yield[b] (%)
		R=	
1	**1a**	H	70
2	**1b**	6-CH_3	89
3	**1c**	6-OCH_3	76
4	**1d**	4-OCH_3	55
5	**1e**	6-Cl	19
6	**1f**	6-NO_2	0

[a] Reaction conditions: substrate (1.0 mmol), $CHCl_3$ (1.5 mL), $Cu(OTf)_2$ (5 mol%), 60 °C, 48 h, under Ar.
[b] Determined by ^1H NMR using internal standard (dibenzy ether) method.

favorable than at 4-position. This can be explained that the substituents at 6-position prevent the coordination of hydroxy group to copper atom, and the cyclization smoothly proceeds without coordination of hydroxy group to catalyst (see mechanistic consideration). In case of **1d**, more electron rich hydroxy group coordinates to copper stronger than that in **1a**. Therefore, the yield of **2d** was lower than that of **2a**.

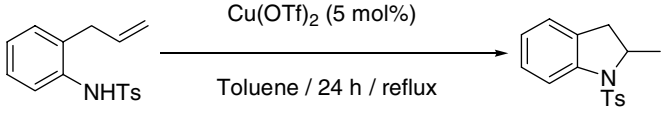
2-(3-Butenyl)phenol (**3**) was converted to 3,4-dihydro-2-methyl-2*H*-1-benzopyran (**4**) in good yield for shorter reaction time by $Cu(OTf)_2$ than by ruthenium catalyst system (72% isolated yield; $RuCl_3 \cdot nH_2O$ (10 mol%), AgOTf (30 mol%), $Cu(OTf)_2$ (50 mol%), 80 °C, 48 h in CH_3CN).



2-Allylaniline derivatives were also tested for this catalysis, and 2-allyl-*N*-tosylaniline (**5**) was found to be a sole reactive substrate among tested. That is, compound **5** was converted to cyclic product **6** in 54% yield by $Cu(OTf)_2$, while 2-allylaniline and 2-allylacetanilide did not react in toluene at reflux in the presence of $Cu(OTf)_2$. This applicability of 2-allylaniline derivatives is similar for cyclization by ruthenium catalyst.

2.2. Silver catalyst

Silver perchlorate was used for survey of solvent. Reaction of **1a** proceeded smoothly in dichloromethane and



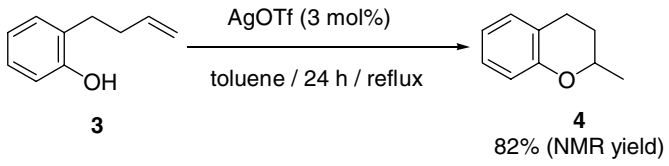
chloroform. Reproducibility was not good in benzene, toluene, hexane, or cyclohexane at lower than 60 °C because of low solubility of silver perchlorate in such solvent. Using ethanol, acetonitrile, DMSO, DMF, and THF retarded the reaction at all.

At higher reaction temperature, yields of **2a** became better, and reaction time could be shortened (entries 10, 11, 115, and 16). Interestingly, loading a lower amount of $AgClO_4$ as a catalyst from 10 mol% to 5 mol% increased the yield of the product **2a** (entries 7, 12, and 17). This observation indicates that the catalyst might decompose the product **2a** (see Table 4).

Next, several silver compounds were investigated as a catalyst for this cyclization. Silver perchlorate and silver trifluoromethanesulfonate catalyzed the reaction efficiently, while silver tetrafluoroborate, silver trifluoroacetate, and silver hexafluorophosphate did not catalyze the reaction. Sunderrajan et al. reported the effect of distance between silver atom and counter anion on the formation of silver–olefin complex. In their report, as the distances between silver and counter anion (0.225 nm in $AgOCOCF_3$ < 0.233 nm in $AgBF_4$ < 0.237 nm in AgOTf) became longer, it was easier to form silver–olefin complexes [10]. Tendency of the formation of silver–olefin complex might be affected for the catalytic activity. Furthermore, coordination ability of counter anion seems to influence the catalytic activity. That is, a silver cation, which has BF_4^- or PF_6^- as a counter anion, is strongly coordinated by oxygen atom and C=C double bond of substrate **1a**, resulted no reaction. In case of ClO_4^- and OTf^-, coordination ability of these counter anions weakens the coordination by phenolic oxygen to promote the reaction efficiently.

