with peptide carbonyls and the remaining ligands to cations and cocrystallized water molecules.

Acknowledgment. This research was supported in part by NIH Grant GM30902.

Supplementary Material Available: Anisotropic thermal parameters for non-hydrogen atoms, atomic coordinates of hydrogen atoms, bond lengths, and bond angles (5 pages); observed and calculated structure factors (12 pages). Ordering information is given on any current masthead page.

Diels–Alder Reaction of Dienes Having Stereogenic Allylic Substituents: Control of Diastereoface Selectivity by the Dienophile

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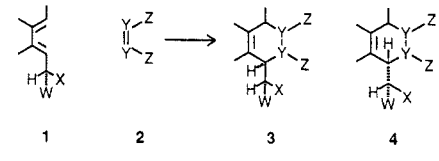
Abstract: The face selectivity of the Diels–Alder reaction of dienes having a stereogenic allylic carbon, as illustrated by structure **5**, has been examined. Whereas *N*-phenylmaleimide and maleic anhydride afforded adducts resulting from like topicity, tetracyanoethylene and 4-phenyl-1,2,4-triazoline-3,5-dione yielded products from unlike approach. The stereochemistries of the products have been established by NOE studies and in one case by an X-ray structure determination. Our results and those of other groups demonstrate that the dienophiles have a significant effect on the face selectivities observed. Recent computational methodologies applied to the face-selectivity problem by Houk and Hehre fail to account for our observations.

The diastereofacial selectivity of the Diels–Alder reaction has been the subject of two recent reviews.[1] The most common approach for obtaining facial selectivity in intermolecular cases is to link the diene or dienophile to a chiral auxiliary. Ideally, the auxiliary blocks one face of the diene or dienophile, a face-selective cycloaddition takes place, the auxiliary is removed, and one obtains an adduct enriched in one enantiomer. Rationalizations of relative topicity are usually based on a conformational analysis of the interaction of the auxiliary with the ground state of the substrate. The alternate approach to face selectivity is to incorporate a stereogenic center within the diene or dienophile, usually at an allylic position. The products of cycloaddition are diastereomers and remain so because the stereogenic center is built into the product. Attempts to rationalize the relative topicity of the Diels–Alder reaction in the presence of allylic centers have involved theoretical arguments. Houk has put forward models that involve calculation of the preferred conformer in cycloaddition transition states,[2] while Hehre has computed the favored electrostatic interactions of the ground states.[3] On the basis of a limited number of results, we had postulated an empirical rule that suggested that relative topicities for Diels–Alder reactions of chirally functionalized dienes and dienophiles should be of opposite sign.[4] In the present paper, we present more complete data covering the cycloaddition of a range of dienophiles with a group of related chirally substituted dienes. Our results and those of other recent reports are consistent with each other and will require a revision of the simple rules for predicting the effects of substituents on the face selectivity of the Diels–Alder reaction.

Results

Table I (Chart I) records the stereochemical outcomes of 20 Diels–Alder reactions carried out in our laboratory or reported in the literature where an acyclic diene of type **1** reacts with a dienophile of type **2** to produce diastereomeric adducts **3** (resulting from a like process) and **4** (resulting from an unlike process)[5] (Scheme I).

Scheme I



1 2 3 4

The first entry records our repetition of the original example (to the best of our knowledge) of a face-selective Diels–Alder reaction controlled by a chiral allylic substituent, namely the reaction of maleic anhydride (**6**) with (*E*)-2-hydroxy-3,5-hexadiene (**5a**).[6] The British group reported a single adduct obtained as

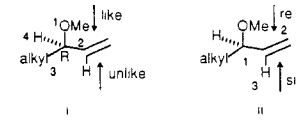
(1) (a) Helmchen, G.; Karge, R.; Weetman, J. *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer Verlag: New York, 1986; p 261. (b) Paquette, L. A. *Asymmetric Synthesis*, Ed. J. D. Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3B, p 455.

(2) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jager, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880–3882.

(3) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 663–666.

(4) Franck, R. W.; Argade, S.; Subramaniam, C. S.; Frechet, D. M.; *Tetrahedron Lett.* **1985**, *26*, 3187–3190.

(5) We use the Seebach–Prelog convention (Seebach, D.; Prelog, V., *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654–660) describing the relative topicities of the approach or addition to the face of an enantiomer, e.g. addition to the *si* face of the double bond with an adjacent *R* allylic center is unlike. Hehre uses "anti" for unlike and Houk applies "erythro" for unlike. To be consistent, we define the configuration of the allylic center by always assigning the sp^2 carbon of the double bond a higher priority than the sp^3 carbon attached to the allylic center (shown in i). Also, in defining the facial configuration of the double bond, we always assign the priority of the allylic carbon as 1 and the vinylic carbon as 2 (shown in ii).



i ii

(6) Heilbron, I. M.; Jones, E. R. H.; McCombie, J. T.; Weedon, B. C. L. *J. Chem. Soc.* **1945**, 88–90.

[†] Author to whom correspondence concerning the X-ray analysis of structure should be addressed.

[‡] Northeastern University.

