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Catalysis with Inorganic Cations. V.[1] Intramolecular Hetero Diels-Alder *versus* Ene Reactions: Effect of Magnesium Perchlorate on Chemoselectivity.[#]

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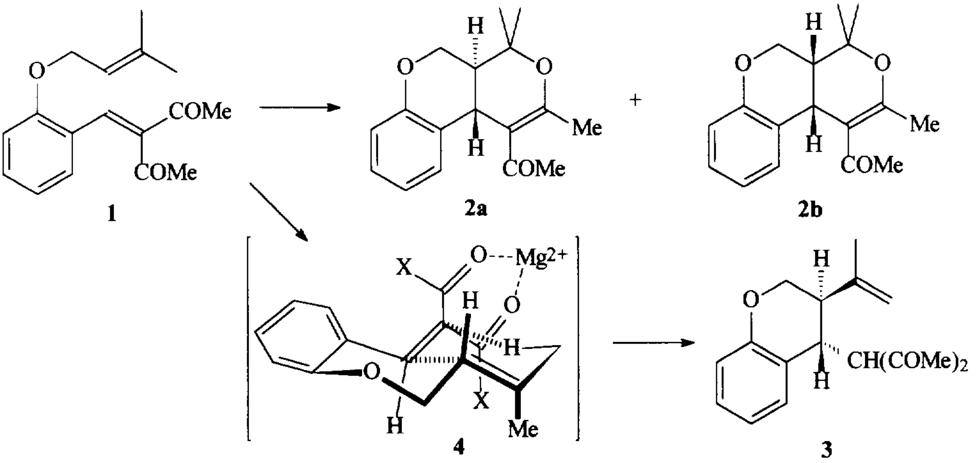
Abstract. The competition between Hetero Diels-Alder (HDA) and intramolecular ene reaction (IER) was tested on (*E*)1-acetyl-3-arylideneindolin-2-one (**5**). Under thermal conditions HDA products **6a,b** are obtained in a quantitative yield stressing the importance of the configuration of the α,β-unsaturated carbonyl system on the reactivity. Both reactivity and chemoselectivity are strongly influenced if the reaction is carried out in the presence of magnesium perchlorate and two IER products **10a,b** are identified by nmr and converted into their thermodynamically stable isomers **11a,b** by silica gel. The importance of two equivalents of ketone, behaving as ligands in the complex between **5** and Mg(II), is emphasized together with its importance in shifting chemoselectivity in favour of the IER. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In the previous paper of this series[2] 3-(3-methyl-2-butenyloxy)benzylidenepentan-2,4-dione (**1**) was made to react under thermal conditions and under catalysis of various inorganic perchlorates (Scheme 1).

Scheme 1



[#] Dedicated to Professor Paolo Grünanger on the occasion of his 70th birthday.

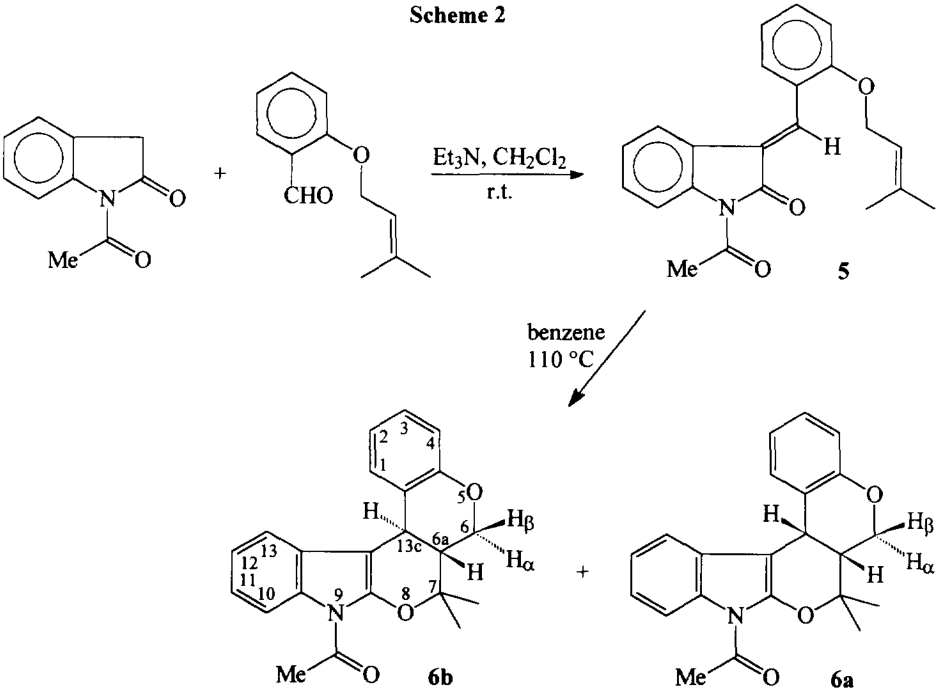
Under thermal conditions and with lithium (LP) and barium perchlorate (BP) at room temperature, the heterodienic cycloaddition preferentially occurred and products **2a,b** were obtained in 70-95% yield. With magnesium perchlorate (MP) the chemoselectivity was strongly influenced, the heterodienic adducts became side-products and the *trans*-ene product **3** was obtained in 93% yield. A rationalization was proposed in terms of specific magnesium cation 1,3-dicarbonyl coordination (**4**) that does not allow the *s-cis* conformation of the α,β-unsaturated carbonyl fragment required for the Hetero Diels-Alder (HDA) cycloaddition.

