

Selected Paper

Diels–Alder Reaction of Cyclopentadienone Acetal with Pyrrole and Indole

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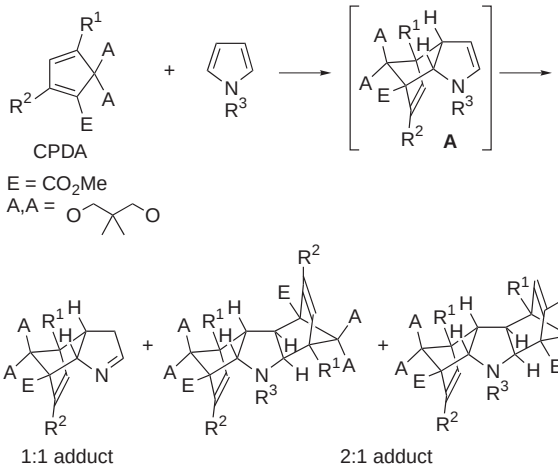
Diels–Alder reactions of a cyclopentadienone acetal with aromatic heterocycles, such as pyrrole or indole, took place with the latter acting as a 2π dienophile. The reaction gave a polycyclic heterocycle in good yield regioselectively. Analysis of the frontier molecular orbitals showed that inverse electron demand interactions control the regioselectivity.

The Diels–Alder reaction involving heterocyclic compounds is a powerful method for the construction of polycyclic heterocycles. Five-membered heterocyclic dienes, such as pyrroles, have been known as important dienes that participate in Diels–Alder reaction as a 4π component.[1,2] The heterocyclic diene, however, does not readily react as a 2π dienophilic component in the Diels–Alder reaction because it is electron-rich and aromatic, and chemical or physical activation is required for such a reaction. For instance, the Diels–Alder reaction of pyrroles takes place with acyclic dienes or *o*-benzoquinones only when the nitrogen atom has an electron-withdrawing group such as a sulfonyl group or an acyl group.[3,4] An entropically favored intramolecular reaction may take place more readily but may still require high reaction temperatures.[5,6] Examples of Diels–Alder reactions of 1*H*-pyrroles are scarce,[7] and, to the best of our knowledge, there are no cases involving unsubstituted 1*H*-pyrrole itself. We, herein, report an efficient Diels–Alder reaction of a substituted cyclopentadienone acetal (CPDA) with indole or pyrrole, in particular 1*H*-pyrrole.

CPDA has been known as a reactive 4π component for the Diels–Alder reaction for some time,[8] but the synthetic scope of the reaction has been rather narrow due to the scarcity of CPDA derivatives. We recently developed a method for the synthesis of new CPDA derivatives that serve as useful dienes toward some olefins.[9,10] We, therefore, decided to examine the Diels–Alder reactivity of a new CPDA towards pyrrole and indole.

Results and Discussion

The Diels–Alder reaction with 1*H*-pyrrole is described first. Both **1** and the pyrrole being cyclic dienes, it was not obvious whether or not these unactivated dienes would react and how they would react with each other. The reaction of CPDA **1** with one equivalent of 1*H*-pyrrole (**2**) was too slow to be useful. However, when **1** was stirred in **2** used as solvent (100 equiv) at ambient temperature, the expected 1:1 Diels–Alder adduct was obtained as a hydrolytically unstable imine product **3** in 92% yield (Eq. 1). We also obtained a small amount of a 2:1 adduct **4**.



