Intramolecular "Diene-Regenerable" Diels-Alder Reaction of 2-Pyrone-6-carboxamides.[1] Preparation and Reaction of Fused 1,3-Cyclohexadiene Systems

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The 2-pyrone-6-carboxamides, prepared from 2-pyrone-6-carbonyl chloride and substituted allylamine, undergo an intramolecular Diels-Alder reaction spontaneously to give 3a,4,5,7a-tetrahydro-1-oxoisoindoline-5,7a-carbolactones, which regenerate the diene moieties by the decarboxylation to afford 3a,4-dihydro-1-oxoisoindolines. 3a,4,4a,5-Tetrahydro-1(2*H*)-isoquinolone and 2,3,4,5,5a,6-hexahydro-1*H*-2-benzazepin-1-one derivatives are obtained similarly from the corresponding amides. These fused 1,3-cyclohexadiene systems reveal to be versatile synthetic intermediates for polycyclic compounds by cycloaddition reaction and for benzo-fused heterocycles by dehydrogenation. The stereochemistries in the successive cycloaddition reactions are also discussed.

Previously, we reported that 2-pyrone-6-carboxylates bearing dienophiles at the ester moieties underwent "diene-regenerable" Diels-Alder reaction intramolecularly to give 3a,4-dihydrophthalide derivatives.[2] The 3a,4-dihydrophthalides behaved as novel functionalized 1,3-cyclohexadiene systems and provided a favorable method for the synthesis of 5,7a-ethanophthalides by the intermolecular Diels-Alder reaction with olefins[2] and of 4-substituted phthalides by oxidation.[3]

In this paper we wish to report that 2-pyrone-6-carboxamides, prepared from 2-pyrone-6-carbonyl chloride and substituted allylamines in situ, undergo an intramolecular Diels-Alder reaction to give tetracyclic adducts, which are smoothly converted to 3a,4-dihydro-1-oxoisoindolines by the extrusion of carbon dioxide. 1(2*H*)-Isoquinolone and 1*H*-2-benzazepin-1-one derivatives are obtained similarly by the intramolecular "diene-regenerable" Diels-Alder reaction of the corresponding 2-pyrone-6-carboxamides. The reaction of the fused 1,3-cyclohexadienes with *N*-phenylmaleimide and the oxidation of the 1,3-cyclohexadienes to benzo-fused heterocycles are also detailed.

Results and Discussion

Intramolecular Diels-Alder Reaction of 2-Pyrone-6-carboxamides. The reaction of 2-pyrone-6-carbonyl chloride (**1**) and *N*-allylaniline (**2a**) in the presence of triethylamine (Et_3N) at room temperature gave a crystalline product **4a** in 60% yield.

Unfortunately, **4a** did not provide satisfactory results on the elemental analysis, and the molecular ion peak on its mass spectrum was not observed because of its instability. Its IR spectrum, however, exhibited strong absorption bands at 1770 and 1700 cm^{-1} assignable to the lactone an lactam carbonyl streching vibrations, respectively. Also, its ^1H NMR spectrum (Table 2) showed two olefinic protons at δ=6.53 and 6.96 and the complicated signals over the region of δ=2 to 4 (total 6H) assigned to methylene and methine protons together with phenyl protons (5H). On the basis of these spectral data and the chemical conversions delineated later, **4a** was deduced to be not the expected *N*-allyl-2-pyrone-6-carboxanilide (**3a**) but 3a,4,5,7a-tetrahydro-1-oxo-2-phenylisoindoline-5,7a-carbolactone, an intramolecular Diels-Alder adduct of **3a**.

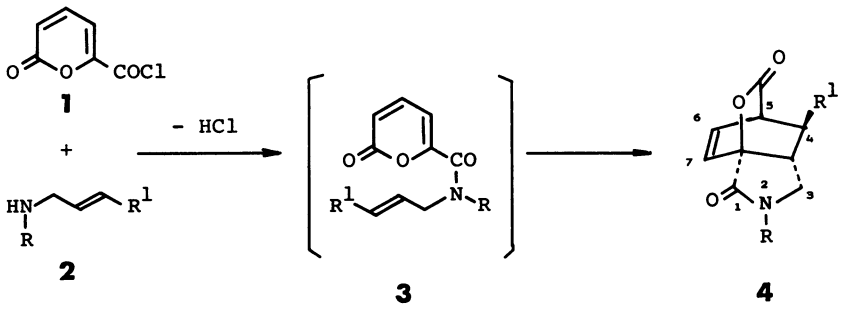
Similarly, the reaction of **1** with *N*-allylbenzylamine (**2b**), *N*-benzyl-*trans*-cinnamylamine (**2c**), *N*-(*trans*-2-butenyl)benzylamine (**2d**), and *N*-methyl-*trans*-cinnamylamine (**2e**) in the presence of Et_3N gave the corresponding Diels-Alder adducts **4b—e** in good yields. These results are summarized in Tables 1 and 2.