This result assumes the chemoselectivity observed with MP as the result of a change in the conformation induced by the specific complexation with the cation. If this conformational change cannot occur is again chemoselectivity affected? To test this a suitable model is required, that can give either HDA or ene intramolecular reaction involving an *s-cis* heterodiene.

RESULTS.

The suitable model molecule, (*E*)1-acetyl-3-[2-(3-methyl-2-butenyloxy)benzylidene]indolin-2-one (**5**) was synthetized by a Knovenagel condensation of 2-(3-methyl-2-butenyloxy)benzaldehyde and 1-acetyl-oxindole[3] (Scheme 2).

Scheme 2

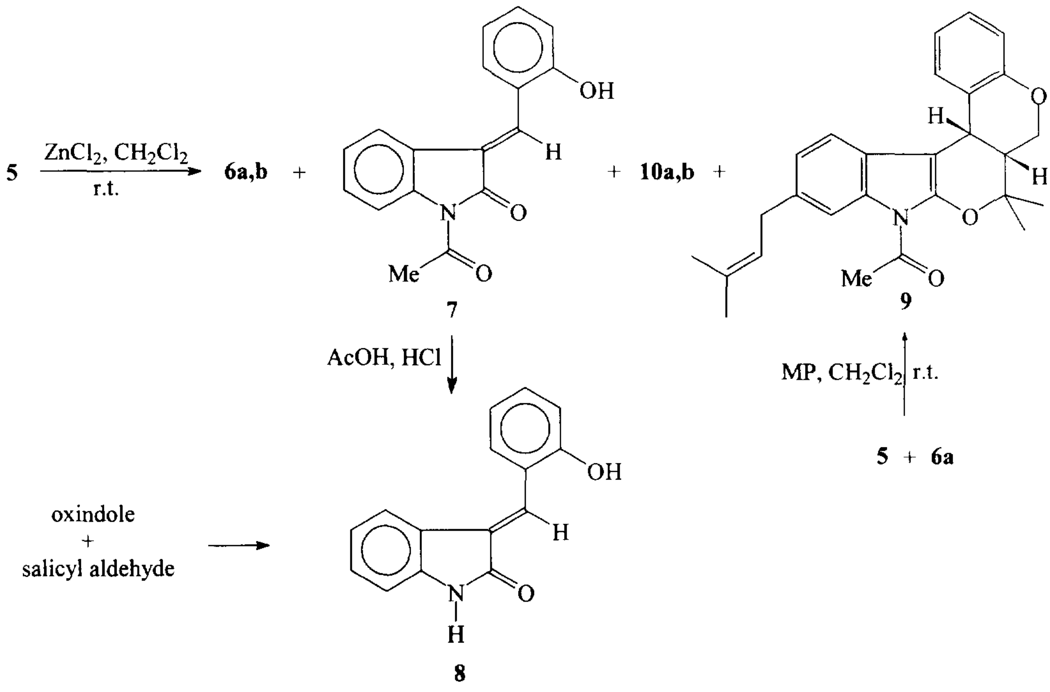


5 is stable at room temperature but, when heated in a sealed tube in benzene at 110 °C, quantitatively gave [6a,13c]-*cis*- and *trans*-9-acetyl-7,7-dimethyl-6,6a,7,13c-tetrahydrochromeno[4',3':4,5]pyrano[2,3-*b*]indoles (**6a,b**) in a ratio 10 : 1. Whereas the main product **6a** was isolated and fully characterized, its stereoisomer **6b** was identified by ^{1}H-Nmr (J_{6a13c} is 5 Hz in **6a** but 11.3 Hz, consistent with a *trans*-diaxial relationship, in **6b**) but never isolated. Hence, under thermal conditions, only the products of the HDA reaction are obtained[4,5] (Table - entry A).

The reaction can be performed in the presence of various Lewis acids. Some of them [*e.g.* Eu(fod)$_3$] had no significant catalytic effect and the reaction does not run at room temperature, while other catalysts (*e.g.* AlCl$_3$) deeply decompose **5**.