This reaction was retarded by adding phosphine (PPh_3, dppe, BINAP) or amine (pyridine). Silver catalyst may promote the reaction using only one or two coordination sites. Therefore, these additives are seemed to block the coordination sites. When using (*R*)-BINOL as an additive, cyclization reaction proceeded smoothly, but no enantiomeric excess of the product was observed (see Table 5).

2-(3-Butenyl)phenol (**3**) was subjected for this reaction to be converted to 3,4-dihydro-2-methyl-2*H*-1-benzopyran (**4**) in good yield by using $AgClO_4$ or AgOTf. Interestingly, loading 3 mol% of AgOTf gave the product **4** in almost similar yield as that (80%) by the reaction using 5 mol% of AgOTf, while using 3 mol% $AgClO_4$ resulted lower yield (74%) of the product **4** than that using 5 mol% catalyst (81%).



3,4-Dihydro-2*H*-1,5-benzodioxepin structure is important framework in Strobilurin I and K that exhibit antifungul activities and cytostatic activities [11]. Therefore, our catalyst system was applied to the reaction of 2-(3-butenyloxy)phenol (**7**). Friedel–Crafts type product **9** was formed selectively by acid (entry 1). Silver triflates showed no catalytic activity, while $Cu(OTf)_2$ gave some extent of the desired product **8** accompanied with **9**. This indicates that the benzene ring in **7** is fairly nucleophilic, compared with the nucleophilicity of oxygen atom in hydroxy group. Addition of phosphine improved the selectivity. Among bidentate phosphines used, diphosphines with larger bite angles increased the selectivity of **8**. Triphenylphosphine was the

Table 4
Intramolecular cyclization of 2-allylphenol (**1a**) with $AgClO_4$[a]

Entry	Solvent (mL)	Temperature (°C)/time (h)	Yield[b] of **2a** (%)
1	CH_2Cl_2 (1.5)	Reflux/24	60
2	CH_2Cl_2 (1.5)	Reflux/48	50
3[c]	CH_2Cl_2 (4.5)	Reflux/48	27 (40)
4	$CHCl_3$ (1.5)	40/48	1 (60)
5	$CHCl_3$ (1.5)	Reflux/24	62
6	$CHCl_3$ (1.5)	Reflux/48	54
7[c]	$CHCl_3$ (4.5)	Reflux/24	81
8	Benzene (1.5)	40/48	2 (23)
10	Benzene (1.5)	60/48	<65
11	Benzene (1.5)	Reflux/24	70
12[c]	Benzene (4.5)	Reflux/24	77
13	Toluene (1.5)	40/48	5 (33)
14	Toluene (1.5)	60/48	<63
15	Toluene (1.5)	80/48	58
16	Toluene (1.5)	Reflux/24	66
17[c]	Toluene (4.5)	Reflux/24	90
18[d]	Toluene (4.5)	Reflux/24	77 (3)

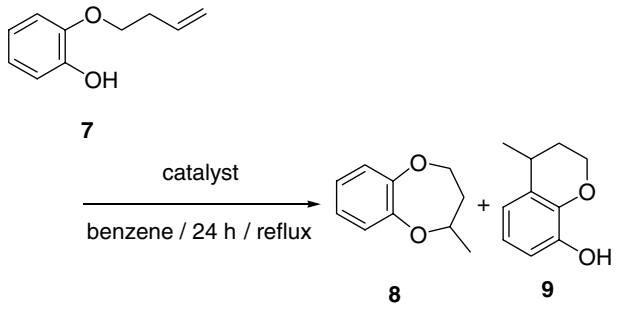
[a] Reaction conditions: **1a** (1.0 mmol), solvent (1.5 mL), $AgClO_4$ (10 mol%), under Ar.
[b] Determined by ^1H NMR analysis using internal standard (dibenzyl ether) method and figures in parenthesis showed yield of recovered starting material.
[c] Reaction conditions: **1a** (3.0 mmol), solvent (4.5 mL), $AgClO_4$ (5 mol%), under Ar.
[d] Reaction conditions: **1a** (3.0 mmol), solvent (4.5 mL), $AgClO_4$ (3 mol%), under Ar.