The stereochemistry at the 3-position of **4** could not be determined only on the basis of the coupling constants between 3-H and 3a-H or 3a-H and 4-H. However, its structure was deduced to be **4**-*endo* from the following inspections using the molecular models of **4**-*endo* and **4**-*exo* as well as the transition states. Firstly, the methylene protons at the 3-position of **4** were observed almost equivalently as shown in Table 2. The methylene protons at the 3-position of **4**-*endo* are possible to be equivalent and, on the other hand, those of **4**-*exo* are not so because of the anisotropic effect arising from the ether-

Table 1. Reactions of 2-Pyrone-6-carbonyl Chloride (**1**) with Alkenylamines (**2**)

Compd	R	R^1	Yield %	IR cm^{-1} ν_{CO}
4a[a]	Ph	H	60	1770, 1700
4b[b]	CH_2Ph	H	94	1765, 1700
4c[b]	CH_2Ph	Ph	88	1770, 1700
4d[b]	CH_2Ph	CH_3	83	1765, 1710
4e[a]	CH_3	Ph	68	1760, 1700

a) Colorless crystals. b) Colorless viscous oil.



Scheme 1.

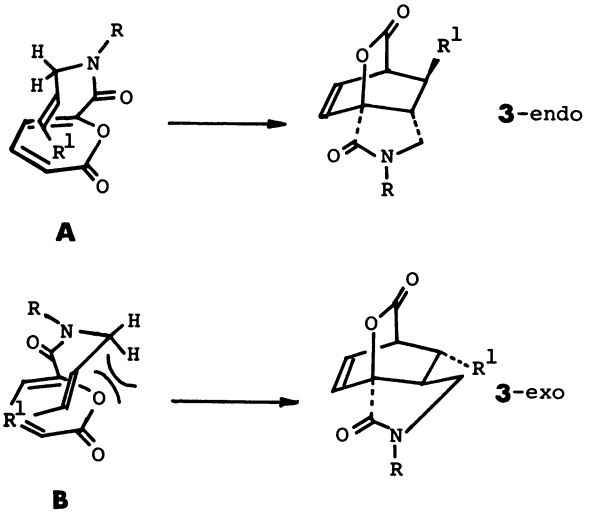
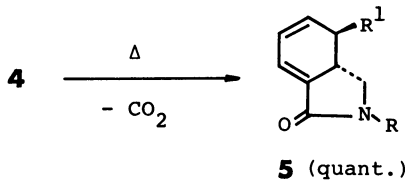


Fig. 1. Possible transition states for the intramolecular Diels–Alder reaction of **3**.



Scheme 2.

oxygen atom of the lactone moiety.

The configurations between 3a- and 4-positions of **4c**, **4d**, and **4e** were determined to be *trans* from those of the 3a,4-dihydro-1-oxoisoindoline derivatives, which were obtained by the decarboxylation of **4** as mentioned later.

The considerations using the molecular models of the possible transition states[4] in this reaction also indicate the predominant formation of **4**-*endo*, i.e., the orientation A leading to **4**-*endo* seems to be more favorable than B leading to **4**-*exo*, in which the sterical repulsion between one of the allylic methylene protons and the ether-oxygen atom of 2-pyrone part in **3** becomes serious along with the progress of the reaction (Fig. 1).

The Diels–Alder adducts from 2-pyrones and dienophiles are not so stable as well-known and only a few examples of the isolation have been reported.[5] To be emphasized is the isolation of the adducts **4**, because **4** possess further strained structures than the adducts reported previously.[5]

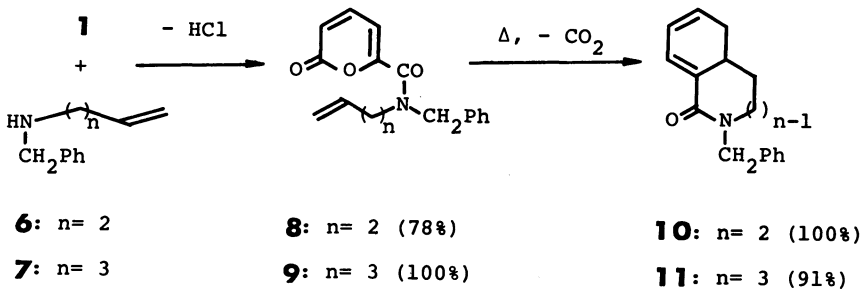
Predictively, the adducts **4** are thermodynamically and photochemically unstable and converted gradually to 3a,4-dihydro-1-oxoisoindoline derivatives by the decarboxylation during the storage in the crystalline or solution state under shield of light in a refrigerator.

For example, **4a** was heated in hexane under reflux for a few minites to give 3a,4-dihydro-1-oxo-4-phenylisoindoline (**5a**) quantitatively. 3a,4-Dihydro-1-oxoisoindolines **5b**—**e** were similarly obtained from the corresponding adducts **4b**—**e** in quantitative yields (Scheme 2).

The analytical and spectroscopic data of **5** were consistent with the proposed structures. Especially, their stereochemical confirmations at the 3a- and 4-positions were accomplished by the following ^{1}H NMR spectral data; for **5a** the vicinal coupling constants (5.9 and 2.2 Hz) between the olefin proton (5-H) and the methylene protons (4-H) were assigned to be $J_{5-4(a)}$ and $J_{5-4(b)}$, respectively. Nextly, the pronounced large coupling constants (17.2 and 9.7 Hz)[6] between 3a-H and 4-H were deduced to be *trans* and *cis*, respectively. These assignments were almost identical with those of 3a,4-dihydrophthalide.[2] Among **4c**, **4d**, and **4e**, the stereochemistry at the 3a- and 4-positions of **4c** was only determined to be *trans* on the basis of the vicinal coupling constants among the adjacent three protons at the 3a-, 4-, and 5-positions (J_{3a-4}=17.0 and J_{4-5}=0.8 Hz) (Table 3).