In the presence of ZnCl$_2$ (Table - entries B and C) the reaction runs both at room temperature (24 hrs) or at 0 °C (6 days). The main difference between these conditions is the amount of **7**, the deallylated product of **5**, that at room temperature becomes the main reaction product. Its structure was demonstrated by deacetylation to **8**, synthetized from oxindole and salicylaldehyde. The fate of the fragmented unsaturated chain was discovered since a small but significant amounts of [6a,13c]*cis*-9-acetyl-7,7-dimethyl-11(3-methyl-2-butenyl)-6,6a,7,13c-tetra-hydrochromeno[4',3':4,5]pyrano[2,3-*b*]indole (**9**) were isolated. Its origin was unambiguously identified since it was obtained from equimolecular amounts of **5** and **6a** in CH$_2$Cl$_2$ in the presence of MP (Scheme 3).

Scheme 3



In addition to **6a,b** and **7**, the ^{1}H-Nmr detected in the reaction mixture the presence of two further products (**10a,b**), both with an isopropenyl group suggesting these were two stereoisomers deriving from an intramolecular ene reaction (IER) on **5**. The ratio between HDA and IER products did not change at room temperature or at 0 °C, and it was about 3 : 1.

The low selectivity in terms of IER products observed with $ZnCl_2$, suggested to test the reaction of **5** in the presence of LP, BP, MP, and sodium perchlorate (SP). Three of them (LP, BP, and SP) were inefficient and either **7** (in CH_2Cl_2) or traces of **6** (in acetone) were obtained after a long standing at room temperature.

MP was a good catalyst, but the nature of the solvent was very important. In CH_2Cl_2 (Table - entry D), **7** was obtained in nearly quantitative yield within one hour. From the reaction run in a 1M solution of MP in acetone (entry E) a result quite similar to that of $ZnCl_2$ was obtained, except the IER products were not **10a,b** but two further isomers **11a,b**. Thus the effect of acetone on the reaction was deeply investigated.

Acetone and MP in a ratio 2 : 1 were added to anhydrous CH_2Cl_2. After stirring 1 hr, **5** (1 equivalent) was added and the reaction was completed within 8 hrs (Entry F). The ^{1}H-Nmr of the quenched solution detected four products: **6a,b** and **10a,b** in a ratio [59 : 5 :12 : 24]. Both **10a** and **10b** are 1-acetyl-3(3'-isopropenylchroman-4'-yl)oxindoles. The minor isomer (**10a**) has the isopropenyl group with the vinyl protons at 5.05 and 4.61 δ, and the methyl at 2.01 δ; the $H_3H_{4'}H_{3'}$ protons are at 3.85, 4.01 and 2.89 δ and $H_{3'}$ is axial since $J_{2'ax3'}$ is 11 Hz. The protons $H_{3'}$ and $H_{4'}$, involved in the ring closure of the IER, are *cis* since $J_{3'4'}$ is 5 Hz. The major isomer (**10b**) has the isopropenyl group with two vinyl protons overlapped at 5.01 δ and the methyl at 1.84 δ. The $H_3H_{4'}H_{3'}$ system has its protons at 4.07, 3.96 and 2.99 δ and $H_{3'}$ is again axial since $J_{2'ax3'}$ is 10 Hz, but the relationship between $H_{3'}$ and $H_{4'}$ is *trans* since $J_{3'4'}$ is 10 Hz.

When the reaction mixture containg the products in a quantitative yield was submitted to the column chromatography over silica gel, the HDA products **6a,b** were isolated in admixture, and two IER products were separated in the expected 12 and 24% yields, but these were not **10a** and **10b**. The new isomers were **11a** (m.p. 141-2 °C - 12% yield) and **11b** (m.p. 111-2 °C - 24% yield) (Scheme 4).

Scheme 4

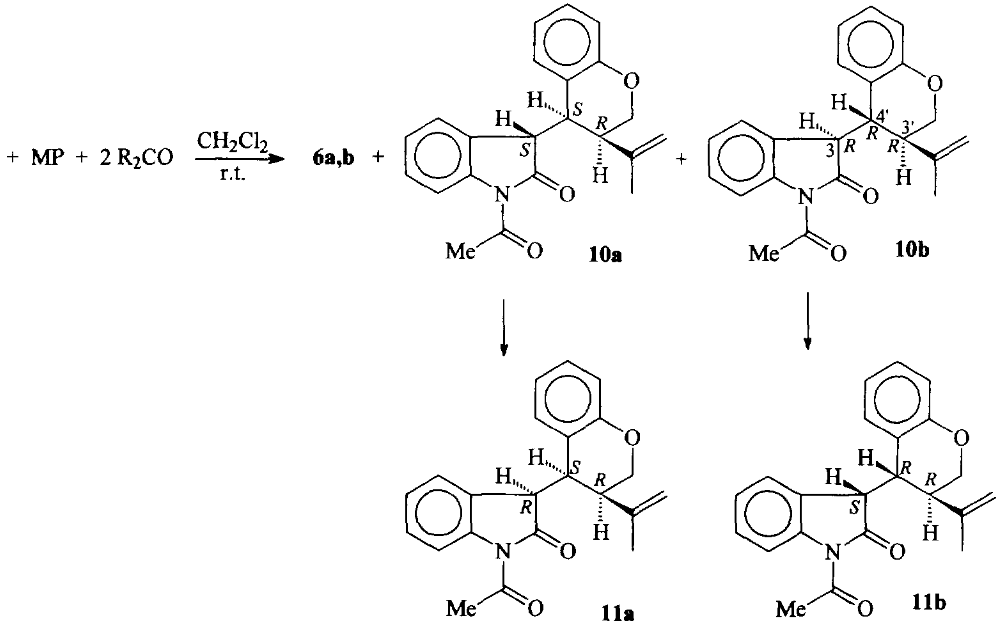


Table. Catalysts, reaction conditions, yields, and product distributions[a] of the intramolecular reaction of **5**