Table 5
Effect of catalysts on intramolecular cyclization of 2-allylphenol (**1a**)[a]

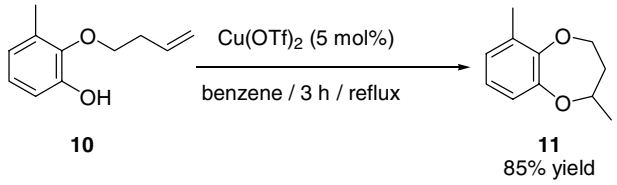
Entry	Catalyst (mol%)	Time (h)	Yield[b] of **2a** (%)
1	$AgBF_4$ (5)	24	0 (86)
2	$AgOCOCF_3$ (5)	24	0 (92)
3	$AgPF_6$ (5)	24	0 (74)
4	AgOTf (5)	24	84
5	AgOTf (3)	24	86
6	AgOTf (2)	24	73 (13)
7	AgOTf (2)	40	83 (1)
8	$AgClO_4$ (5)	24	90
9	$AgClO_4$ (3)	24	77 (3)

[a] Reaction condition; 2-allylphenol (**1a**, 3 mmol), toluene (4.5 mL), reflux, under Ar.
[b] Determined by ^1H NMR analysis using internal standard (dibenzyl ether) method, and figures in parenthesis were yield of recovered starting material.

best among the additives used. The amount of PPh_3 largely influenced the selectivity and reactivity. Using 2.2 equiv. of PPh_3 to copper atom resulted the best selectivity of 1.32 ratio of **8/9**, while adding less amount of PPh_3 decreased the selectivity, and employing 3 equiv. of PPh_3 made the reaction sluggish. Other monodentate phosphines resulted in low reactivity with low selectivity at all (see Table 6).



For obtaining seven-membered ring selectively, substrate **10**, in which ortho position was blocked by methyl substituent, was used for this reaction. Copper(II) triflate catalyzed the cyclization of **10** efficiently to give the desired product **11** in 85% yield even in 3 h.



2.3. Mechanistic consideration

Plausible reaction mechanism is postulated in Scheme 1. At first, carbon–carbon double bond is activated by coordination to Lewis acidic copper (II) center. Then oxygen or nitrogen atom attacks to carbon–carbon double bond coordinated to copper intramolecularly to give alkylcopper intermediate **B** and trifluoromethanesulfonic acid (TfOH). This alkylcopper intermediate **B** is hydrolyzed by TfOH to afford product and $Cu(OTf)_2$. As electron withdrawing groups (Cl, NO_2) decreased the yields of the products, nucleophilic attack by oxygen atom is included in the mechanism. Coordination of hydroxy group to copper atom prevents the reaction in some extent, because 6-position substituents increased the yield of the products. Therefore, intermediate **A** is written as a copper–olefin complex without coordination by oxygen of substrate. But the weak coordination by oxygen atom of substrate to copper as a bidentate fashion is still possible.

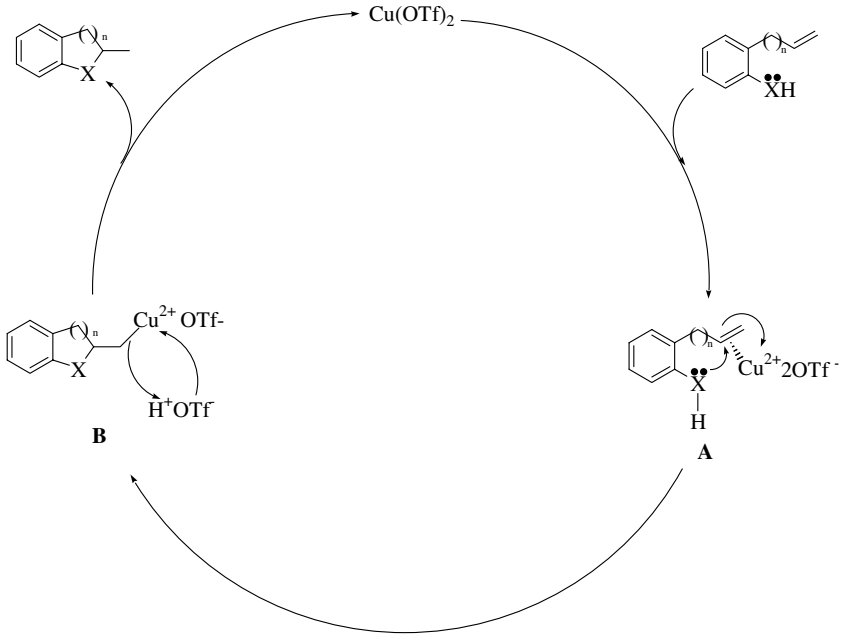
2.4. Claisen rearrangement and intramolecular cyclization of allyl phenyl ether