This means that the intramolecular Diels–Alder reaction of amide **3c** is carried out with the retention of the stereochemistry on the dienophile moiety. Taking the integrity of the stereocontrol in this reaction into consideration, the stereochemistries at the 3a- and 4-positions of **5d** and **5e** were suggested to be also *trans*.

The above findings revealed that the "diene-regenerable" Diels–Alder reaction of 2-pyrone-6-



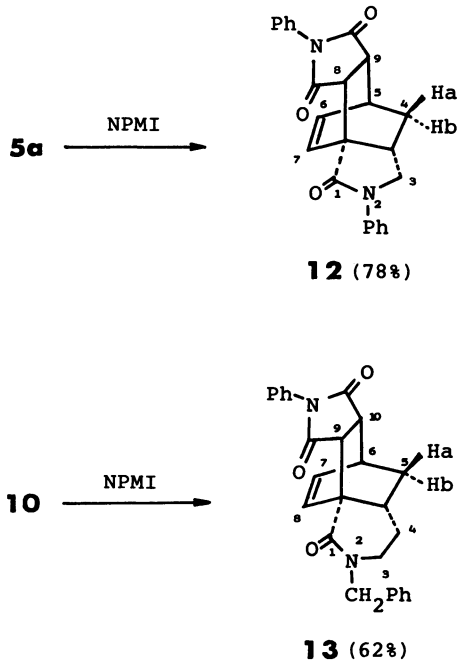
Scheme 3.

carboxamides **3** provided an attractive route to obtain 3a,4-dihydro-1-oxoisoindolines, so we attempted to apply this method to the preparation of the 1,3-cyclohexadiene systems fused by six- and seven-membered heterocycles containing nitrogen atom.

The reaction of **1** with *N*-(3-butenyl)benzylamine (**6**) and *N*-(4-pentenyl)benzylamine (**7**) in the presence of Et_3N at room temperature gave the 2-pyrone-6-carboxamides **8** and **9**. The successive intramolecular Diels–Alder reaction of **8** and **9** proceeded only under the severer conditions, i.e., under reflux in toluene for **8** and in *o*-dichlorobenzene for **9**, to give 2-benzyl-3,4,4a,5-tetrahydro-1(2*H*)-isoquinolone (**10**) and 2-benzyl-2,3,4,5,5a,6-hexahydro-1*H*-2-benzazepin-1-one (**11**), respectively (Scheme 3).

Cycloaddition Reaction of Fused 1,3-Cyclohexadienes 5a and 10 with *N*-Phenylmaleimide (NPMI). In order to obtain the stereochemical aspect on the Diels–Alder reaction of the fused 1,3-cyclohexadiene systems, the reaction of **5a** and **10** with NPMI was investigated.

The reaction of **5a** or **10** with an equimolar NPMI in xylene under reflux and the successive working-up gave the cycloadduct **12** or **13** as a sole product (Scheme 4).



Scheme 4.

The structure of **12** was deduced to be a 3a,4,5,7a-tetrahydro-5,7a-ethano-1-oxoisoindoline derivative on the basis of its spectral data. It was confirmed that the stereochemistry at the 3a- and 7a-junctions was *cis* and the configurations of the protons at the 8- and 9-positions were both *exo* from the analysis of its ^1H NMR spectrum compared with that of cycloadduct[2] from 3a,4-dihydrophthalide and NPMI or of the related similar ring systems.[7]

The structure of **13** was deduced to be a 3,4,4a,5,6,8a-hexahydro-6,8a-ethano-1(2*H*)isoquinolone derivative also from its spectral data. The sufficient assignment of the signals in its ^1H NMR spectrum was not accomplished, because some of the methylene and methine protons were superimposed one another. However, the signal patterns[8] of the olefin protons of **13** were almost identical with those of **12**; δ=6.24 (dd, 1H, J=6.8 and 8.5 Hz) and 6.77 (d, 1H, J=8.5 Hz) for **12** and δ=6.26 (dd, 1H, J=5.7 and 9.0 Hz) and 6.86 (d, 1H, J=9.0 Hz) for **13**, so the stereochemistry at the 4a- and 8a- junctions of **13** was concluded to be also *cis*. Although the configurations of the protons at the 9- and 10-positions were obscure, they were tentitatively assigned to be both *exo* similarly to those of **12** according to the reaction pathway.

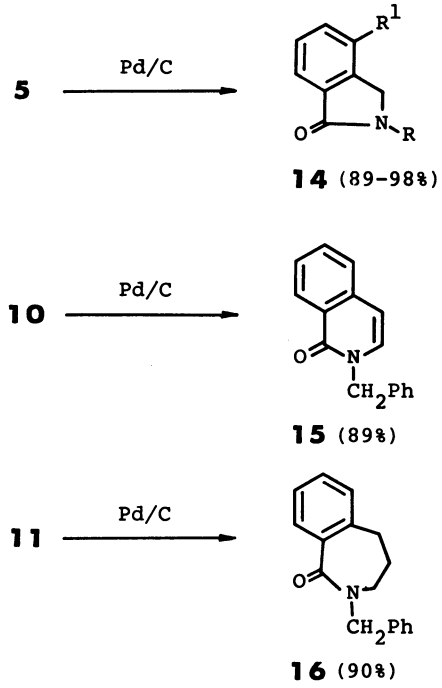
These findings indicate that the Diels–Alder reaction of **5a** and **10** with NPMI proceeds in a highly stereoselective manner. Therein, an only approarch of NPMI to 1,3-diene moiety of **5a** or **10** leading to *cis*-fused lactam ring seems to be possible owing to the less ring distorsion at the transition state in the reaction.