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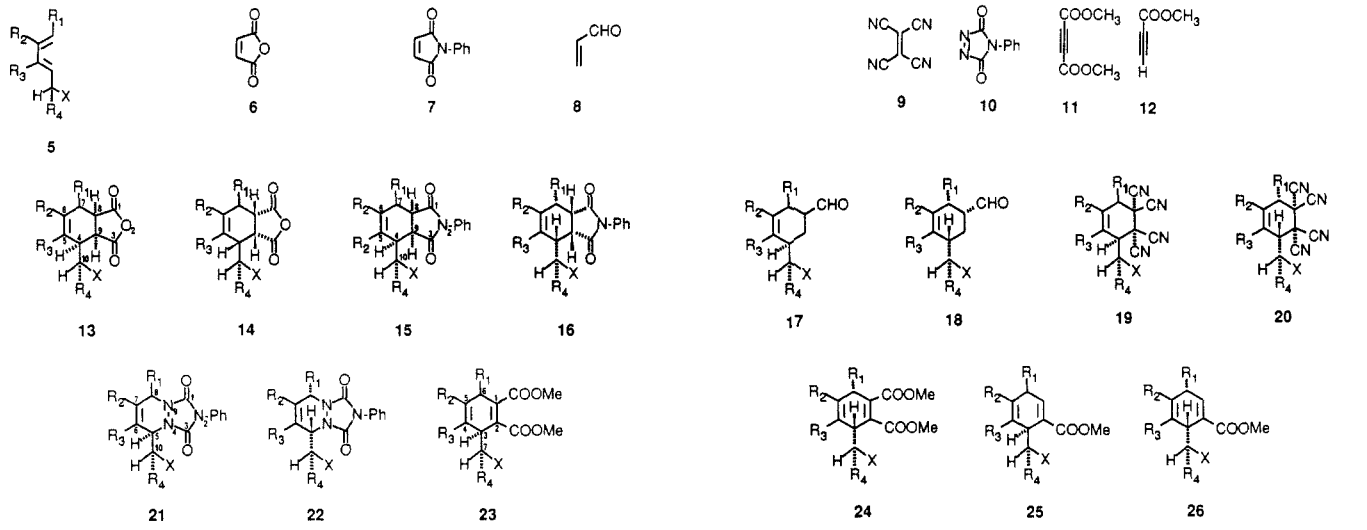
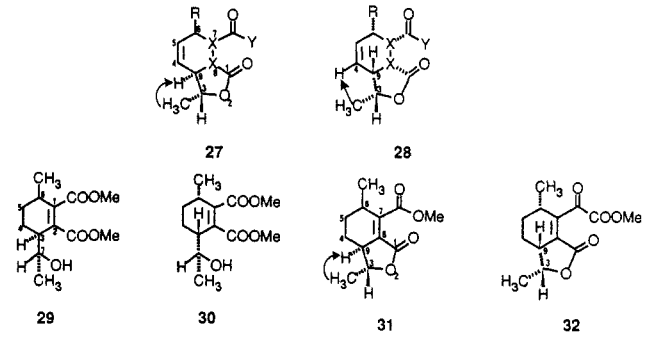
Chart I. Dienes, Dienophiles, and Initial Cycloaducts Listed in Table I[a]



[a] **a**: R_1 = H, R_2 = H, R_3 = H, R_4 = CH_3, X = OH. **b**: R_1 = H, R_2 = H, R_3 = H, R_4 = CH_3, X = OTMS. **c**: R_1 = H, R_2 = H, R_3 = H, R_4 = CH_3, X = OTBDMS. **d**: R_1 = CH_3, R_2 = H, R_3 = H, R_4 = CH_3, X = OH. **e**: R_1 = CH_3, R_2 = H, R_3 = H, R_4 = CH_3, X = OCH_3. **f**: R_1 = CH_3, R_2 = H, R_3 = H, R_4 = CH_3, X = OTMS. **g**: R_1 = $CH(OCH_3)CH_3$, R_2 = H, R_3 = H, R_4 = CH_3, X = OCH_3. **h**: R_1 = $CH(CH_3)_2$, R_2 = H, R_3 = OMOM, R_4 = CH_3, X = OH. **i**: R_1 = $CH(CH_3)_2$, R_2 = H, R_3 = OMOM, R_4 = CH_3, X = OTMS. **j**: R_1 = CN, R_2 = H, R_3 = OBn, R_4 = CH_2OBN, X = OH. **k**: R_1 = OTBDMS, R_2 = H, R_3 = H, R_4 = $(CH_2)_3OPMB$, X = OBn. **m**: R_1 = H, R_2 = OTBDMS, R_3 = H, R_4 = $CH(OTBDMS)CH_3$, X = NHCbz.