Entry	Lewis acid	Solvent	Ligand (equivalents)	T/°C (time)	Yield %	Heterodienic products		Enic products		By-product	[**6**]/[**10**]
						6a	**6b**	**10a**	**10b**	**7**	
A	---	Benzene	---	110 (48 h)	quant.	90	10	---	---	---	100 : 0
B	$ZnCl_2$	CH_2Cl_2	---	r.t. (24 h)	85	36[b]	7	4	13	40	72 : 28
C	$ZnCl_2$	CH_2Cl_2	---	0 (6 d)	95	61	6	4	17	12	76 : 24
D	MP[c]	CH_2Cl_2	---	r.t. (1 h)	quant.	d	---	---	d	100	---
E	MP[c]	Acetone	---	r.t. (4 d)	85	76	7	6[e]	11[f]	---	83 : 17
F	MP[c]	CH_2Cl_2	Me_2CO (2 eq.)	r.t (8 h)	quant.	59	5	12	24	---	64 : 36
G	MP[c]	CH_2Cl_2	Ph_2CO (2 eq.)	r.t. (8 h)	quant.	45	5	19	31	b	50 : 50
H	MP[c]	CH_2Cl_2	$MeCOCH_2COMe$ (1 eq.)	r.t. (24 h)	quant.	46[b]	4	1	11	30	75 : 25
I	MP[c]	CH_2Cl_2	$MeCOC(Me)_2COMe$ (1 eq.)	r.t. (8 h)	quant.	54	5	13	28	---	59 : 41
J	MP[g]	CH_2Cl_2	---	r.t. (5 h)	95	59	6	14	21	---	65 : 35
K	MP[c]	CH_2Cl_2	(1*R*)-Camphor (2 eq.)	r.t. (8 h)	quant.	52	4	15	29	---	56 : 44

[a] The product distributions reported in the Table are the average of at least three independent experiments; [b] significative amounts of **9** were isolated; [c] one equivalent; [d] trace amounts detected by tlc; [e] largely isomerized into **11a**; [f] largely isomerized into **11b**; [g] 0.5 equivalents.

11a has the isopropenyl group with the vinyl protons at 4.97 and 4.49 δ and the methyl at 1.98 δ. The diagnostic $H_3H_{4'}H_{3'}$ system has its protons at 3.94, 3.85 and 2.80 δ and $H_{3'}$ is axial ($J_{2'ax3'}$ = 10 Hz) and the relationship with $H_{4'}$ is *cis* ($J_{3'4'}$ = 5 Hz). Clearly **11a** derived from the kinetically formed **10a** that isomerized over silica gel retaining the original chromane configuration and inverting H_3.

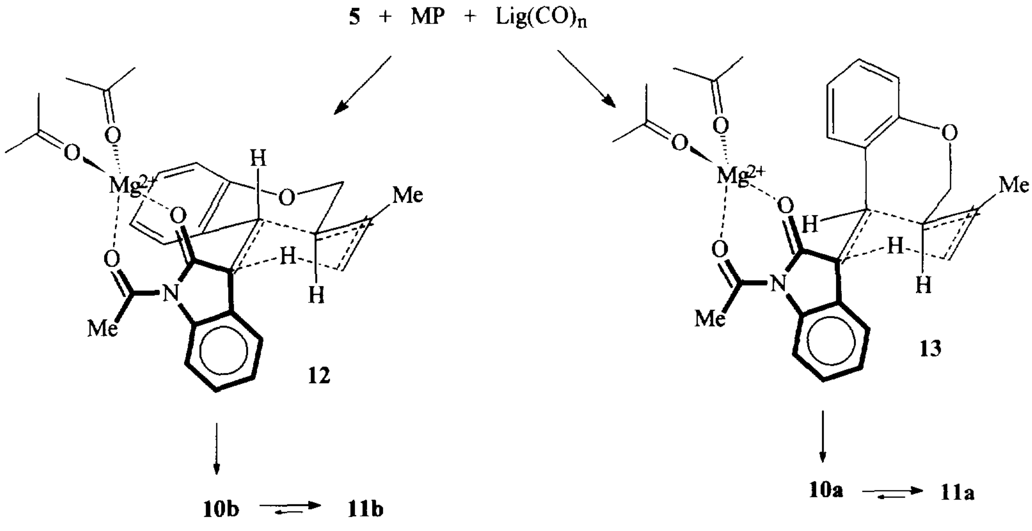
The major thermodynamically stable isomer **11b**, deriving from **10b**, has the isopropenyl group with the methyl at 1.68 δ and two vinyl protons at 4.78 and 4.53 δ. The protons $H_3H_{4'}H_{3'}$ resonate at 4.23, 4.03 and 2.53 δ, $H_{3'}$ is axial ($J_{2'ax3'}$ = 10.2 Hz) and the relationship with $H_{4'}$ is, as expected, *trans*-diaxial ($J_{3'4'}$ = 10 Hz). Again the chromane configuration of **10b** was retained and H_3 inverted over silica gel.