(1)

CPDA (R^1, R^2)	pyrrole (R^3; eq.)	conditions	yield			
			1:1 adduct	2:1 adduct		
1 (Ph, E)	**2** (H; 100)	rt, 16 h	92% (**3**)	6% (**4**)	nd	(**5**)
1 (Ph, E)	**2** (H; 14)	rt, 16 h	59% (**3**)	40% (**4**)	nd	(**5**)
6 ($SiMe_3$, E)	**2** (H; 100)	rt, 24 h	94% (**7**)	nd (**8**)	nd	(**9**)
10 ($SiMe_3$, H)	**2** (H; 100)	100 °C, 24 h	nd (**11**)	nd (**12**)	nd	(**13**)
1 (Ph, E)	**14** (Me; 14)	100 °C, 16 h	nd	72% (**15**)	22%	(**16**)

nd: not detected

The formation of products **3** and **4** indicates the formation of a simple 1:1 Diels–Alder adduct **A** as an initial product, which underwent rapid enamine/imine isomerization to **3** before reacting a second time with **1**. When a smaller amount of **1** (14 equiv) was used, the yield of the 2:1 adduct increased to 40% at the expense of **3**, which suggests that isomerization from adduct **A** to compound **3** and the double Diels–Alder addition compete with each other.

The Diels–Alder reaction with **2** also proceeded with CPDA having a trimethylsilyl substituent **6** to give the 1:1 adduct **7** in 94% yield. However, neither CPDA **10** nor 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene reacted with **2**, which suggests that the high reactivity of compounds **1** and **6** originates from the presence of the two ester groups.

The structures of the products provide a few interesting mechanistic details. First, CPDA having two ester groups is

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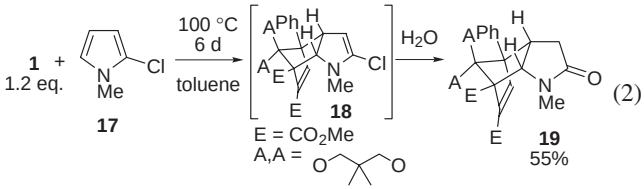
a quite reactive electron-deficient diene, to which pyrrole reacts as a 2π-electron dienophile rather than as a 4π-diene. Second, both the first and the second Diels–Alder reactions took place *endo*-selectively (Fig. 1a) as shown by NMR analysis of **3** and **4**.[11] This selectivity is not unexpected in light of steric hindrance of the acetal group in addition to the secondary orbital interactions.[12] Third, the results indicate that the Diels–Alder reaction of 1*H*-pyrrole first generates an enamine product such as adduct **A**, which either undergoes spontaneous isomerization to a potentially unstable imine, such as compound **3**, or undergoes further intermolecular reactions. This complexity in the reaction pathways is likely the reason why there are no reports of a Diels–Alder reaction involving 1*H*-pyrrole in the literature. In addition, the fact that an excess of compound **2** cannot compete effectively with intermediate **A** in the Diels–Alder reaction indicates that aromatic pyrrole **2** is indeed a quite unreactive dienophile.

From the energy diagram of the frontier molecular orbital (FMO) interactions (Fig. 1b), the LUMO of the diene **1** and the HOMO of the pyrrole **2** interact with each other, and therefore, that the reaction falls is an inverse electron demand Diels–Alder reaction allowing pyrrole to act as a dienophile.[12] Due to the interaction, the observed regioselectivity (**TS-1** leading to **A**) agrees with the selectivity expected on the basis of the FMO coefficients of the reacting carbon atoms (Fig. 1b). The regioselectivity of the second Diels–Alder reaction between adduct **A** (enamine) and the diene **1** through **TS-2** leading to the 2:1 adducts also conforms to the standard FMO rule.[13]