a lactonic acid where their crystallization process enriched the diastereomer ratio. We treated the crude adduct with diazomethane and found the ratio of like/unlike listed in the table. Prior ester formation between the anhydride and the free alcohol followed by intramolecular cycloaddition would have required a like process. To rule out this pathway as the reason for the like product, we repeated the sequence with the silyl ether of the dienol (entry 2) and observed an improved like process. In general, the tabulated results reveal that dienes with free hydroxyl groups give poorer selectivities than their silylated analogues. The favorable effect of silyl blocking groups in 3 + 2 cycloadditions has been noted by Trost.[7] Diene **5d** with maleic anhydride is reported to be not selective by Kessabi.[8] However, in our hands, diene **5d** (entry 4) exhibited modest like selectivity, similar to its reaction with *N*-phenylmaleimide (entry 7). Again, the selectivity was improved when the free OH of the diene was blocked (entries 6, 8, and 9). Extremely high face selectivities in the same like sense were observed by McDougal[9] and Reitz[10] (entries 11 and 12) with *N*-phenylmaleimide with chiral dienes bearing an additional 2-alkoxy group. Furthermore, McDougal observed like selectivity with acrolein (entry 13). In contrast to the consistent observation of preferred like selectivity of dienes **5b,c,e,f** with maleic anhydride and *N*-phenylmaleimide, diene **5e** and tetracyanoethylene (TCNE) afford the adduct derived from unlike addition (entry 14).[11] The doubly allylic diene **5g** also reacts with TCNE to give the product of unlike attack with enhanced selectivity (entry 15). Also, dienes **5d** and **5f** react with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD), favoring unlike attack (entries 16 and 17). Further examples of unlike attack in our series include cycloadditions with acetylenic dienophiles (entry 18). Kozikowski's program for the total synthesis of actinobolin was handicapped by the unlike selectivity of acetylenic dienophiles with complex allylically functionalized diene **5m** (entry 20).[12] The unlike selectivity produced in entry 19 with an acetylenic dienophile was in the desired sense for Kozikowski's forskolin synthesis.[13] Since Bartlett had reported that variation of solvent caused a reversal of face selectivity in the addition of

Chart II. Conversion Products Derived from Initial Adducts[a]



[a] **a**: R = H, X = CH, Y = OH; **b** R = H, X = CH, Y = OCH_3; **c** R = H, X = CH, Y = NHC_6H_5; **d** R = CH_3, X = CH, Y = NHC_6H_5; **e** R = CH_3, X = N, Y = NHC_6H_5.

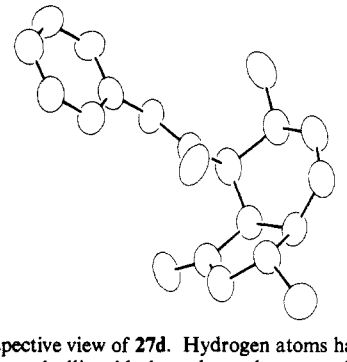


Figure 1. A perspective view of **27d**. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids have been drawn at 50% probability.

(7) Trost, B. M.; Lynch, J.; Renaut, P. *Tetrahedron Lett.* **1985**, *26*, 6313–6316.
(8) Kessabi, J. Thesis; Dr. IIIeme Cycle, L'Universite de Rennes, 1985.
(9) McDougal, P. G.; Rico, J. G.; VanDerveer, D. *J. Org. Chem.* **1986**, *51*, 4492–4494.
(10) Reitz, A. B.; Jordan, A. D., Jr.; Maryanoff, B. E. *J. Org. Chem.* **1987**, *52*, 4800.
(11) (a) Messager, J. C.; Toupet, L. *Acta Crystallogr., Sect. B: Struct. Sci.* **1986**, *B42*, 371–78. (b) Gree, R.; Kessabi, J.; Mosset, P.; Martelli, J.; Carrie, R. *Tetrahedron Lett.* **1984**, *25*, 3697–3700. Part of the confusion about rules for face selectivity stems from the 1984 report where the selectivity was reported to be like, but as corrected in 1986, the outcome was in fact from unlike approach.
(12) (a) Kozikowski, A. P.; Nieduzak, T. R. *Tetrahedron Lett.* **1986**, *27*, 819–822. (b) Kozikowski, A. P.; Konoike, T.; Nieduzak, T R. *J. Chem. Soc., Chem. Commun.* **1986**, 1350–1352. (c) Kozikowski, A. P.; Nieduzak, T. R.; Konoike, T.; Springer, J. P. *J. Am. Chem. Soc.* **1987**, *109*, 5167.
(13) Kozikowski, A. P.; Jung, S. H.; Springer, J. P. *J. Chem. Soc., Chem. Commun.* **1988**, 167. We thank Professor Kozikowski for a preprint of this work.

Table I. Relative Topicities of the Diels–Alder Reaction of a Series of Dienophiles with Dienes Bearing a Stereogenic Allylic Carbon