Whereas, as reported above, the configuration of the chromane fragment can be easily determined, the value of $J_{34'}$ and the other spectral data do not allow a convincing attribution of the relative configuration of each isomer. This was unambiguously solved through an X-ray structure determinations of **11b**,[6] shown to be (3*S*,3'*R*,4'*R*)-1-acetyl-3(3'-isopropenylchroman-4'-yl)oxindole.[7] Therefore **10b** was the (3*R*,3'*R*,4'*R*) isomer, as reported in Scheme 4.

A "chair chair-like" transition state (**12**) is required to **5**, coordinated by Mg(II) and acetone, to give the *trans* ring closure to **10b**. It looks obvious that the delivery of the hydrogen at C3 must occur from the same side giving rise to the CC bond and this gives the (3*R*,3'*R*,4'*R*) isomer **10b** that isomerizes to the (3*S*,3'*R*,4'*R*) isomer **11b**. The IER can occur through the t.s. of the coordinated (*E*)-**5** to give the *cis* ring closure. This has the "boat chair-like" configuration **13**, suitable to give **10a**. Again the delivery of the hydrogen atom to C3 must occur on the same side giving the CC bond and the isomer (3*S*,3'*R*,4'*S*) **10a** is the kinetically formed product that isomerized to the stable (3*R*,3'*R*,4'*S*) isomer **11a**. These considerations are depicted in Scheme 5.

To support the relative stability of the above isomers, MM2 calculations were performed. **11a** is more stable than **10a** by 1.0 kcal/mol, and **11b** is more stable than **10b** by 2.0 kcal/mol, thus rationalizing the observed equilibration.

Scheme 5



DISCUSSION AND CONCLUSION

The oxindolidene derivative **5** is a system suitable to test the chemoselectivity induced by cations of inorganic perchlorates.

In the absence of any coordination, **5** gives HDA only; with $ZnCl_2$ the IER begins to become competitive and certainly the steric hindrance of the Lewis acid has a specific role on this.[8]

When the magnesium cation (deriving from MP) is added to the reaction in the presence of an auxiliary ligand (acetone as solvent or two equivalents of acetone in CH_2Cl_2) four carbonyl groups, two from **5** and two from the auxiliary ligand, are coordinated in the most probable tetrahedral form. This becomes the effective substrate undergoing the reaction and, due to the steric overcrowding around the oxindole carbonyl group, IER becomes an important pathway.

To test this model, the effect of ketones on the reactivity of **5** with MP was inferred performing some experiments.

If the steric hindrance of the ketone used as a ligand is increased, an increase of the intramolecular ene reactivity could be expected. The reaction was performed with 2 equivalents of benzophenone (Table - Entry G) and again four products were obtained in a quantitative yield. The ratio **[6a,b]** : **[10a,b]**, hence the ratio [HDA] : [IER], was found to be 50 : 50 (with acetone - Entry G - this was 64 : 36).

If two equivalents of ketone are required, a good alternative to these could be the use of *one equivalent* of acetyl acetone. This experiment (Table - Entry H) underestimates the intrinsic acidity of the ligand. Thus the ratio [HDA] : [IER] was 75 : 25, but a 30% yield of **7** was also obtained.

To avoid this, 3,3-dimethyl-2,4-pentandione (1 equivalent - Entry I) was tested and, nicely, the ratio [HDA] : [IER] was 59 : 41, the four product products being obtained in a quantitative yield without any formation of **7**.

In conclusion, two carbonyl groups, added as further ligands to Mg(II) coordinated to **5**, give the intermediates of the reaction represented in Scheme 5. These auxiliary ligands could be provided by a further equivalent of **5** if the ratio **[5]** : [MP] is 2 : 1. This experiment (entry J) was run and within 5 hours all **5** converted into **6a,b** and **10a,b** in a ratio 65 : 35, and **7** was not obtained under these conditions.

All these experiments emphasize the importance of carbonyl compounds, behaving as ligands around Mg(II), in changing the chemoselectivity of the reaction, and suggest that, being IER so influenced by the auxiliary ligands coordinated to magnesium ion, an enantiotopically-oriented ligand belt could induce enantioselectivity in the ring closure of **5**. The reaction of **5**, MP, and two equivalents of (1*R*)-camphor (Table - Entry K) was tested and a satisfactory result in terms of chemoselectivity was obtained, since the ratio [HDA]:[IER] was 56 : 44. The result in terms of enantioselectivity was fully disappointing and both **6** and **11** were isolated almost optically inactive, but the development of these concepts are the topic of the forthcoming paper.