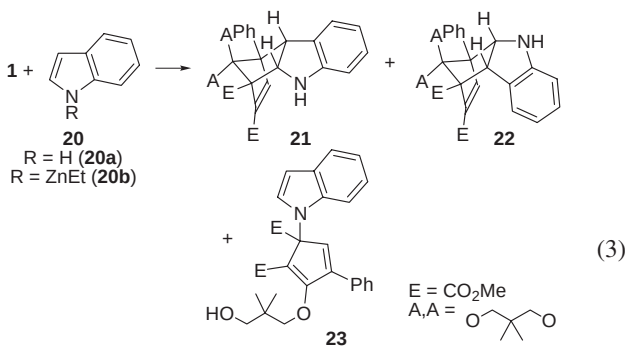
Based on the above discussion, 1-methylpyrrole (**14**) will give a 2:1 adduct, rather than a 1:1 adduct. Indeed, **14** reacted twice with **1**, to give two regioisomeric 2:1 adducts **15** (72%) and **16** (22%). Both were found to be *endo*-adducts. Note the formation of isomer **5** was not observed in the reaction with 1*H*-pyrrole (less than several percent at most). The exact reasons for the formation of compound **16** are unclear. However, the less selectivity may be caused by the higher reaction temperature that was required to activate substrate **14**, which has a low reactivity. The lower reactivity of 1-methylpyrrole, compared to the unsubstituted congener, may be due to the steric interaction between the 1-methyl group and the ester (E) substituent in **1** in the transition state of the Diels–Alder reaction (See Fig. 1a).

Hoping to control the reaction and to produce a stable product, we examined the reaction of **1** with 2-chloro-1-methylpyrrole (**17**) (Eq. 2). The initial 1:1 adduct **18** was unreactive and, upon aqueous workup, the halo enamine moiety underwent spontaneous hydrolysis to give the expected lactam **19** with a yield of 55%.



(2)

Unprotected indole **20a** also underwent a Diels–Alder reaction with **1**. Because the adducts do not possess a reactive enamine moiety, **21** and **22** were isolated as they were formed in 76 and 17% yield, respectively (Eq. 3). While attempting to accelerate the cycloaddition reaction under the influence of a Lewis acidic metal, the zincated indole **20b** was found to react much more rapidly than the parent indole (room temperature vs 80 °C).[14,15] The reaction, however, afforded the Diels–Alder adduct **21** only as a minor product (29%), and the substitution product **23** was the major product (55%).



(3)

20	conditions	yield		
		21	22	23
20a (10 eq.)	80 °C, 12 h, toluene	76%	17%	nd
20b (1.1 eq.)	rt, 5 h, CH_2Cl_2	29%	nd	55%

nd: not detected

Conclusion

Substituted CPDA having two ester groups is a reactive diene that undergoes Diels–Alder reactions with pyrrole and indole. The present report describes the use of unsubstituted 1*H*-pyrrole in a Diels–Alder reaction and a few ways to control

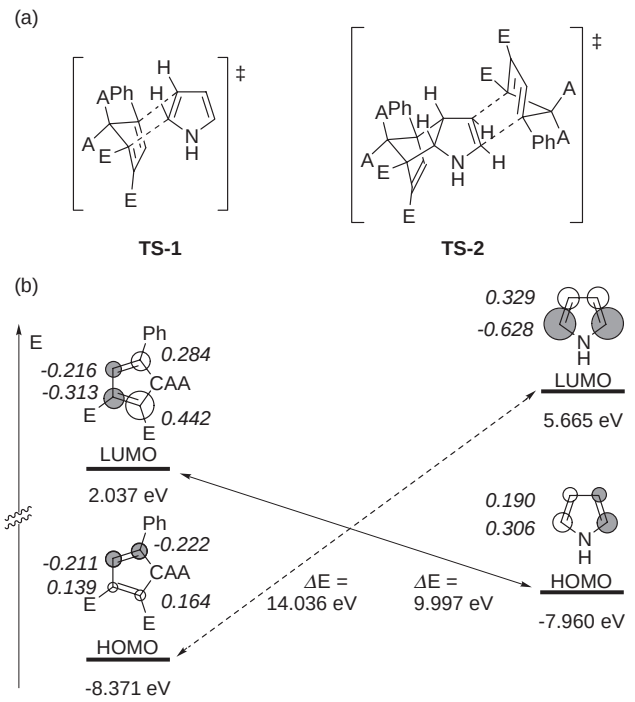


Fig. 1. (a) Structures of the transition states for the major adducts with the bonds being formed shown as broken lines. The transition structures **TS-1** and **TS-2** result in the formation of 1:1 adduct **3** and 2:1 adduct **4**, respectively. (b) Frontier molecular orbitals of **1** and **2** (HF/6-31G*). Orbital coefficients are shown in italic.

the reactivity of pyrroles in Diels–Alder reactions, which also suggested reasons why 1*H*-pyrrole did not appear to be a useful dienophile in Diels–Alder reactions.