				products				
entry	diene	dienophile	% yield	like	(ratio)	unlike	structure	ref
1	**5a**	6	82.5	**13a**[a]	(2.7/1)	**14a**[a,b]	NOE	*c*, 6
2	**5b**	6	68.4	**13b**[a]	(4/1)	**14b**[a,b]	NOE	*c*
3	**5c**	6	64.9	**13c**	(4.5/1)	**14c**[b]	NOE	*c*
4	**5d**	6		**13d**[a,d]	(2.5/1)	**14d**[a,d]	X-ray	8, *c*
5	**5a**	7	53	**15a**[a]	(1.3/1)	**16a**[a]	NOE	*c*
6	**5b**	7	91.5	**15b**	(3.5/1)	**16b**	NOE	*c*
7	**5d**	7	78.3	**15d**[a]	(1.7/1)	**16d**	NOE, X-ray	*c*
8	**5e**	7		**15e**	(5/1)	**16e**	NOE	4
9	**5f**	7	74.5	**15f**	(7.3/1)	**16f**	NOE	4, *c*
10	**5h**	7		**15h**[e]	(5/1)	**16h**[e]		9
11	**5i**	7		**15i**	(99+)		X-ray	9
12	**5j**	7	51	**15j**	(99+)		*J* values	10
13	**5i**	8		**17**[f]	(en, 99+)			9
				18[f]	(ex, 99+)			
14	**5e**	9		**19e**	(1/2)	**20e**	X-ray	11
15	**5g**	9	89	**19g**	(1/5.7)	**20g**	X-ray	11
16	**5d**	10	97	**21d**[b,g]	(1/2.8)	**22d**	NOE	*c*
17	**5f**	10	92	**21f**[b]	(1/5.5)	**22f**	NOE	*c*
18	**5d**	11	71.5	**23d**	(1/2.7)	**24d**	NOE	*c*
19	**5k**	11	41	**23k**	(1/2)	**24k**		13
20	**5m**	12	85	**25m**[h]	(1/1.7)	**26m**	X-ray	12

[a] Unstable, cyclizes to the corresponding lactone. [b] Stereochemistry is not proven rigorously. [c] Present work. [d] The ratio shown was obtained in $CHCl_3$, and this result does not agree with the reported 1/1 ratio (ref 7). [e] The stereochemistry was not assigned. We are assuming the relative topicity. [f] The ratio of endo(1) to exo(1) was 93/7. [g] One additional minor compound (relative ratio) was also isolated. [h] The ratio changed from 1:1.5 to 1:10 with application of 6 kbar.

Table II. NOE Data Used To Prove Stereochemistry of Adducts

			enhancement observed (in %)	
entry	lactone	peak irradiated	at H-9	at H-4
1	**27b**	1.48	4.5	
2	**27c**	1.44	8.3	
3	**28c**	1.49		6.8
4	**27d**	1.43	11.6	
5	**28d**	1.47		10.3
6	**28e**	1.48		16.4
7	**31**	1.47	7.5	
8	**32**[a]	1.19		

[a] It showed enhancement at the methine proton at C3 only.

Table III. *J* Values for Epimeric Vicinal Protons at C3 and C9 on the Lactone Ring

entry	lactone	cis/trans	$J_{3,9}$, Hz
1	**27c**	t	1.71
2	**28c**	c	4.81
3	**27d**	t	2.44
4	**28d**	c	3.66
5	**31**	t	9.15
6	**32**	c	7.93

"isodicyclopentadiene" and maleic anhydride[14] and Trost had observed some solvent effects in the face selectivities in his 3 + 2 work,[7] we repeated entries 7 and 17 in DMF and observed small changes (like increase from 1.7 to 2.1 in entry 7, unlike decrease from 5.5 to 3.5 in entry 17).

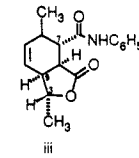
Generally, our Diels–Alder adducts were converted to lactones, either spontaneously or by acid catalysis. For adducts **23d** and **24d** (entry 18) it was necessary to reduce their unconjugated double bonds with H_2 over Pt/EtOAc to form **29** and **30** (Chart II), which were then lactonized. The stereochemistry of our adducts was determined by NOE experiments with the derived, rigid, bicyclic lactones. In structures in the **27** and **31** stereochemical series, the methyl group at C3 of the lactone was irradiated, the signal of H9 increased, thus demonstrating that the lactone and its precursor Diels–Alder adduct arose from a like process. Conversely, with lactones of type **28**, the NOE experiment revealed an interaction between the methyl at C3 and the vinyl proton at C4. These data are recorded in Table II. It must be noted that lactone **32**, with no vinyl H, exhibited no NOE enhancements so our assignment of stereochemistry is done by analogy. Further NMR data derived from the lactones that we did not use for structure assignments were the coupling constants between the methine protons at C3 and C9. The data in Table III reveal that there is no convincing difference between the cis and trans *J* values.[15] For lactone **27d**, derived from like **15d** of entry 7, an X-ray analysis confirmed our NOE-based conclusion. Figure 1 shows a perspective drawing of the X-ray model of this molecule. The amido group is twisted with respect to the cyclohexene ring with the carbonyl group pointed toward the concave face of the molecule.

Discussion

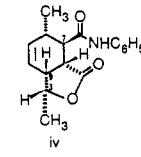
An important conclusion that we can draw from the data in Table I is that the theories put forward by Houk and Hehre as well as the simple selection rule postulated by our group are not adequate. Our interpretation of Houk's theory is that it would uniformly predict unlike attack, whereas Hehre's rule clearly requires like attack when the stereogenic center bears oxygen. If one limits the dienophile data set to *N*-phenylmaleimide, maleic anhydride, and acrolein, then there is a consistent like preference that is in accord with our selection rule and Hehre's theory. Implicit in our rule was the importance of reactive conformation A proposed by McDougal, which follows from arguments put forward by Fleming and McGarvey.[16] If A were more reactive

(14) Watson, W. H.; Galloy, J.; Bartlett, P. D.; Roof, A. A. M. *J. Am. Chem. Soc.* **1981**, *103*, 2022–2031.