EXPERIMENTAL SECTION

Melting points were determined by the capillary method and are uncorrected. Elemental analyses were made on C. Erba CHN analyzer mod. 1106. ^{1}H-Nmr ($CDCl_3$, TMS as standard) were recorded on a Bruker

AC 300 spectrometer, ir spectra (nujol mulls) on a Perkin Elmer 881 spectrophotometer. Column chromatography: silica gel 230-400 mesh.

(E)-1-Acetyl-3-[2-(3-methyl-2-butenyloxy)benzylidene]-2-oxindole (5). A solution of 1-acetyloxindole (3.5 g - 20 mmol) and 2-(3-methyl-2-butenyloxy)benzaldehyde (3.8 g - 20 mmol) in dichloromethane (30 ml) and triethylamine (1.5 ml) was stirred at room temperature for 3 days. The solvent was evaporated and the yellow residue was crystallized from cyclohexane. **5** was obtained (3.3 g) as yellow needles and a further crop of analytically pure product was obtained by column chromatography of the mother liquors, cyclohexane-ethyl acetate 93:7 as eluant (total 4.8 g - 69%), m.p. 123-4 °C. Ir: ν_{CO} 1747 and 1697 cm^{-1}. ^{1}H-Nmr, δ: 8.32 (1H, d, H_7), 8.05 (1H, s, arylidenic proton), 7.7-7.9 (7H, aromatic protons), 5.43 (1H, m, vinylic proton), 4.59 (2H, d, -OCH$_2$-), 2.77 (3H, s, acetyl), 1.76 and 1.725 (3H + 3H, s + s, isopropylidene protons). Elem. anal.; calc. for $C_{22}H_{21}NO_3$: C, 76.1; H, 6.1; N, 4.0. Found: C, 76.3; H, 6.1; N, 4.1%.

Thermal intramolecular HDA reaction of 5 (Entry A). A solution of **5** (0.20 g - 0.58 mmol) in benzene (5 ml) was heated 48 hours at 110 °C in a sealed vial. The clear solution was evaporated and the residue was monitored by ^{1}H-Nmr and shown to contain **6a** and **6b** in a ratio 91 : 9.

6b; ^{1}H-Nmr, δ: 8.46 (1H, dd, H_{10}), 6.83-7.77 (7H, aromatic protons), 4.44 (1H, dd, $H_{6\beta}$),[9] 4.13 (1H, dd, $H_{6\alpha}$, $J_{6\alpha,6\beta}$ = 9.7 Hz), 3.83 (1H, d, H_{13c}), 2.65 (3H, s, acetyl), 2.35 (1H, ddd, H_{6a}, $J_{6a,13c}$ = 11.3 Hz, $J_{6a,6\beta}$ = 6.2 Hz, $J_{6a,6\alpha}$ = 12.2 Hz), 1.55 and 1.32 (3H + 3H, s + s, 7-methyls).

A short column chromatography gave **6a** in more than 90% yield as white crystals, m.p. 151-2 °C from cyclohexane (contaminated by a trace of **6b**). Ir: ν_{CO} 1703 cm^{-1}. ^{1}H-Nmr, δ: 8.40 (1H, dd, H_{10}), 6.80-7.62 (7H, aromatic protons), 4.48 (1H, ddd, $H_{6\beta}$, $J_{6\beta,13c}$ = 1 Hz), 4.31 (1H, bd, H_{13c}), 4.18 (1H, dd, $H_{6\alpha}$, $J_{6\alpha,6\beta}$ = 11.5 Hz), 2.63 (3H, s, acetyl), 2.25 (1H, ddd, H_{6a}, $J_{6a,13c}$ = 5.0 Hz, $J_{6a,6\beta}$ = 4.2 Hz, $J_{6a,6\alpha}$ = 8.6 Hz), 1.52 and 1.58 (3H + 3H, s + s, 7-methyls). Elem. anal.; calc. for $C_{22}H_{21}NO_3$: C, 76.1; H, 6.1; N, 4.0. Found: C, 75.9, H, 6.1; N, 4.1%.