Dehydrogenation of Fused 1,3-Cyclohexadiene Systems 5, 10, and 11 to Benzo-Fused Heterocycles. As described above, 4-substituted phthalides were prepared by the facial oxidation of 3a,4-dihydrophthalides with palladium-charcoal (Pd/C), so we investigated the dehydrogenation of 3a,4-dihydro-1-oxoisoindolines **5** and their higher homologs, **10** and **11**, to the benzo-fused heterocycles.

The heating of **5** in refluxing xylene in the presence of Pd/C gave the expected 1-oxoisoindolines **14** almost quantitatively. While the similar treatment of **11** with Pd/C in refluxing *o*-dichlorobenzene yielded 2-benzyl-2,3,4,5-tetrahydro-1*H*-2-benzazepin-1-one (**16**)[9], **10** gave 2-benzyl-1(2*H*)-isoquinolone(**15**)[10] with the elimination of two equimolar hydrogen under similar dehydrogenating conditions (Scheme 5).

Finally, the possibility of the one-pot preparation of the benzlactams **15** and **16** from **8** and **9**, respectively, was surveyed. Heating of the amide **8** in refluxing toluene in the presence of Pd/C gave 2-benzyl-3,4-dihydro-1(2*H*)-isoquinolone (**17**;[9] 43%) and **14d** (47%). A similar reaction of **9** furnished 2-benzyl-3,4-dihydro-5-methyl-1(2*H*)-isoquinolone (**18**; 87%) as a sole product. In both cases, the terminal olefins of the dienophile moieties were isomerized by the Pd/C to the inner ones, which cycloadded to the 4π-components of 2-pyrones (Scheme 6). Interestingly, the dehydrogenation of the dihydro-1(2*H*)-isoquinolones **17** and **18** to 1(2*H*)-isoquinolone systems was suppressed under these reaction conditions.

In conclusion, the intramolecular "diene-regenerable" Diels–Alder reaction of 2-pyrone-6-carboxamides provided an attractive synthetic method for the 1,3-cyclohexadiene systems fused by pyrrole, pyridine, and azepine rings, which are versatile intermediates for polycyclic compounds and benzo-fused heterocycles. Among them, it should be emphasized that the stereochemistries of the final polycyclic compounds depend upon those of the successive intra- and intermolecular cycloaddition reactions.

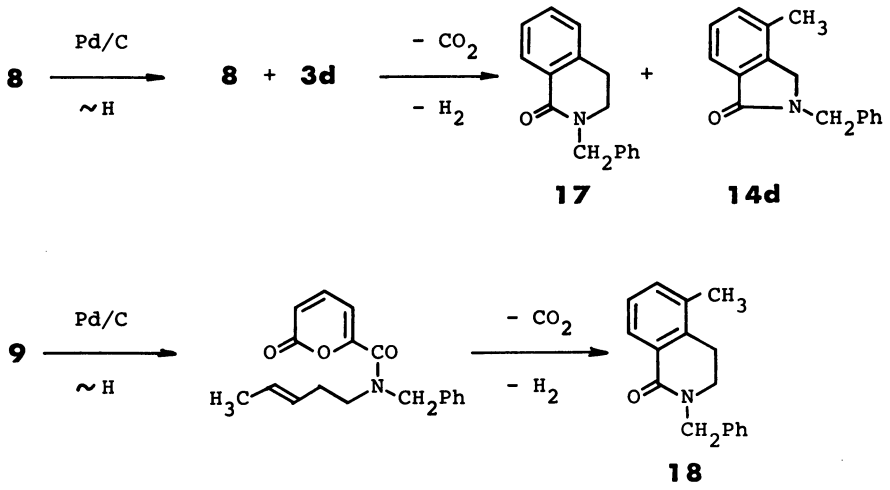


Scheme 5.

Experimental

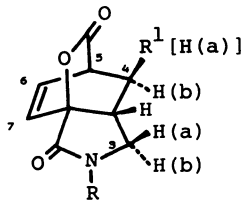
General. All melting points are uncorrected. The IR spectra were measured on a JASCO IRA-1 spectrometer. The ^{1}H NMR spectra were obtained on JEOL FX-200 and JMN-MH-100 spectrometers with tetramethylsilane as an internal standard. The mass spectra were determined with JEOL JMS-012G-2 and JMS-D mass spectrometers equipped with direct inlets and at an ionization energy of 75 eV. The elemental analyses were performed on a Hitachi 026 CHN analyzer. The thin-layer chromatography was accomplished on 0.2 mm precoated plates of silica gel 60F-254 (Merck) or on 0.2 mm precoated plates of aluminium oxide 60F-254 Type E (Merck). The visualization was made with ultraviolet light (254 and 365 nm). For the preparative column chromatography, Wakogel C-300 was used.

Preparation of 3a,4,5,7a-Tetrahydro-1-oxoisoindoline-5,7a-carbolactones 4 from 2-Pyrone-6-carbonyl Chloride (1)



Scheme 6.