Allyl phenyl ether (**11**) has been known to be converted to 2,3-dihydro-2-methylbenzofuran (**2a**) in moderate to good yields using heterogeneous catalyst, [12] In(III), [13] or $Mo(CO)_6$ [14]. We also tested the reaction of **11** using our catalysts and found that **11** was converted to **2a** in moderate yield using $Cu(OTf)_2$ or silver catalysts. GC-mass analysis of the reaction mixture using $Cu(OTf)_2$ in chloroform revealed that it was a mixture of substrate **12**, product **2a**, and 2-allylphenol (**1a**).

Table 6
Cyclization of **7**[a]

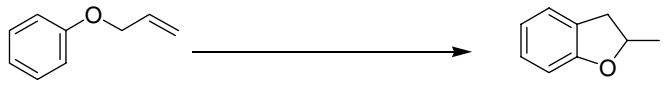
Entry	Catalyst (mol%)	Additive (mol%)	Recovery[b] of **7** (%)	Yield[b] of **8** (%)	Yield[b] of **9** (%)	Ratio of **8/9**
1	TfOH (10)		0	0	68	0
2	AgOTf (5)		100	0	0	
3	$Cu(OTf)_2$ (5)		0	25	67	0.37
4[c]	$Cu(OTf)_2$ (10)	Dppm (10)	0	22	67	0.33
5[c,d]	$Cu(OTf)_2$ (10)	Dppe (10)	0	41	59	0.69
6[c]	$Cu(OTf)_2$ (10)	Dppp (10)	60	17	20	0.85
7[c]	$Cu(OTf)_2$ (10)	PPh_3 (10)	0	24	57	0.42
8[c]	$Cu(OTf)_2$ (10)	PPh_3 (20)	0	46	40	1.15
9[c]	$Cu(OTf)_2$ (10)	PPh_3 (21)	0	48	40	1.20
10[c]	$Cu(OTf)_2$ (10)	PPh_3 (22)	0	54	41	1.32
11[c,d]	$Cu(OTf)_2$ (10)	PPh_3 (30)	86	7	0	100
12[c]	$Cu(OTf)_2$ (10)	$P(OPh)_3$ (22)	0	Trace	68	0
13[c]	$Cu(OTf)_2$ (10)	$P(4\text{-}FC_6H_4)_3$ (22)	0	40	54	0.74
14[c]	$Cu(OTf)_2$ (10)	PPh_2Cy (22)	20	40	40	1.00
15[c]	$Cu(OTf)_2$ (10)	$P(4\text{-}MeC_6H_4)_3$ (22)	70	16	13	1.23
16[c]	$Cu(OTf)_2$ (10)	$P(2\text{-}MeC_6H_4)_3$ (22)	35	36	28	1.29
17[c]	$Cu(OTf)_2$ (10)	$P(4\text{-}MeOC_6H_4)_3$ (12)	0	26	59	0.44
18[c]	$Cu(OTf)_2$ (10)	$P(4\text{-}MeOC_6H_4)_3$ (20)	76	12	10	1.20
19[c]	$Cu(OTf)_2$ (10)	$P(4\text{-}MeOC_6H_4)_3$ (22)	100	0	0	

[a] Reaction conditions: **7** (1.0 mmol), catalyst, additive, benzene (2.0 mL), reflux, 24 h.
[b] Determined by 1H NMR using internal standard (dibenzyl ether) method.
[c] In toluene for 48 h.
[d] In toluene for 72 h.