Experimental

General. IR spectra were obtained on an ASI Applied Systems REACT IR1000 equipped with an attenuated total reflection (ATR) instrument. NMR spectra were obtained on JEOL ECX-400 and ECA-500 spectrometers. ^{1}H NMR spectra in $CDCl_3$ were referenced internally to tetramethylsilane as a standard. ^{13}C NMR spectra in $CDCl_3$ were referenced to the solvent resonance. Nuclear Overhauser effects were measured by the DPFGSE-NOE method.[16] The three-bond coupling constant ($^3J_{CH}$) was determined as reported.[9,17] Mass spectra were recorded using a JEOL JMS-T100LC spectrometer and polyethylene glycol (MW 600) as a calibration standard. Melting points were determined on a Mel-Temp capillary melting-point apparatus and were uncorrected. The X-ray diffraction study was carried out on a MacScience DIP2030 Imaging Plate diffractometer. Space group determination, structural solution, and refinement were performed using the maXus software program. Ab initio calculations were performed using a Spartan 04, 1.0.3 package (Wavefunction).

Materials. CPDA **1**[9] and 2-chloro-1-methylpyrrole[18] were synthesized as reported. Pyrrole, 1-methylpyrrole, and indole were purchased and purified by distillation or recrystallization. All solvents were purified by distillation and dried on molecular sieves 4 Å.

Diels–Alder Reaction of CPDA 1 and 1*H*-Pyrrole (2). A mixture of CPDA **1** (35.8 mg, 100 μmol) and 1*H*-pyrrole (**2**) (0.694 mL, 10.0 mmol) was stirred at rt for 16 h. After removal of the excess 1*H*-pyrrole in vacuo, NMR analysis of the crude materials using dibromomethane as an internal standard showed that the 1:1 adduct **3** and the 2:1 adduct **4** were obtained in 92% (91.9 μmol) and 6% yield (6.1 μmol), respectively. When the reaction was carried out between 35.8 mg of CPDA **1** (100 μmol) and 0.100 mL of 1*H*-pyrrole (**2**) (1.44 mmol), the 1:1 adduct **3** and the 2:1 adduct **4** were obtained in 59% (27.4 mg, 58.9 μmol) and 40% (15.9 mg, 20.3 μmol) yield, respectively, after purification by silica gel column chromatography (eluent: 30% ethyl acetate/hexane then 5% methanol/ethyl acetate). Physical data of **3**:[11] mp 83–84 °C (dec); IR (powder) 3213, 2954, 1731, 1713, 1617, 1603, 1501, 1436, 1358, 1293, 1275, 1246, 1223, 1164, 1104, 1071, 1055, 1023, 976, 903, 770, 758, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.44 (s, 3H), 0.72 (s, 3H), 1.93 (dddd, J = 1, 4, 4, 19 Hz, 1H), 2.51 (dd, J = 11, 19 Hz, 1H), 3.04 (dd, J = 1, 11 Hz, 1H), 3.27 (dd, J = 1, 11 H, 1H), 3.36 (d, J = 11 Hz, 1H), 3.52 (d, J = 11 Hz, 1H), 3.61–3.68 (m, 1H), 3.73 (s, 3H), 3.88 (s, 3H), 5.55–5.59 (m, 1H), 7.06 (s, 1H), 7.29–7.34 (m, 1H), 7.34–7.39 (m, 3H), 7.48–7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 23.0, 30.3, 38.4, 39.8, 52.0, 52.4, 66.6, 72.5, 72.6, 81.4, 119.3, 127.9, 128.3, 129.1, 135.9, 136.4, 145.3, 163.1, 168.3, 170.5; MS (APCI) calcd for $C_{24}H_{28}NO_6$ ($[M + H]^+$) 426.2, found 426.2. Physical data of **4**:[11] mp 249–250 °C (dec); IR (powder) 3257, 2956, 1733, 1713, 1603, 1439, 1341, 1281, 1227, 1164, 1109, 1098, 762, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.36 (s, 3H), 0.39 (s, 3H), 0.55 (s, 3H), 0.63 (s, 3H), 2.76 (d, J = 11 Hz, 1H), 2.95 (d, J = 11 Hz, 1H), 3.07 (d, J = 11 Hz, 1H), 3.09 (d, J = 11 Hz, 1H), 3.16 (d, J = 11 Hz, 1H), 3.20 (dd, J = 4, 8 Hz, 1H), 3.25 (d, J = 11 Hz, 1H), 3.26 (d, J = 11 Hz, 1H), 3.29 (d, J = 11 Hz, 1H), 3.31 (s, 3H), 3.75 (s, 3H), 3.83 (s, 3H), 3.87 (dd, J = 4, 8 Hz, 1H), 3.89 (s, 3H), 4.53 (d, J = 8 Hz, 1H), 4.59 (d, J = 8 Hz, 1H), 7.13 (s, 1H), 7.24–7.45 (m, 8H), 7.55 (s, 1H), 7.65 (d, J = 8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5, 22.6, 22.8, 22.9, 30.2, 30.3, 48.3, 49.5, 51.8, 52.1, 52.1, 68.3, 68.3, 68.8, 69.2, 71.3, 71.5, 72.1, 72.3, 72.4, 77.3, 77.8, 118.4, 119.1, 127.4, 127.4, 127.7, 128.2, 129.0, 129.7, 135.4, 136.1, 136.2, 136.6, 146.8, 149.0, 164.9, 165.3, 169.9, 171.2; MS (APCI) calcd for $C_{44}H_{50}NO_{12}$ ($[M + H]^+$) 784.3, found 784.3.