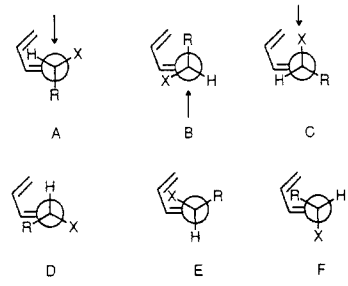
(15) In our preliminary communication, ref 4, the conditions described for the preparation of the lactones also caused an epimerization of the carboxanilido functions. Thus, the structures were (iii) and (iv). These lactones could also be prepared by MeO epimerization of lactones **27d** and **28d**. With (iii) and (iv) the coupling between the protons on C3 and C9 were 7.3 and 6.7 Hz, respectively. Again, this demonstrates that *J* values should not be used to prove the stereochemistry of lactones.



iii



iv



than B, like selectivity would be the outcome. Hehre implies that a third conformer, C, is determining with dienophile approach syn to oxygen. The outcome is identical with reaction with A. Houk suggests that B is dominant, requiring a different topicity in the reaction. These rationalizations are described in terms of ground-state conformations. But, in terms of transition-state effects, one would argue that like selectivity would derive from a transition state stabilized by interaction with the substituents oriented as in A. Conversely, substituents oriented as in B would interact with the transition state to favor unlike attack. Now, as Kozikowski suggested, the approach of a linear acetylenic dienophile to A would produce repulsions between the outside alkoxy and the activating group of the dienophile, thus the normally less favored inside alkoxy conformers B and/or E would react, giving product of unlike attack. Conformers D and F, because of steric hindrance to the inside R group, have not been considered. A prediction developing from this rationalization is that the reactivity of the McDougal–Reitz dienes, which cannot readily achieve an inside alkoxy conformation, would be greatly diminished toward DMAD. But, a propiolate dienophile, because its regiochemistry in a cycloaddition with a 2-alkoxy diene would not force the dienophile ester function against the outside alkoxy of Reitz–McDougal dienes, might react and give like selectivity. At this time, we have no satisfying rationale for the unlike topicity of TCNE and PTAD with our standard diene. Vogel has reported reversal of face selectivity with cycloadditions of deuterium-labeled 2,3-dimethylidenebicyclo[2.2.1]heptane with TCNE and NPTAD on the one hand and maleic anhydride, DMAD, and benzoquinone on the other.[17] Their rationalization of the data includes stereoelectronic factors, differential steric repulsive effects, and a possible change in mechanism. Their results are similar but not exactly parallel to ours; and theirs is a rigid, bicyclic system. Ginsburg, in his classic studies with propellane dienes, did observe a reversal in topicity between *N*-phenylmaleimide and *N*-phenyltriazolinedione. However, in his rationale, the PTAD had a bonding interaction with the allylic group. Such a bonding interaction in our system would have favored a like approach, contrary to our observation.[18] Clearly the small energy differences between the like and unlike transition states (for example ~2 kcal/mol between entry 9 and entry 17) for the cycloadditions described in our table are controlled by some factor, which still needs elucidation. Will the difference between like and unlike pathways be a function of how early or late in the reaction coordinate the transition state is developed? Will it turn out that the unlike TCNE and PTAD cases are not really Diels–Alder reactions?[19] The one conclusion that we are confident of is that dienes with stereogenic allylic centers are very subtle probes into the mechanism of the Diels–Alder reaction. Further experimentation at Hunter will examine dienic control of face selectivity in dienophiles with stereogenic allylic centers and also control via double diastereoselection.[20]

Experimental Section

NMR spectra were recorded on JEOL GX (400 MHz) and GE QE (300 MHz) instruments with tetramethylsilane as internal standard and $CDCl_3$ as the solvent. Infrared spectra were recorded on a Perkin-Elmer 1310 spectrophotometer. Elemental analyses were performed by the Spang Micronalytical Laboratory, Eagle Harbor, MI. The high-resolution mass spectra were obtained by the mass spectral facility, The Pennsylvania State University, University Park, PA. Melting points were uncorrected and were determined on a Fisher-Johns melting point apparatus. Thin-layer chromatograms were done on precoated TLC sheets of silica gel 60 F_{254} (E. Merck) with potassium permanganate spray and/or short- and long-wave ultraviolet light to visualize the spots. PLC plates were prepared by using Kieselgel 60 PF_{254} (E. Merck), and chromatotron (radial chromatography) plates were prepared by using Kieselgel 60 PF_{254} gipshaltig (E. Merck). Flash chromatography was performed with silica gel 60 (230–400 mesh) purchased from Aldrich Chemical Co.