Table 2. ^{1}H NMR Spectral Data for 3a,4,5,7a-Tetrahydro-1-oxoisoindoline-5,7a-carbolactones **4** in $CDCl_3$: δ



Compd	3-H(a)	3-H(b)	3a-H	4-H(a)	4-H(b)	5-H	6-H	7-H	Others
	3.90	3.99	2.55	1.95	1.95	3.53	6.53	6.96	7.2—7.6 (phenyl)
4a[a]	t	dd	dddd	ddd		ddd	dd	t	
	J (Hz) 3(a),3(b)=3(a),3a=9.0, 3(b),3a=9.2, 3a,4(a)=6.3, 3a,4(b)=6.0, 4(a),5=4(b),5=0.3, 5,6=7.2, 5,7=0.3, 6,7=8.0								
	3.24	3.18	2.30	1.75	1.75	3.52	6.42	6.84	7.1—7.3 (phenyl)
4b[b]	t	dd	m	m		m	t	d	4.5 (-CH_2-)
	J (Hz) 3(a),3(b)=3(a),3a=8.5, 3(b),3a=9.1, 5,6=6,7=7.0								
	3.48	3.40	2.55	—	3.16	3.64	6.50	7.06	7.1—7.4 (phenyl)
4c[a]	dd	t	ddd		dd	ddd	dd	dd	4.55 (-CH_2-)
	J (Hz) 3(a),3(b)=3(a),3a=6.2, 3(b),3a=5.4, 3a,4=6.0, 4,5=0.8, 5,6=5.9, 5,7=0.8, 6,7=6.4								
	3.2 — 3.5		1.6		2.0	2.94	6.34	6.80	7.2—7.3 (phenyl)
4d[b]	m		m			m	dd	d	4.5 (-CH_2-)
	J (Hz) 5,6=5.5, 6,7=7.0								1.1 (Me)
	3.58	3.58	2.62	—	3.20	3.69	6.50	7.02	7.2—7.4 (phenyl)
4e[a]	d		dd		d	d	dd	d	2.98 (Me)
	J (Hz) 3(a),3a=3(b),3a=8.0, 3a,4=6.0, 4,5=0, 5,6=7.0, 6,7=7.5								

a) Measured at 200-MHz. b) Measured at 100-MHz.

and Allylamines 2. Typical Procedure: To a stirred and cooled at 0 °C solution of *N*-allylaniline (**2a**)(32 mmol) and Et_3N (35 mmol) in THF (40 mL), **1**[11] (32 mmol) in THF (10 mL) was added dropwise for 30 min and the reaction mixture was stirred for additional 12 h at room temperature. The resultant triethylamine hydrochloride was filtered off and the filtrate was evaporated in vacuo at room temperature. The crystallization and successive washing with ethanol gave 4.8 g (60%) of **4a**.

A similar reaction of **1** with **2e** gave **4e** also as a crystalline form. On the other hand, **4b**, **4c**, and **4d** were obtained as oily products, so their purification was accomplished with a column chromatography (silica gel-ether).

Some efforts to purify **4** enough to obtain the satisfactory elemental analyses, e.g., recrystalization or purification with a performance liquid chromatography, were made without success.

Heating of **4a** in a capillary at 45 °C showed some changes of its crystalline form and **4a** melted at 94—95 °C. The melting point was identical with that of the decarboxylated product **5a**. The mass spectrum of **4a** under the ordinarily-measured conditions was also identical with that of **5a**.

The results of these reactions and the spectral data of the products **5** are summarized in Tables 1 and 2, respectively.

Decarboxylation of 3a,4,5,7a-Tetrahydro-1-oxoisoindoline-5,7a-carbolactones 4. Typical Procedure: A solution of **4a** (500 mg, 1.96 mmol) in hexane (30 mL) was refluxed for a few minutes and cooled at −30 °C to give 410 mg (99%) of the crystalline **5a**.

5a: Colorless plates (hexane-ethanol); mp 94—95 °C; IR (KBr) 1675 cm^{-1} (CO); MS *m/z* (relative intensity) 211 (M^+, base peak), 107 (22), 106 (72), 105 (Ph-CH=NH^+, 92), 104 (27), 92 (M^+−PhNCO, 37), 91, 77.

Found: C, 79.75; H, 6.34; N, 6.68%. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63%; M, 211.

5b: Yield 100%; colorless plates (hexane-ethanol); mp 90—91.5 °C; IR (KBr): 1670 cm^{-1} (CO); MS *m/z* (relative intensity) 225 (M^+, base peak), 106 (42), 105 (Ph-CH=NH^+, 88), 91 (77), 77 (20).

Found: C, 80.13; H, 6.78; N, 6.19%. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%; M, 225.

5c: Yield 100%; colorless needles (hexane-benzene); mp 139—141 °C; IR (KBr): 1680 cm^{-1} (CO); MS *m/z* (relative intensity) 301 (M^+, 11), 167 (Ph-$C_7H_6^+$, 44), 106 (13), 91 ($C_7H_7^+$, base peak).

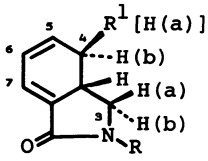
Found: C, 83.65; H, 6.41; N, 4.74%. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65%; M, 301.

5d: Yield 97%; colorless plates (hexane-benzene); mp 136.5—138.5 °C; IR (KBr): 1680 cm^{-1} (CO); MS *m/z* (relative intensity) 239 (M^+, 13), 106 (33), 91($C_7H_7^+$, base peak), 77 (33).

Found: C, 80.31; H, 7.23; N, 5.81%. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%; M, 239.