Scheme 1. Possible mechanism for the intramolecular cyclization reaction with $Cu(OTf)_2$.

Therefore, the reaction proceeded through **1a** by Claisen rearrangement.



$Cu(OTf)_2$ (5 mol%) in $CHCl_3$, at reflux, 48 h	14%
$Cu(OTf)_2$ (5 mol%) in benzene, at reflux, 48 h	50%
AgOTf (5 mol%) in $CHCl_3$, at reflux, 48 h	54%
$AgClO_4$ (5 mol%) in $CHCl_3$, at reflux, 24 h	64%

3. Experimental

3.1. General

Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured using a JEOL JNM A-400 (400 MHz) spectrometer using tetramethylsilane as the internal standard. IR spectra were measured on a Shimadzu IR-408 spectrometer. Mass spectral (GC–MS) data were recorded on a Shimadzu QP2000A instrument. Melting points were measured on a Yanako Model MP and were not corrected. Substrates purchased were used without further purification. Solvents were purified according to the literature method, and stored under argon.

2-Allyl-4-methoxyphenol (**1d**), [15] 2-allyl-6-chlorophenol (**1e**), [16] 2-allyl-6-nitrophenol (**1f**), [17] 2-(3-butenyl)-phenol (**3**), [18] 2-allylaniline, [19] *N*-(2-allylphenyl)acetamide, [20] 2-allyl-*N*-tosylaniline (**5**), [21] 2-(3-butenyloxy)phenol (**7**), [22] and 2-(3-butenyloxy)-3-methylphenol (**10**) [23] were prepared according to the literature method.

3.2. Intramolecular cyclization

Typical procedure: to two-necked flask were added a solution of substrates (1.0 mmol) in solvent (1.5 mL) and $Cu(OTf)_2$ (0.05 mmol), and the resulting mixture was stirring under reflux for 24 h under argon atmosphere. After the reaction, solvent was removed in vacuum, and distilled water and dibenzyl ether were added to the residue. Organic materials were extracted with chloroform. Analysis of the crude mixture containing internal standard was analyzed by ^{1}H NMR to determine the yield of the product.

3.3. 2,3-Dihydro-2-methylbenzofuran (*2a*)

^{1}H NMR($CDCl_3$) δ 1.46 (3H, d, $J = 6.4$, CH_3), 2.81 (1H, dd, $J = 14.4$, 7.2, CH_2), 3.30 (1H, dd, $J = 14.4$, 7.2, CH_2), 4.88–4.94 (1H, m, CH), 6.75 (1H, d, $J = 7.6$, Ar), 6.82 (1H, t, $J = 7.6$, Ar), 7.10 (1H, t, $J = 7.6$, Ar), 7.15 (1H, d, $J = 7.6$, Ar). GC–MS (*m*/*z*) 134.

3.4. 2,3-Dihydro-2,7-dimethylbenzofuran (*2b*)

^{1}H NMR($CDCl_3$) δ 1.47 (3H, d, $J = 6.4$, CH_3), 2.20 (3H, s, CH_3), 2.81 (1H, dd, $J = 15.2$, 7.6, CH_2), 3.30 (1H, dd, $J = 15.2$, 7.6, CH_2), 4.86–4.94 (1H, m, CH), 6.73 (1H, d, $J = 7.6$, Ar), 6.92 (1H, d, $J = 7.6$, Ar), 6.98 (1H, d, $J = 7.6$, Ar). GC–MS (*m*/*z*) 148.

3.5. 2,3-Dihydro-7-methoxy-2-methylbenzofuran (*2c*)

^{1}H NMR($CDCl_3$) δ 1.51 (3H d, $J = 6.0$, CH_3), 2.84 (1H, dd, $J = 15.2$, 7.6, CH_2), 3.32 (1H, dd, $J = 15.2$, 7.6, CH_2),

3.87 (3H, s, OCH_3), 4.93–5.02 (1H, m, C*H*), 6.72–6.81 (3H, m, Ar). GC–MS (*m*/*z*) 164.