Diels–Alder Reaction of CPDA 6 and 1*H*-Pyrrole (2). A mixture of CPDA **6** (35.5 mg, 100 μmol) and 1*H*-pyrrole (**2**) (0.694 mL, 10.0 mmol) was stirred at rt for 24 h. After removal of the excess 1*H*-pyrrole in vacuo, NMR analysis of the crude materials using 1,1,2,2-tetrachloroethane as an internal standard showed that the 1:1 adduct **7** was obtained in 94% yield (93.5 μmol). Physical data of **7** (analyzed as crude materials): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.16 (s, 9H), 0.68 (s, 3H), 1.09 (s, 3H), 1.85 (ddd, J = 3, 5, 19 Hz, 1H), 2.39 (dd, J = 11, 19 Hz, 1H), 3.04 (ddd, J = 5, 8, 11 Hz, 1H), 3.30 (dd, J = 2, 12 Hz, 1H), 3.42 (dd, J = 2, 12 Hz, 1H), 3.54 (d, J = 12 Hz, 1H), 3.66 (s, 3H), 3.82 (s, 3H), 3.91 (d, J = 12 Hz, 1H), 5.46–5.49 (m, 1H), 6.91 (s, 1H), 7.27–7.28 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −1.62, 22.7, 23.7, 29.4, 39.2, 39.5, 51.8, 52.2, 54.9, 66.2, 72.5, 72.5, 82.4, 121.5, 137.8, 146.2, 163.6, 168.0, 172.4.