Preparation of Dienes. Dienes **5a** and **5d** were prepared by using literature procedures.[21] Trimethylsilylated dienes **5b** and **5f** were prepared by treating **5a** and **5d** with excess of bis(trimethylsilyl)acetamide, and the crude silylated dienes were used directly without further purification. Diene **5c** was obtained from **5a** by treatment with *tert*-butyldimethylsilyl chloride and DBU in 63.5% yield.[22]

General Procedure for the Diels–Alder Reactions of Dienes 5a–d and 5f with Maleic Anhydride (6), *N*-Phenylmaleimide (7), and DMAD (11). A mixture of diene (1 mmol) and dienophile (1 mmol) in dry benzene (3–5 mL) was stirred (under nitrogen) at room temperature for 3–10 days. The reaction mixture with DMAD (**11**) was refluxed for 48 h. Removal of the solvent gave the crude product, and the diastereomer ratio was determined by NMR before separation by chromatotron/flash chromatography/preparative thin-layer chromatography.

3aα,4α,7,7aα-Tetrahydro-4(*S)-(1(*R**)-hydroxyethyl)isobenzofuran-1,3-dione (Adduct 13a) and 3aβ,4β,7,7aβ-tetrahydro-4(*R**)-(1(*R**)-hydroxyethyl)isobenzofuran-1,3-dione (adduct 14a) from the reaction of diene 5a and maleic anhydride (6)**: reaction time, 3 days; yield, 82.5%; ratio **13a**:**14a**, 2.7:1. Both the adducts were unstable and lactonized to **27a** and **28a**, respectively. The lactone mixture was isolated as a white solid and was not separable by chromatographic means. The crude product (33.5 mg, 17 mmol) was dissolved in 10 mL of Et_2O, and a solution of diazomethane in 10 mL of ether was added dropwise until the yellow color persisted. Evaporation of the solvent gave a crude yellow solid (34.5 mg, yield 96.6%), which also could not be separated by chromatography. Crystallization from water gave 12 mg of pure lactone **27b** as white needles, mp 153 °C (lit.[6] mp 151 °C). The minor lactone **28b** could not be further purified.

1β, 3,3aα, 4α,5,7aα-Hexahydro-1-methyl-3-oxo-4-carbomethoxyisobenzofuran (lactone 27b): IR ($CHCl_3$) 1765, 1725 cm^{-1}; ^1H NMR (300 MHz) δ 5.96–5.89 (m, 1 H, C5-H), 5.69–5.64 (m, 1 H, C_4-*H*), 4.42 (dq, $J_{Me,3}$ = 6.56 Hz, $J_{3,9}$ = 1.01 Hz C_3-*H*), 3.82 (s, 3 H, -OCH_3), 3.66(dd, 1 H, $J_{7,8}$ = 4.08 Hz, $J_{8,9}$ = 7.85 Hz, C_8-*H*), 2.90–2.78 (m, 2 H, C_7-*H* and C_9-*H*), 2.42–2.36 (m, 2 H, CH_2), 1.48 (d, 3 H, $J_{Me,3}$ = 6.56 Hz, CH_3).

3aα,4α,7,7aα-Tetrahydro-4(*S)-[1(*R**)-(trimethylsiloxy)ethyl]isobenzofuran-1,3-dione (adduct 13b) and 3aβ,4β,7,7aβ-tetrahydro-4(*R**)-[1(*R**)-(trimethylsiloxy)ethyl]isobenzofuran-1,3-dione (adduct 14b) from the reaction of diene 5b and maleic anhydride (6)**: reaction time, 5 days; yield, 82.5%; Ratio **13b**:**14b**, 4:1. Attempts to separate the product mixture by PLC (Petroleum ether/EtOAc, 4:1) failed, and both of the products lactonized to **27a** and **28a**, respectively.

3aα,4α,7,7aα,-Tetrahydro-4(*S)-[1(*R**)-*tert*-butyldimethylsiloxy)-ethyl]isobenzofuran-1,3-dione (adduct 13c) and 3aβ,4β,7,7β-tetrahydro-4(*R**)-[1(*R**)-(*tert*-butyldimethylsiloxy)ethyl]isobenzofuran-1,3-dione (adduct 14c) from the reaction of diene 5c and maleic anhydride (6)**: reaction time, 7 days; yield 64.9%; ratio **13c**:**14c**, 4.5:1. Products were separated by flash chromatography (petroleum ether/EtOAc, 4:1).

Adduct 13c: mp 66–68 °C; IR ($CHCl_3$) 1765 cm^{-1}; ^1H NMR (300 MHz) δ 6.04 (m, 1 H, C_6-*H*), 5.88 (m, 1 H, C_5-*H*), 4.47 (overlapping dq, 1 H, $J_{Me,10}$ = 5.95 Hz, C_{10}-*H*), 3.82 (dd, 1 H, *J* = 5.17 and 9.67 Hz, C_9-*H*), 3.47 (m, 1 H, C_8-*H*), 2.76 (overlapping ddd, 1 H, CH_2),

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2.32–2.16 (m, 2 H, CH_2 and C_4-*H*), 1.29 (d, 3 H, $J_{Me,10}$ = 5.99 Hz, CH_3), 0.93 (s, 9 H, $SiC(CH_3)_3$), 0.19 (s, 3 H, $SiCH_3$), 0.16 (s, 3 H, $SiCH_3$).