3.6. 2,3-Dihydro-5-methoxy-2-methylbenzofuran (**2d**)

^{1}H NMR($CDCl_3$) δ 1.43 (3H, d, $J = 6.79$, CH_3), 2.77 (1H, dd, $J = 15.2$, 7.6, CH_2), 3.25 (1H, dd, $J = 15.2$, 7.6, CH_2), 3.73 (3H, s, OCH_3), 4.83–4.91 (1H, m, C*H*), 6.61–6.67 (2H, m, *Ar*), 6.73 (1H, d, $J = 2.4$, *Ar*). GC–MS (*m*/*z*) 164.

3.7. 7-Chloro-2,3-dihydro-2-methylbenzofuran (**2e**)

^{1}H NMR($CDCl_3$) δ 1.51 (3H, d, $J = 6.4$, CH_3), 2.89 (1H, dd, $J = 16.0$, 7.6, CH_2), 3.41 (1H, dd, $J = 16.0$, 8.8, CH_2), 5.07–5.16 (1H, m, C*H*), 6.77 (1H, d, $J = 8.8$, *Ar*), 8.06–8.16 (2H, m, *Ar*). GC–MS (*m*/*z*) 179.

3.8. 3,4-Dihydro-2-methyl-2H-1-benzopyran (**4**)

^{1}H NMR ($CDCl_3$) δ 1.39 (3H, d, $J = 6.0$, CH_3), 1.65–1.48 (1H, m, CH_2CH_2CH), 1.94–2.00 (1H, m, CH_2CH_2CH), 2.70–2.76 (1H, ddd, $J = 16.4$, 3.2, CH_2CH_2CH), 2.81–2.90 (1H, ddd, $J = 16.4$, 6.4, 3.2, CH_2CH_2CH), 4.08–4.18 (1H, m, C*H*), 6.78–6.83 (2H, m, *Ar*), 7.02–7.09 (2H, m, *Ar*). GC–MS (*m*/*z*) 148.

3.9. 2-Methyl-N-tosylindoline (**6**)

^{1}H NMR ($CDCl_3$) δ 1.46 (3H, d, $J = 6.4$, $CHCH_3$), 2.38 (3H, s, $ArCH_3$), 2.46 (1H, dd, $J = 6.4$, 3.2, CH_2), 4.34–4.42 (1H, m, C*H*), 7.03–7.09 (2H, m, *Ar*), 7.187.26 (3H, m, *Ar*), 7.58 (2H, d, $J = 8.4$, *Ar*),7.69 (1H,d, $J = 8.0$, *Ar*). GC–MS (*m*/*z*) 287.

3.10. 3,4-Dihydro-2-methyl-2H-1,5-benzodioxepin (**8**)

^{1}H NMR ($CDCl_3$) δ 1.40 (3H, d, $J = 6.3$, CH_3), 1.95–2.07 (1H, m, CH_2CHHCH), 2.10–2.20 (1H, m, CH_2CHHCH), 4.00–4.07 (1H, m, $OCHHCH_2$), 4.20–4.27 (1H, m, C*H*), 4.33–4.41 (1H, m, $OCHHCH_2$), 6.87–6.97 (4H, m, Ar). GC–MS (*m*/*z*) 164.

3.11. 3,4-Dihydro-4-methyl-2H-1-benzopyran-8-ol (**9**)

^{1}H NMR ($CDCl_3$) δ 1.30 (3H, d, $J = 6.9$, CH_3), 1.67–1.79 (1H, m, CH_2CHHCH), 2.05–2.15 (1H, m, CH_2CHHCH), 4.17–4.31 (2H, m, OCH_2CH_2), 5.51 (1H, s, O*H*), 6.67–6.78 (3H, m, Ar). GC–MS (*m*/*z*) 164.

3.12. 3,4-Dihydro-2,6-dimethyl-2H-1,5-benzodioxepin (**11**)

^{1}H NMR ($CDCl_3$) δ 1.46 (3H, d, $J = 6.3$, CH_3), 2.01–2.23 (2H, m, CH_2CH_2CH), 2.30 (3H, s, CH_3), 4.02–4.10 (1H, m, $OCHHCH_2$), 4.20–4.31 (1H, m, C*H*), 4.40–4.48 (1H, m, $OCHHCH_2$), 6.81–6.91 (3H, m, Ar). GC–MS (*m*/*z*) 178.