5e: Yield 99%; colorless prisms (hexane-benzene); mp 105.5—106.5 °C; IR (KBr): 1670 cm^{-1} (CO); MS *m/z* (relative intensity) 225 (M^+, base peak), 167 (Ph-$C_7H_6^+$, 40),

Table 3. ^{1}H NMR Spectral Data for 3a,4-Dihydro-1-oxoisoindolines **5** in $CDCl_3$: δ



Compd	3-H(a)	3-H(b)	3a-H	4-H(a)	4-H(b)	5-H	6-H	7-H	Others
5a[a]	4.13	3.51	2.90	2.62	2.09	6.15	6.29	6.86	7.1, 7.8 (phenyl)
	t	dd	m	ddd	dddd	dddd	ddd	t	
	J (Hz) 3(a),3(b)=3(a),3a=9.0, 3(b),3a=9.6, 3a,4(a)=9.0, 3a,4(b)=17.2, 4(a),4(b)=17.0, 3a,5=1.2, 3a,7=3.2, 4(a),5=5.9, 4(b),5=4(b),6=2.2, 5,6=8.8, 6,7=3.2								
5b[b]	3.50	2.5——3.1		2.0——2.2		5.8——6.3		6.6	7.2 (phenyl)
	m	m		m		m		m	4.5 ($-CH_2-$)
5c[a]	3.26	2.8——3.0			3.40	5.96	6.28	6.78	7.1—7.3 (phenyl)
	m	m			ddd	dd	ddd	dd	3.95, 4.10 ($-CH_2-$)
	J (Hz) 3a,4=17.0, 3a,7=2.2, 4,5=0.8, 4,6=1.2, 5,6=8.8, 6,7=3.2								
5d[a]	3.55	2.85	2.1——2.5			5.82	6.19	6.74	7.2—7.4 (phenyl)
	t	dd	m			dd	ddd	dd	4.53, 4.60 ($-CH_2-$)
	J (Hz) 3(a),3(b)=3(a),3a=9.3, 3(b),3a=8.1, 3a,4=15.6, 3a,7=1.4, 4,5=0.7, 4,6=1.2, 5,6=9.0, 6,7=3.2								1.10 (Me)
5e[a]	2.8——3.5					6.02	6.33	6.78	7.2—7.4 (phenyl)
	m					dd	ddd	t	2.93 (Me)
	J (Hz) 3a,7=1.4, 4,5=0.8, 4,6=0.8, 5,6=9.0, 6,7=3.2								

a) Measured at 200-MHz. b) Measured at 100-MHz.

154 (70), 153 (47), 134 ($M^+-C_7H_7$, 92), 42 (60).

Found: C, 80.16; H, 6.79; N, 6.41%. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%; M, 225.

The ^{1}H NMR spectral data of **5** are summarized in Table 3.

Preparation of 2-Pyrone-6-carboxamides 8 and 9 from 1 and Amines 6 and 7. Similarly to the preparation of **4**, the reaction of **1** (7.6 mmol) and **6** (7.6 mmol) in THF (40 mL) in the presence of a little excess of Et_3N at room temperature for 15 h gave an oily product, which was purified with a short column chromatography (aluminium oxide–ether) to afford 1.68 g (78%) of **8**.

8: Pale yellow viscous oil; IR (Neat) 1740 and 1635 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ=2.40 (m, 2H, >N-CH_2-), 3.40 (m, 2H, -CH_2-CH=), 4.50 (s, 2H, -CH_2-Ph), 5.15 (m, 2H, =CH_2), 5.7 (m, 1H, -CH=), 6.45 (m, 1H, 5-H), 6.65 (m, 1H, 4-H), and 7.3—7.4 (m, 6H, 3-H and phenyl protons); MS m/z (relative intensity) 283 (M^+, 17), 242 ($M^+-C_3H_5$, 85), 239 (M^+,$-CO_2$, 13), 95 (42), 91 ($C_7H_7^+$, base peak).

Found: C, 71.86; H, 6.09; N, 5.06%. Calcd for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05; N, 4.94%; M, 283.

9: Colorless viscous oil; IR (neat): 1740 and 1635 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ=1.6—2.2 (m, 4H, >N-CH_2-CH_2-), 3.4 (m, 2H, -CH_2-CH=), 4.65 (s, 2H, -CH_2-Ph), 4.90 (m, 2H, =CH_2), 5.68 (m, 1H, -CH=), 6.32 (m, 1H, 5-H), 6.60 (m, 1H, 4-H), and 7.2—7.3 (m, 6H, 3-H and phenyl protons); MS m/z (relative intensity) 297 (M^+, 4), 269 (M^+-CO, 5), 242 ($M^+-C_4H_7$, 5), 174 (30), 106, 104, 91 ($C_7H_7^+$, base peak).

Found: C, 72.92; H, 6.71; N, 4.99%. Calcd for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71%; M, 297.

Diene-Regenerable Diels-Alder Reaction of 2-Pyrone-6-carboxamides 8 and 9. A solution of **8** (1.30 g, 4.6 mmol) in toluene (30 mL) was heated under reflux for one day and the toluene was evaporated to dryness, which was treated with a short column chromatography (silica gel–benzene) to give 1.10 g (100%) of **10**.

10: Colorless plates (hexane); mp 64—65 °C; IR (KBr): 1640 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ=1.68(m, 1H, 5-H), 1.96 (m, 2H, 4-H), 2.26 (m, 1H, 5-H), 2.72 (m, 1H, 4a-H), 3.3 (m, 2H, 3-H), 4.54, 4.83 (2d, 1H each, -CH_2-Ph, J=14 Hz), 6.12 (m, 2H, 6- and 7-H), and 7.16 (m, 1H, 8-H); MS m/z (relative intensity) 239 (M^+, base peak), 210 (17), 148 ($M^+-C_7H_7$, 17), 134 (23), 120 (23), 106 (27), 105 ($PhCO^+$, 70), 91 (45), 77 (41).