Reaction of 5 catalyzed by ZnCl$_2$ (Entry B). **5** (174 mg - 0.5 mmol) was added to a stirred suspension of crushed anhydrous ZnCl$_2$ (200 mg - 1.5 mmol) in anhydrous CH$_2$Cl$_2$ (1.5 mL). Stirring was continued at room temperature for 24 hours until tlc showed no more starting product in the solution. The reaction mixture was poured in water, acidified with few drops of acetic acid and extracted with CH$_2$Cl$_2$. A portion of the crude mixture was monitored by Nmr and showed the ratios of **6a**, **6b**, **7**, **9**, **10a**, and **10b** reported in the table. The reaction mixture was column chromatographed over silica gel. Eluant cyclohexane - ethyl acetate 97 : 3 was suitable to separate **11a**, **11b**, **9**, and **6a,b** in the order. **9** (12 mg - 6% yield) was isolated as a clourless oil, ^{1}H-Nmr, δ: 8.26 (1H, d, H_{10}, J_{meta} = 1.8 Hz), 7.62 (1H, dd, H_{12}, J_{ortho} = 7.8 Hz, J_{meta} = 1.8 Hz), 7.43 (1H, dd, H_{13}), 6.75-7.2 (4H, $H_{1\text{-}4}$), 5.32 (1H, m, vinylic proton, J = 7.2 and 1.2 Hz), 4.46 (1H, ddd, $H_{6\beta}$, $J_{6\beta,13c}$ = 1 Hz), 4.28 (1H, bd, H_{13c}, $J_{6a,13c}$ = 5 Hz), 4.16 (1H, dd, $H_{6\alpha}$, $J_{6\alpha,6\beta}$ = 11.5 Hz), 3.38 (2H, d, allylic CH$_2$, J = 7.2 Hz), 2.61 (3H, s, acetyl), 2.22 (1H, ddd, H_{6a}, $J_{6a,6\beta}$ = 4 Hz, $J_{6a,6\alpha}$ = 9 Hz), 1.71 and 1.72 (3H + 3H, d + d, vinylic methyls, J = 1.2 Hz), 1.51 and 1.58 (3H + 3H, s + s, 7-methyls).

The eluant was changed to cyclohexane - ethyl acetate 70 : 30 and **7** was separated as yellow needles, m.p. 162-3 °C from acetic acid - water 1 :1 (50 mg, 36% yield). Ir: ν_{OH} 3220 bb cm^{-1}, ν_{CO} 1755 and 1675 cm^{-1}. ^{1}H-Nmr, δ: 8.30 (1H, bd, H_7, J = 8 Hz), 7.97 (1H, s, vinylic proton), 6.9-7.6 (7H, aromatic protons), 5.61 (1H, bs, OH), 2.77 (3H, s, acetyl). Elem. anal. (after drying under vacuum at 120 °C for 24 hrs); calc. for $C_{17}H_{13}NO_3$: C, 73.1; H, 4.7; N, 5.0. Found: C, 73.3, H, 4.7; N, 4.9%.

The experiment described in entry C was worked-up analogously.

Transfer of the 3-methyl-2-butenyl group from 5 to 6a. To a stirred mixture of **6a** (70 mg - 0.2 mmol) and MP (45 mg - 0.2 mmol) in anhydrous CH_2Cl_2 (0.5 mL) at room temperature, **5** (70 mg - 0.2 mmol) was added. Within one hour no more **5** was detected by tlc and, in addition to some trace products not investigated, the column chromatography (eluant cyclohexane - ethyl acetate first 96 : 4, then 70 : 30) gave in the order: **9** (40 mg - 48%) whose ^{1}H-Nmr was identical to that previously described, **6a** (70 mg) coming partly from the unreacted reagent and partly from **5**, and finally **7** (25 mg - 44%).

Hydrolytic deacetylation of 7. **7** (30 mg - 0.11 mmol) was dissolved in acetic acid (3.0 mL) and conc. HCl (0.2 mL). This mixture was warmed at 100 °C for about 10 minutes. Cooling at room temperature gave yellow crystals of **8** (20 mg), m.p. 189-190 °C. This product had identical m.p. and ir spectrum of a sample synthetized from oxindole and salicyl aldehyde following the literature method.[10]

Reaction of 5 catalyzed by MP and acetone in CH_2Cl_2 (Entry F). This and the conditions described under entry J are best methods to synthetize the IER products. Anhydrous MP (446 mg - 2 mmol) and acetone (232 mg - 4 mmol) were stirred at room temperature in anhydrous CH_2Cl_2 (20 mL) for 2 hours. **5** (700 mg - 2 mmol) was added and the clear yellow solution was stirred for 8 hours. The reaction mixture was decomposed in water and extracted with CH_2Cl_2. A portion of the crude reaction mixture was monitored by ^{1}H-Nmr and showed the presence only of **6a,b** and **10a,b** in the ratio reported in the table.

10a; ^{1}H-Nmr, δ: 8.13 (1H, bd, H_7, J = 8 Hz), 5.05 and 4.61 (1H + 1H, bs + bs, vinylic protons), 4.50 (1H, ddd, $H_{2'eq.}$, $J_{2'eq.,4'}$ = 1.8 Hz), 4.31 (1H, t, $H_{2'ax.}$, $J_{2'eq.,2'ax.}$ = 11 Hz, $J_{2'ax.,3'}$ = 11 Hz), 4.01 (1H, m, $H_{4'}$, $J_{3',4'}$ = 5 Hz, $J_{3,4'}$ = 2 Hz), 3.85 (1H, bs, H_3), 2.89 (1H, dt, $H_{3'}$, $J_{2'eq.,3'}$ = 4 Hz), 2.70 (3H, s, acetyl), 2.01 (3H, s, methyl isopropenyl).