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References

[1] (a) A.P. Monte, D. Marona-Lewicka, M.A. Parker, D.B. Wainscott, D.L. Nelson, D.E. Nichols, J. Med. Chem. 39 (1996) 2953;
(b) G. Turan-Zitouni, S. Demirayak, K. Erol, M. Ozdemir, Ann. Pharma. Franc. 54 (1996) 109, Chem. Abstr. 125 (1996) 75341;
(c) D. Fancelli, C. Caccia, M.G. Fornaretto, R. McArthur, D. Severino, F. Vaghi, M. Varasi, Bioorg. Med. Chem. Lett. 6 (1996) 263;
(d) L. Pieters, T. De Bruyne, M. Claeys, A. Vlietinck, M. Calomme, D. Vanden Berghe, J. Natur. Prod. 56 (1993) 899;
(e) N. Hirose, S. Kuriyama, S. Ozaki, S. Toyoshima, Chem. Pharma. Bull. 24 (1976) 2912;
(f) T. Ohgoh, N. Hirose, N. Hashimoto, A. Kitahara, K. Miyao, Jpn. J. Pharma. 21 (1971) 119.

[2] (a) A. Shah, Y. Naliapara, D. Sureja, N. Motohashi, T. Kurihara, M. Kawase, K. Satoh, H. Sakagami, J. Molnar, Anticancer Res. 18 (1998) 61;
(b) A.E. Fenwick, Tetrahedron Lett. 34 (1993) 1815;
(c) D.A. Clark, S.W. Goldstein, R.A. Volkmann, J.F. Eggler, G.F. Holland, B. Hulin, R.W. Stevenson, D.K. Kreutter, E.M. Gibbs, J. Med. Chem. 34 (1991) 319;
(d) R. Mechoulam, N. Lander, M. Srebnik, A. Breuer, M. Segal, J.J. Feigenbaum, T.U.C. Jarbe, P. Consroe, NIDA Res. Monogr. 79 (1987) 15, Chem. Abstr. 108 (1988) 124050;
(e) M. Shiratsuchi, K. Kawamura, T. Akashi, M. Fujii, H. Ishihama, Y. Uchida, Chem. Pharm. Bull. 35 (1987) 632;
(f) A.K.M.N. Gohar, F.F. Abdel-Latif, M.S. El-Ktatny, Ind. J. Chem., Sect. B: Org. Chem. Med. Chem. 25B (1986) 404;
(g) R.C. Schnur, R. Sarges, M.J. Peterson, J. Med. Chem. 25 (1982) 1451.

[3] (a) A. Wissner, D.M. Berger, D.H. Boschelli, M.B. Floyd Jr., L.M. Greenberger, B.C. Gruber, B.D. Johnson, N. Mamuya, R. Nilakantan, M.F. Reich, R. Shen, H.-R. Tsou, E. Upeslacis, Y.F. Wang, B. Wu, F. Ye, N. Zhang, J. Med. Chem. 43 (2000) 3244;
(b) V. Dauksas, P. Gaidelis, E. Udrenaite, L. Labanauskas, G. Gasperaviciene, Chemija (1991) 116, Chem. Abstr. 118 (1993) 234026;
(c) M.R. Stillings, C.B. Chapleo, R.C.M. Butler, J.A. Davis, C.D. England, M. Myers, P.L. Myers, N. Tweddle, A.P. Welbourn, J. Med. Chem. 28 (1985) 1054;
(d) C.S. Rooney, W.C. Randall, K.B. Streeter, C. Ziegler, E.J. Cragoe Jr., H. Schwam, S.R. Michelson, H.W.R. Williams, E. Eichler, J. Med. Chem. 26 (1983) 700.