Found: C, 80.48; H, 7.21; N, 5.92%. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%; M, 239.

Heating of **9** in *o*-dichlorobenzene under reflux for one day gave **11** in 91% yield.

11: Pale yellow viscous oil; IR(Neat): 1635—1610 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ=1.3—1.9 (m, 4H, 4- and 5-H), 1.9—2.3 (m, 2H, 6-H), 2.4 (m, 1H, 5a-H), 3.1—3.4 (m, 2H, 3-H), 4.62 (s, 2H, -CH_2-Ph), 6.0—6.1 (m, 2H, 7- and 8-H), 6.6 (m, 1H, 9-H), and 7.2—7.4 (m, 5H, phenyl protons); MS m/z (relative intensity) 253 (M^+, 11), 251 (M^+-H_2, 4), 106 (8), 105 (12), 104 (12), 91 ($C_7H_7^+$, base peak), 77 (26).

Found: m/z 253.1466. Calcd for $C_{17}H_{19}NO$: M, 253.1466.

Cycloaddition Reaction of 5a and 10 with *N*-Phenylmaleimide (NPMI). Typical Procedure: An equimolar (2.4 mmol) mixture of **5a** and NPMI in xylene (20 mL) was heated under reflux for 20 h and the xylene was evaporated in vacuo to give a residue. The residue was treated with a short column chromatography (silica gel–chloroform) to afford 0.71 g (78%) of **12**.

12: Colorless prisms (benzene–hexane); mp 280—281 °C;

IR (KBr): 1690 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=1.45 (ddd, 1H, 4-H, J_{gem}=12.8, $J_{3a,4}$=8.6, and $J_{4,5}$=0.6 Hz), 1.91 (ddd, 1H, 4'-H, J_{gem}=12.8, $J_{3a,4'}$=10.2, and $J_{4',5}$=4.2 Hz), 2.25 (m, 1H, 3a-H), 3.16 (dd, 1H, 9-H, $J_{8,9}$=8.4 and $J_{5,9}$=3.8 Hz), 3.24 (d, 1H, 8-H, $J_{8,9}$=8.4 Hz), 3.49 (m, 1H, 5-H), 3.61 (t, 1H, 3-H, J_{gem}=$J_{3,3a}$=9.6 Hz), 4.00 (dd, 1H, 3'-H, J_{gem}=9.6 and $J_{3',3a}$=7.2 Hz), 6.24 (dd, 1H, 6-H, $J_{5,6}$=6.8 and $J_{6,7}$=8.5 Hz), 6.77 (d, 1H, 7-H, $J_{6,7}$=8.5 Hz), and 7.1—7.7 (m, 10H, phenyl protons); MS *m/z* (relative intensity) 384 (M^+, 63), 279, 265, 252, 236, 221 (M^+—NPMI, 36), 173 (NPMI$^+$, 18), 119 (PhNCO$^+$, 25), 105 (Ph-CH=NH$^+$, base peak), 77 (92).

Found: C, 75.14; H, 5.31; N, 7.39%. Calcd for $C_{24}H_{20}N_2O_3$: C, 74.98; H, 5.24; N, 7.29%; M, 384.

13: Yield 62%; colorless prisms (benzene-hexane); mp 229—230 °C; IR (KBr): 1700 and 1630 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=1.16 (m, 1H, 5-H), 1.7—2.1 (m, 4H, 4-, 4'-, 4a-, and 5'-H), 3.08 (dd, 1H, 10-H, $J_{9,10}$=7.6 and $J_{6,10}$=3.4 Hz), 3.2—3.4 (m, 3H, 3-, 3'-, and 6-H), 4.07, 5.20 (2d, 1H each, -CH_2-Ph, J_{gem}=13.6 Hz), 6.26 (dd, 1H, 7-H, $J_{6,7}$=5.7 and $J_{7,8}$=9.0 Hz), 6.86 (d, 1H, 8-H, $J_{7,8}$=9.0 Hz), and 7.1—7.5 (m, 10H, phenyl protons); MS *m/z* (relative intensity) 412 (M^+, 18), 383, 357, 321, 252, 239 (M^+—NPMI, 16), 210 (23), 173 (NPMI$^+$, 16), 145 (6), 119 (PhNCO$^+$, 14), 105 (Ph-CH=NH$^+$, 51), 91 ($C_7H_7^+$, base peak), 77 (48).

Found: C, 75.70; H, 5.89; N, 6.89%. Calcd for $C_{25}H_{24}N_2O_3$: C, 75.70; H, 5.89; N, 6.79%; M, 412.

Dehydrogenation of Fused 1,3-Cyclohexadiene Systems 5, 10, and 11 to Benzo-Fused Heterocycles 14, 15, and 16. Typical Procedure: A solution of **4a** (300 mg, 1.4 mmol) in xylene (20 mL) in the presence of 10% Pd/C (150 mg) was heated under reflux for one day, the Pd/C was filtered off, and the filtrate was evaporated to dryness. The residue was chromatographed on silica gel (chloroform) to give 291 mg (98%) of 2-phenylphthalimidine (**14a**).

14a: Colorless plates (ethanol); mp 160—162 °C (lit,[12] mp 166—167 °C); IR (KBr): 1675 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=4.65 (s, 2H, 3-H) and 7.0—7.9 (m, 9H, 4-, 5-, 6-, and 7-H and phenyl protons); MS *m/z* 209 (M^+).