Diels–Alder Reaction of CPDA 1 and 1-Methylpyrrole (14). A mixture of CPDA **1** (35.8 mg, 100 μmol) and 1-methylpyrrole (**14**) (0.128 mL, 1.44 mmol) was stirred at 100 °C. After removal of 1-methylpyrrole in vacuo, purification by silica gel column chromatography (eluent: 3–5% ethyl acetate/dichloromethane) afforded the 2:1 adduct **15** (28.7 mg, 36.0 μmol) and **16** (8.4 mg, 11 μmol) in 72 and 22% yield, respectively. Physical data of **15**:[11] mp 202–203 °C (dec); IR (powder) 3257, 2956, 2873, 1725, 1611, 1436, 1270, 1227, 1167, 1106, 1063, 762, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.30 (s, 3H), 0.33 (s, 3H), 0.53 (s, 3H), 0.67 (s, 3H), 2.06 (s, 3H), 2.65 (d, J = 3 Hz, 1H), 2.67 (d, J = 3 Hz, 1H), 3.09 (d, J = 8 Hz, 1H), 3.11 (d, J = 8 Hz, 1H), 3.14–3.20 (m, 4H), 3.33 (d, J = 11 Hz, 1H), 3.35 (s, 3H), 3.73 (s, 3H), 3.77 (s, 3H), 3.92 (s, 3H), 3.97 (dd, J = 3, 8 Hz, 1H), 4.28 (d, J = 8 Hz, 1H), 4.65 (d, J = 7 Hz, 1H), 7.22–7.32 (m, 6H), 7.37 (t, J = 8 Hz, 2H), 7.45 (s, 1H), 7.45–7.51 (br, 1H), 7.65 (d, J = 8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 22.8, 22.9, 22.9, 30.2, 30.3, 35.9, 47.6, 48.5, 51.6, 51.8, 51.9, 52.1, 68.1, 68.1, 68.7, 68.8, 72.0, 72.1, 72.2, 72.2, 75.2, 76.1, 118.0, 118.3, 127.2, 127.4, 127.8, 127.9, 128.1, 129.8, 135.7, 136.2, 136.6, 137.1, 145.1, 145.2, 163.5, 165.3, 169.8, 171.4; MS (APCI) calcd for $C_{45}H_{52}NO_{12}$ ($[M + H]^+$) 798.3, found 798.3. Physical data of **16**: mp 204–205 °C (dec); IR (powder) 2956, 2879, 1723, 1436, 1275, 1210, 1167, 1100, 1067, 917, 760, 695 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.27 (s, 6H), 0.61 (s, 6H), 2.46 (s, 3H), 2.61 (d, J = 11 Hz, 2H), 3.11 (d, J = 11 Hz, 2H), 3.18 (s, 4H), 3.22 (d, J = 7 Hz, 2H), 3.74 (s, 6H), 3.81 (s, 6H), 4.49 (d, J = 6 Hz, 2H), 6.93 (t, J = 7 Hz, 4H), 7.03–7.09 (m, 6H), 7.51 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 23.0, 30.4, 33.7, 49.0, 51.7, 51.9, 67.0, 68.5, 71.9, 72.1, 75.0, 118.7, 127.1, 127.7, 129.0, 134.5, 136.7, 145.9, 163.1, 171.1; HRMS (APCI) calcd for $C_{45}H_{52}NO_{12}$ ($[M + H]^+$) 798.3490, found 798.3452.

Diels–Alder Reaction of CPDA 1 and 2-Chloro-1-methylpyrrole (17). A solution of CPDA **1** (179 mg, 500 μmol) and 2-chloro-1-methylpyrrole (**17**) (48.4 mg, 420 μmol) in toluene (2.0 mL) was stirred at 100 °C for 6 days. After removal of excess substrate and solvent in vacuo, purification by silica gel column chromatography (eluent: 40% ethyl acetate/hexane) afforded the 1:1 adduct **19** (84.5 mg, 186 μmol) in 55% yield. Physical data of **19**: mp 254–255 °C (dec); IR (powder) 2962, 1709, 1688, 1597, 1439, 1360, 1296, 1216, 1098, 1061, 961, 897, 789, 770,