[4] (a) Acidic conditions see: D. Barton, W.D. Ollis, J.F. Stoddart (Eds.), Comprehensive Organic Chemistry, vol. I, Pergamon, Oxford, 1979;
(b) J. March, Advanced Organic Chemistry, Reactions, Mechanisms, and Structure, fourth ed., Wiley, New York, 1992, Chapter 15;
(c) J. Meinwald, J. Am. Chem. Soc. 77 (1955) 1617;
(d) P.E. Peterson, E.V.P. Tao, J. Org. Chem. 29 (1964) 2322;
(e) A.O. Fitton, R.K. Smalley, Practical Heterocyclic Chemistry, Academic Press, New York, 1968, p. 16;

(f) C.D. Hurd, W.A. Hoffman, J. Org. Chem. 5 (1940) 212;
(g) A.B. Sen, R.P. Rastogi, J. Indian Chem. Soc. 30 (1953) 355;
(h) C.M. Evans, A.J. Kirby, J. Chem. Soc., Perkin Trans. 2 (1984) 1259.
[5] Photocatalytic, see: G. Fráter, H. Schmid, Helv. Chim. Acta 50 (1967) 255.
[6] Intramolecular cyclization of heterofunctionalities to olefins, see: (a) C.-G. Yang, N.W. Reich, Z. Shi, C. He, Org. Lett. 7 (2005) 4553;
(b) J.-S. Ryu, T.J. Marks, F.E. McDonald, J. Org. Chem. 69 (2004) 1038;
(c) S. Geresh, O. Levy, Y. Markovits, A. Shani, Tetrahedron 31 (1975) 2803;
(d) M.F. Grundon, D. Stewart, W.E. Watts, J. Chem. Soc., Chem. Commun. (1973) 573.
[7] K. Hori, H. Kitagawa, A. Miyoshi, T. Ohta, I. Furukawa, Chem. Lett. (1998) 1083.
[8] Our intermolecular addition to olefins, see: (a) Y. Oe, T. Ohta, Y. Ito, Chem. Commun. (2004) 1620;
(b) Y. Oe, T. Ohta, Y. Ito, Synlett (2005) 179.
[9] Recent intramolecular cyclization to olefins, see: H. Qian, X. Han, R.A. Widenhoefer, J. Am. Chem. Soc. 126 (2004) 9536.
[10] S. Sunderrajan, B.D. Freeman, C.K. Hall, Ind. Eng. Chem. Res. 38 (1999) 4051.
[11] V. Hellwig, J. Dasenbrock, D. Klostermeyer, S. Kroib, T. Sindlinger, P. Spiteller, B. Steffan, W. Steglich, Tetrahedron 55 (1999) 10101.
[12] (a) N.T. Mathew, S. Khaire, S. Mayadevi, R. Jha, S. Sivasanker, J. Catal. 229 (2005) 105;
(b) R.A. Sheldon, J.A. Elings, S.K. Lee, H.E.B. Lempers, R.S. Downing, J. Mol. Catal. A 134 (1998) 129.
[13] A.M. Bernard, M.T. Cocco, V. Onnis, P.P. Piras, Synthesis (1997) 41.
[14] V.H. Grant, B. Liu, Tetrahedron Lett. 46 (2005) 1237.
[15] D.E. Nichols, A.J. Hoffman, R.A. Oberlender, R.M. Riggs, J. Med. Chem. 29 (1986) 302.
[16] C.F.H. Allen, J.W. Gates, Org. Synth Coll. vol. III (1995) 418.
[17] M. Moreno-Manas, R. Pleixats, A. Santamaria, Synlett (2001) 1784.
[18] P. Yates, T.S. Macas, Can. J. Chem. 66 (1988) 1.
[19] N. Takamatsu, S. Inoue, Y. Kishi, Tetrahedron Lett. (1971) 4661.
[20] S. Jolidon, H.-J. Hansen, Helv. Chem. Acta 101 (1977) 978.
[21] M. Muehlstadt, K. Hollmann, R. Widera, Zeits. Chem. 28 (1988) 436.
[22] D.J. Miller, M. Bashir-Uddin Surfraz, M. Akhtar, D. Gani, R.K. Allemann, Org. Biomol. Chem. 2 (2004) 671.
[23] Y. Kajihara, Y. Suzuki, N. Yamamoto, K. Sasaki, T. Sakakibara, L.R. Juneja, Chem. A Eur. J. 10 (2004) 971.