10b; ^{1}H-Nmr, δ: 8.23 (1H, bd, H_7, J = 8 Hz), 5.05 (2H, bs, vinylic protons), 4.30 (1H, dd, $H_{2'eq.}$), 4.07 (1H, d, H_3, $J_{3,4'}$ = 2.5 Hz), 3.99 (1H, dd, $H_{2'ax.}$, $J_{2'eq.,2'ax.}$ = 11 Hz, $J_{2'ax.,3'}$ = 10 Hz), 3.96 (1H, dd, $H_{4'}$, $J_{3',4'}$ = 10 Hz), 2.99 (1H, dt, $H_{3'}$, $J_{2'eq.,3'}$ = 3.8 Hz), 2.79 (3H, s, acetyl), 1.84 (3H, s, methyl isopropenyl).

The reaction mixture was absorbed on a small amount of silica gel and set aside for one night. Then was placed on a chromatographyc column and eluted with cyclohexane - ethyl acetate 97 : 3. **11a**, **11b**, and **6a,b** separated in the order.

11a (84 mg - 12% yield) was obtained as colourless needles, m.p. 141-2 °C from light petrol ether. Ir: ν_{CO} 1752 and 1709 cm^{-1}. ^{1}H-Nmr, δ: 8.18 (1H, bd, H_7, J = 8 Hz), 7.4-6.6 (7H, aromatic protons), 4.97 and 4.49 (1H + 1H, bs + bs, vinylic protons), 4.23 (1H, dd, $H_{2'ax.}$, $J_{2'eq.,2'ax.}$ = 10.5 Hz, $J_{2'ax.,3'}$ = 12 Hz), 4.17 (1H, ddd, $H_{2'eq.}$, $J_{2'eq.,4'}$ = 1.7 Hz), 3.94 (1H, bs, H_3), 3.85 (1H, ddd, $H_{4'}$, $J_{3',4'}$ = 5 Hz, $J_{3,4'}$ = 2.5 Hz), 2.80 (1H, ddd, $H_{3'}$, $J_{2'eq.,3'}$ = 4 Hz), 2.38 (3H, s, acetyl), 1.98 (3H, s, methyl isopropenyl). Elem. anal.; calc. for $C_{22}H_{21}NO_3$: C, 76.1; H, 6.1; N, 4.0. Found: C, 75.9, H, 6.2; N, 4.2%.

11b (147 mg - 21% yield) was obtained as soft white needles, m.p. 111-2 °C from light petrol ether. Ir: ν_{CO} 1763 and 1703 cm^{-1}. ^{1}H-Nmr, δ: 8.20 (1H, bd, H_7, J = 8 Hz), 7.4-6.4 (7H, aromatic protons), 4.78 and 4.53 (1H + 1H, bs + bs, vinylic protons), 4.23 (1H, d, H_3, $J_{3,4'}$ = 3 Hz), 4.03 (1H, dd, $H_{4'}$, $J_{3',4'}$ = 10 Hz), 3.91 (1H, dd, $H_{2'eq.}$), 3.85 (1H, t, $H_{2'ax.}$, $J_{2'eq.,2'ax.}$ = 10.5 Hz), 2.60 (3H, s, acetyl), 2.53 (1H, dt, $H_{3'}$, $J_{2'eq.,3'}$ = 4.5

Hz, $J_{2'ax.,3'}$ = 10.2 Hz), 1.68 (3H, s, methyl isopropenyl). Elem. anal.; calc. for $C_{22}H_{21}NO_3$: C, 76.1; H, 6.1; N, 4.0. Found: C, 76.2, H, 6.1; N, 4.1%.

The experiment described under entry E was worked-up analogously, but a check of the crude reaction mixture by Nmr showed that **10a** and **10b** were largely isomerized to **11a** and **11b**. Control experiments cleared this is due to the experimental conditions since a reaction mixture deriving from entry F, dissolved in an acetonic solution of MP 1M for the time required for entry E, isomerized **10a,b** into **11a,b**.

Further reactions of 5 catalyzed by MP (Entries G-J). All experiments were run under the conditions described in the Table. MP was first stirred one hour in CH_2Cl_2 in the presence of benzophenone or camphor (2 equivalents) or acetylacetone or 3,3-dimetilpentan-2,4-dione[11] (1 equivalent), then **5** was added. After the time reported in the Table, the reaction was worked-up as descrbed for entry F and monitored by Nmr. The column chromatography gave benzophenone (when present) as first fraction eluted; camphor or dimethylpentandione (when present) were eluted between **11b** and **6a,b**. The presence of these fractions is the reason to suggest entry F as best method to prepare IER products in spite of the somewhat lower yields.

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