Adduct 14c: syrupy mass; ^{1}H NMR (300 MHz) δ 6.17 (m, 1 H, C_6-*H*), 6.05 (m, 1 H, C_5-*H*), 4.37 (m, 1 H, C_{10}-*H*), 3.43 (m, 2 H, C_8-*H* and C_9-*H*), 2.69 (overlapping dd, CH_2), 2.31–2.18 (m, 2 H, CH_2 and C_4-*H*), 1.4 (d, 3 H, $J_{Me,10}$ = 5.99 Hz, CH_3), 0.92 (s, 9 H, $SiC(CH_3)_3$), 0.18 (s, 3 H, $SiCH_3$), 0.15 (s, 3 H, $SiCH_3$).

3aα,4α,7,7aα-Tetrahydro-4(*S)-(1(*R**)-hydroxyethyl)-2-phenylisoindole-1,3(2*H*)-dione (adduct 15a) and 3aβ,4β,7,7aβ-tetrahydro-4-(*R**)-(1(*R**)-hydroxyethyl)-2-phenylisoindole-1,3(2*H*)-dione (adduct 16a) from the reaction of diene 5a and *N*-phenylmaleimide (7)**: reaction time, 3 days; yield, 53% ratio **15a**:**16a**, 1.3:1. Both the products lactonized spontaneously to **27c** and **28c**, respectively. The lactone mixture could not be separated by chromatography or by fractional crystallization.

3aα,4α,7,7aα-Tetrahydro-4(*S)-[1(*R**)-(trimethylsiloxy)ethyl]-2-phenylisoindole-1,3(2*H*)-dione (adduct 15b) and 3aβ,4β,7,7aβ-tetrahydro-4(*R**)-[1(*R**)-(trimethylsiloxy)ethyl]-2-phenylisoindole-1,3-(2*H*)-dione (adduct 16b) from the reaction of diene 5b and *N*-phenylmaleimide (7)**: reaction time, 5 days; yield, 91.5%; ratio **15b**:**16b**, 3.5:1; the compounds were separated by PLC (petroleum ether/EtOAc, 4:1).

Adduct 15b: colorless syrup, IR ($CHCl_3$) 1700 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.5–7.2 (m, 5 H, Ar *H*), 6.07–5.99 (m, 1 H, C_6-*H*), 5.90–5.85 (m, 1 H, C_5-*H*), 4.68 (dq, 1 H, *J* = 6.00 and 10.47 Hz, C_{10}-*H*), 3.70 (dd, 1 H, *J* = 8.85 and 4.90 Hz, C_9-*H*), 3.33 (overlapping ddd, 1 H, C_8-*H*), 2.83 (dd, 1 H, *J* = 7.30 and 14.85 Hz, CH_2), 2.31–2.24 (m, 2 H, CH_2 and C_4-*H*), 1.30 (d, 3 H, $J_{Me,10}$ = 6.02 Hz, CH_3), 0.23 (s, 9 H, $Si(CH_3)_3$); high-resolution mass spectrum calcd for $C_{21}H_{25}NO_3Si$ 343.1604, found 343.1594.

Adduct 16b: pale yellow liquid contaminated with *N*-phenylmaleimide (7); ^{1}H NMR (300 MHz) δ 7.54–7.23 (m, 5 H, Ar *H*), 6.10–6.02 (m, 2 H, C_6-*H* and C_5-*H*), 4.5 (overlapping dq, 1 H, $J_{Me,10}$ = 5.92 Hz, C_{10}-*H*), 3.39–3.35 (m, 2 H, C_9-*H*, and C_8-*H*) 2.82 (overlapping ddd, 1 H, CH_2), 2.32–2.24 (m, 2 H, CH_2 and C_4-*H*), 1.47 (d, 3 H, $J_{Me,10}$ = 5.92 Hz, CH_3), 0.19 (s, 9 H, $Si(CH_3)_3$); high-resolution mass spectrum calcd for $C_{19}H_{25}NO_3Si$ 343.1604, found 343.1599.

3aα,4α,7α,7aα-Tetrahydro-4(*S)-(1(*R**)-hydroxyethyl)-7-methyl-2-phenylisoindole-1,3(2*H*)-dione (adduct 15d) and 3aβ,4β,7β,7aβ-tetrahydro-4(*R**)-(1(*R**)-hydroxyethyl)-7-methyl-2-phenylisoindole-1,3-(2*H*)-dione (adduct 16d) from the reaction of diene 5d and *N*-phenylmaleimide (7))**: reaction time, 5 days; yield, 78.3%; ratio **15d**:**16d**, 1.7:1; **15d** lactonizes spontaneously to **27d**. The lactone alcohol mixture was separated by multiple elution on PLC (CH_2Cl_2/acetone, 19:1).