700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.42 (s, 3H), 0.72 (s, 3H), 1.83 (dd, $J = 5$, 18 Hz, 1H), 2.41 (dd, $J = 11$, 18 Hz, 1H), 2.88 (s, 3H), 3.06 (d, $J = 11$ Hz, 1H), 3.24 (d, $J = 11$ Hz, 1H), 3.32 (d, $J = 11$ Hz, 1H), 3.37 (d, $J = 11$ Hz, 1H), 3.74 (s, 3H), 3.84 (s, 3H), 3.79–3.85 (m, 1H), 4.90 (d, $J = 9$ Hz, 1H), 7.14 (s, 1H), 7.36–7.41 (m, 3H), 7.49 (d, $J = 7$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 22.6, 29.3, 30.0, 31.0, 35.9, 51.6, 52.0, 66.2, 66.5, 66.6, 72.2, 72.2, 118.2, 127.8, 128.2, 128.5, 134.5, 135.5, 145.8, 162.6, 170.9, 174.8; Anal. Calcd for $C_{25}H_{29}NO_7$: C, 65.92; H, 6.42; N, 3.08%. Found: C, 65.72; H, 6.45; N, 2.91%.

X-ray Crystallographic Study of 19. Suitable crystals of **19** were obtained by recrystallization from dichloromethane/pentane. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre: Deposition number CCDC-600526. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from CCDC, 12, Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk). Selected data: $C_{25}H_{29}NO_7$, monoclinic, $C2/c$, $a = 19.5980(14)$ Å, $b = 11.5910(9)$ Å, $c = 21.2100(7)$ Å, $\beta = 106.249(4)^\circ$, $V = 4625.6(5)$ Å^3, $Z = 8$, $D_{calcd} = 1.308$ g cm^{-3}, $R = 0.051$, $R_w = 0.136$.

Diels–Alder Reaction of CPDA 1 and 1*H*-Indole (20a). A solution of CPDA **1** (71.7 mg, 200 µmol) and 1*H*-indole (**20a**) (234 mg, 2.00 mmol) in toluene (0.400 mL) was stirred at 80 °C for 12 h. After removal of solvent in vacuo, purification by silica gel column chromatography (eluent: 10–20% ethyl acetate/hexane) afforded the Diels–Alder adducts **21** (72.5 mg, 152 µmol) mol) and **22** (16.4 mg, 39.4 µmol) in 76 and 17% yield, respectively. Physical data of **21**:[11] mp 184–185 °C (dec); IR (powder) 3386, 2952, 1729, 1704, 1603, 1486, 1463, 1441, 1335, 1291, 1216, 1169, 1069, 1040, 980, 753, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.44 (s, 3H), 0.71 (s, 3H), 2.97 (d, $J = 11$ Hz, 1H), 3.33 (d, $J = 2$ Hz, 1H), 3.43 (s, 3H), 3.44 (d, $J = 11$ Hz, 1H), 3.86 (s, 3H), 4.93 (d, $J = 9$ Hz, 1H), 5.29 (d, $J = 9$ Hz, 1H), 6.34 (d, $J = 8$ Hz, 1H), 6.58 (td, $J = 1$, 8 Hz, 1H), 6.88 (t, $J = 7$ Hz, 1H), 7.18 (s, 1H), 7.29 (d, $J = 8$ Hz, 1H), 7.32–7.37 (m, 1H), 7.37–7.43 (m, 3H), 7.59–7.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 23.1, 30.6, 51.3, 51.5, 52.1, 64.6, 67.2, 68.5, 72.4, 72.6, 108.8, 118.3, 118.3, 126.8, 127.1, 127.8, 128.3, 128.4, 128.9, 135.6, 136.0, 146.2, 153.1, 162.6, 171.4; HRMS (APCI) calcd for $C_{28}H_{30}NO_6$ ($[M + H]^+$) 476.2073, found 476.2091. Physical data of **22**: mp 139–140 °C (dec); IR (powder) 3404, 3054, 1722, 1711, 1617, 1495, 1455, 1416, 1337, 1245, 1223, 1094, 1011, 909, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.49 (s, 3H), 0.72 (s, 3H), 2.95 (d, $J = 11$ Hz, 1H), 3.32 (d, $J = 11$ Hz, 1H), 3.34 (d, $J = 11$ Hz, 1H), 3.44 (t, $J = 11$ Hz, 1H), 3.66 (s, 3H), 3.87 (s, 3H), 4.92 (d, $J = 9$ Hz, 1H), 5.19 (d, $J = 9$ Hz, 1H), 6.33 (d, $J = 8$ Hz, 1H), 6.36 (d, $J = 7$ Hz, 1H), 6.65 (d, $J = 7$ Hz, 1H), 6.80 (s, 1H), 6.85 (t, $J = 8$ Hz, 1H), 7.34–7.46 (m, 3H), 7.63 (d, $J = 8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 22.9, 30.4, 49.8, 51.8, 52.3, 63.6, 67.8, 68.5, 72.4, 72.7, 108.3, 117.4, 117.5, 124.1, 126.8, 127.8, 128.3, 128.3, 129.3, 134.2, 135.6, 147.1, 153.4, 164.2, 171.4; MS (APCI) calcd for $C_{28}H_{30}NO_6$ ($[M + H]^+$) 476.2, found 476.2.