14b: Yield 94%; colorless needles (hexane); mp 85—88 °C (lit,[12] mp 90 °C); ^1H NMR ($CDCl_3$) δ= 4.25 (s, 2H, 3-H), 4.82 (s, 2H, -CH_2-Ph), 7.30 (br s, 5H, phenyl protons), 7.3—7.5 (m, 3H, 4-, 5-, and 6-H), and 7.88 (m, 1H, 7-H); MS *m/z* 223 (M^+).

14c: Yield 89%; colorless plates (hexane); mp 135—136 °C; IR (KBr): 1680 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=4.30 (s, 2H, -CH_2-Ph), 4.76 (s, 2H, 3-H), 7.2 (br s, 5H, phenyl protons), 7.3 (br s, 5H, phenyl protons), 7.4 (m, 2H, 5- and 6-H), and 7.9 (m, 1H, 7-H); MS *m/z* (relative intensity) 299 (M^+, base peak), 208 (M^+—C_7H_7, 43), 195 (29), 165 (52), 91 ($C_7H_7^+$, 71).

Found: C, 84.52; H, 5.88; N, 4.80%. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68%; M, 299.

14d: Yield 90%; colorless prisms (hexane); mp 116—117 °C; IR (KBr): 1680 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=2.22 (s, 3H, -CH_3), 4.13 (s, 2H, -CH_2-Ph), 4.77 (s, 2H, 3-H), 7.1—7.4 (m, 2H, 5- and 6-H), 7.27 (br s, 5H, phenyl protons), and 7.67 (m, 1H, 7-H); MS *m/z* (relative intensity) 237 (M^+, base peak), 146 (M^+—C_7H_7, 41), 133 (34), 91 ($C_7H_7^+$, 94), 77 (32), 65 (38).

Found: C, 80.75; H, 6.47; N, 5.90%; Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.91%; M, 237.

14e: Yield 95%; colorless needles (hexane-benzene); mp 138.5—139.5 °C; IR (KBr): 1670 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=3.44 (s, 3H, -CH_3), 4.50 (s, 2H, 3-H), 7.54 (br s, 5H, phenyl protons), 7.6 (m, 2H, 5- and 6-H), and 7.9 (m, 1H, 7-H); MS *m/z* (relative intensity) 223 (M^+, base peak), 194 (72), 165 (38), 91 ($C_7H_7^+$, 55).

Found: C, 80.96; H, 5.90; N, 6.44%. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27%; M, 223.

Heating of **10** in xylene under reflux in the presence of Pd/C for 3 d gave similarly **15** in 90% yield.

15: Colorless needles (hexane); mp 67—69 °C (lit,[10] mp 69—71 °C); IR (KBr): 1640 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=5.25 (s, 2H, -CH_2-Ph), 6.50 (d, 1H, 4-H, J=7 Hz), 7.13 (d, 1H, 3-H, J=7 Hz), 7.4 (br s, 5H, phenyl protons), 7.5—7.8 (m, 3H, 5-, 6-, and 7-H), and 8.5 (m, 1H, 8-H); MS *m/z* 235 (M^+).

16: Colorless prisms (hexane-benzene); mp 83—86 °C lit,[9] mp 82—85 °C); IR (KBr): 1635 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=1.6—2.0 (m, 2H, 4-H), 2.75 (t, 2H, 3-H, J=7 Hz), 3.21 (t, 2H, 5-H, J=7 Hz), 4.90 (s, 2H, -CH_2-Ph), 7.1—7.6 (m, 8H, 6-, 7-, and 8-H and phenyl protons), and 7.95 (m, 1H, 9-H); MS *m/z* 251 (M^+).

One-Pot Preparation of Benzo-Fused Heterocycles from Amides 8 and 9. Typical Procedure: A solution of **8** (500 mg, 1.77 mmol) in toluene (20 mL) in the presence of 10% Pd/C (500 mg) was refluxed for one day and the solvent was evaporated to dryness. The residure was chromatographed on silica gel to give 190 mg (47%) of **14d** and 170 mg (43%) of **17** as benzene and benzene-chloroform (1:1) eluents, respectively.

17: Yellow oil; IR (Neat): 1640 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=2.84 (t, 2H, 3-H, J=7 Hz), 3.44 (t, 2H, 4-H, J=7 Hz), 4.74 (s, 2H, -CH_2-Ph), 7.1—7.4 (m, 8H, 5-, 6-, and 7-H and phenyl protons), and 8.12 (m, 1H, 8-H); MS *m/z* 237 (M^+).

The above ^1H NMR spectral data were identical with the reported ones.[9]

18: Colorless plates (hexane); mp 79—80 °C; IR (KBr): 1640 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ=2.62 (s, 3H, -CH_3), 2.85 (t, 2H, 3-H, J=7 Hz), 3.44 (br t, 2H, 4-H, J=7 Hz), 4.76 (s, 2H, -CH_2-Ph), 7.2—7.4 (m, 7H, 6- and 7-H and phenyl protons), and 8.0 (m, 1H, 8-H); MS *m/z* (relative intensity) 251 (M^+, base peak), 174 (M^+—Ph, 18), 160 (M^+—C_7H_7, 31), 147 (26), 132 (30), 119 (PhCH_2CH=NH$^+$, 15), 104 (45), 91 (C_7H_7, 92), 77 (58).

Found: C, 81.52; H, 6.88; N, 5.69%. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57%; M, 251.

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