Diels–Alder Reaction of CPDA 1 and Zincated Indole 20b. A solution of diethylzinc (1.1 M in dichloromethane; 54.5 µL, 60.0 µmol) was added to 1*H*-indole (**20a**) (6.44 mg, 55.0 µmol) and stirred at rt for 12 h. After addition of CPDA **1** (17.9 mg, 50.0 µmol), the mixture was stirred at rt for another 5 h. After aqueous workup, purification by silica gel column chromatography (eluent: 10–40% ethyl acetate/hexane) afforded the Diels–Alder adduct **10** (6.70 mg, 14.1 µmol) in 28% yield and indolyl cyclopentadiene **23** (13.0 mg, 27.3 mmol) in 55% yield. Physical data of **23**: mp 138–139 °C; IR (powder) 3253, 2952, 2925, 1723, 1710, 1692, 1602, 1459, 1434, 1241, 1052, 1015, 743, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (s, 3H), 0.88 (s, 3H), 2.57 (m, 1H), 3.35–3.45 (m, 2H), 3.64 (s, 3H), 3.84 (s, 3H), 4.01 (d, $J = 10$ Hz, 1H), 4.05 (d, $J = 10$ Hz, 1H), 6.48 (d, $J = 3$ Hz, 1H), 6.94 (s, 1H), 7.08 (td, $J = 1$, 7 Hz, 1H), 7.12 (td, $J = 1$, 7 Hz, 1H), 7.17 (d, $J = 4$ Hz, 1H), 7.25 (d, $J = 8$ Hz, 1H), 7.38–7.43 (m, 3H), 7.55–7.61 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5, 21.5, 37.3, 51.7, 53.7, 68.5, 74.6, 80.7, 101.9, 112.0, 114.1, 120.0, 121.3, 121.7, 128.0, 128.1, 128.7, 129.5, 129.6, 131.3, 135.9, 136.5, 144.7, 162.9, 168.2, 170.6; MS (APCI) calcd for $C_{28}H_{30}NO_6$ ($[M + H]^+$) 476.2, found 476.2.

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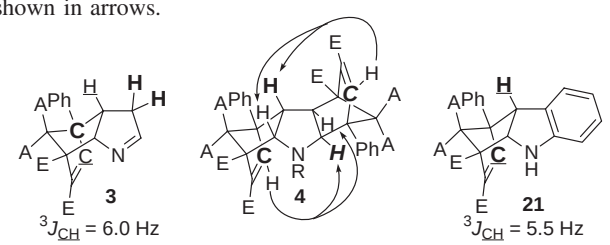

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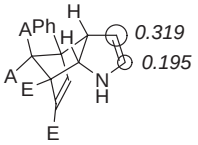
13 HOMO coefficients of **A** are calculated as shown at HF/6-31G* level, which indicates the preference for the 2:1 adduct **4** over **5**.



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