1β,3aα,4α,5α,7aα-Hexahydro-1,5-dimethyl-3-oxo-*N*-phenyl-4-isobenzofurancarboxamide (lactone 27d): colorless cubes; mp 125 °C (EtOAc); IR ($CHCl_3$) 3420, 3330, 1755, 1675 cm^{-1}; ^{1}H NMR (400 MHz) δ 9.98 (br, 1 H, N*H* Ar), 7.58–7.06 (m, 5 H, Ar *H*), 5.89 (m, 1 H, C_5-*H*), 5.57 (d br, $J_{4,5}$ = 10.38 Hz, C_4-*H*), 4.4 (dq, 1 H, $J_{Me,3}$ = 6.71 Hz, $J_{3,9}$ = 2.44 Hz, C_3-*H*), 3.38 (dd, 1 H, $J_{8,9}$ = 7.93 Hz, $J_{8,7}$ = 4.27 Hz, C_8-*H*), 3.01 (dd, 1 H, $J_{7,6}$ = 5.50 Hz, $J_{7,8}$ = 4.27 Hz C_7-*H*), 2.80 (m, 2 H, C_9-*H* and C_6-*H*), 1.43 (d, 3 H, $J_{Me,3}$ = 6.71 Hz, CH_3 at C_3), 1.13 (d, 3 H, $J_{Me,6}$ = 7.32, CH_3 at C_6). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.57; H, 6.66; N, 4.91. Found: C, 71.38; H, 7.05; N, 4.97.

Adduct 16d: waxy solid; IR ($CHCl_3$) 3450, 1700 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.46–7.15 (m, 5 H, Ar *H*), 6.27 (m, 1 H, C_6-*H*), 5.84 (m, 1 H, C_5-H), 4.45 (dq, 1 H, $J_{Me,10}$ = 6.1 Hz, $J_{10,4}$ = 3.05 Hz, C_{10}-*H*), 3.66 (d, 1 H, *J* = 2.45 Hz, O*H*), 3.38 (dd, 1 H, $J_{9,4}$ = 8.55 Hz, $J_{9,8}$ = 5.50 Hz, C_9-*H*), 3.23 (overlapping dd, 1 H, C_8-*H*), 2.54 (m, 1 H, C_4-*H*), 2.26 (br m, 1 H, C_7-*H*), 1.46 (d, 3 H, $J_{Me,7}$ = 7.32 Hz, CH_3 at C_7), 1.36 (d, 3 H, $J_{Me,10}$ = 6.11 Hz, CH_3 at C_{10}); high-resolution mass spectrum calcd for $C_{17}H_{19}NO_3$ 285.1365, found 285.1365.

3aα,4α,7α,7aα-Tetrahydro-4(*S)-[1(*R**)-trimethylsiloxy)ethyl]-7-methyl-2-phenylisoindole-1,3(2*H*)-dione (adduct 15f) and 3aβ,4β,7β,7aβ-tetrahydro-4(*R**)-[1(*R**)-(trimethylsiloxy)ethyl]-7-methyl-2-phenylisoindole-1,3(2*H*)-dione (adduct 16f) from the reaction of diene 5f and *N*-phenylmaleimide (7)**: reaction time, 10 days; yield, 74.5%; ratio **15f**:**16f**, 7.3:1. The two silyl ether adducts were separated by PLC (petroleum ether/EtOAc, 4:1).

Adduct 15f: white needles, mp 135 °C (petroleum ether/EtOAc); IR (CCl_4) 1710 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.42–7.13 (m, 5 H, Ar *H*), 5.75 (m, 2 H, C_6-*H* and C_5-*H*) 4.68 (overlapping dq, 1 H, $J_{Me,10}$ = 6.10 Hz, C_{10}-*H*), 3.62 (dd, 1 H, *J* = 4.88 and 8.55 Hz, C_9-*H*) 3.13 (dd, 1 H, *J* = 7.94 and 8.54 Hz, C_8-*H*), 2.49 (m, 1 H, C_7-*H*), 2.20 (m, 1 H, C_4-*H*), 1.40 (d, 3 H, $J_{Me,7}$ = 7.33 Hz, CH_3 at C_7), 1.24 (d, 3 H, $J_{Me,10}$ = 6.1 Hz, CH_3 at C_{10}), 0.15 (s, 9 H, $Si(CH_3)_3$); high-resolution mass spectrum calcd for $C_{20}H_{27}NO_3Si$ 357.1761, found 357.1740.

Adduct 16f: gummy yellow mass, contaminated with *N*-phenylmaleimide; ^{1}H NMR (400 MHz) δ 7.43–7.14 (m, 5 H, Ar *H*), 5.97 (ddd, 1 H, *J* = 9.16, 6.10, 3.15 Hz, C_6-*H*), 5.74 (ddd, 1 H, *J* = 9.15, 6.10, 3.05 Hz, C_5-*H*), 4.48 (overlapping dq, 1 H, C_{10}-*H*), 3.31 (dd, 1 H, *J* = 8.55 and 5.50 Hz, C_9-*H*), 3.17 (dd, 1 H, *J* = 8.55 and 7.32 Hz, C_8-*H*), 2.49 (m, 1 H, C_7-*H*), 2.20 (m, 1 H, C_4-*H*), 1.44 (d, 3 H, $J_{Me,7}$ = 7.32 Hz, CH_3 at C_6), 1.41 (d, 3 H, $J_{Me,10}$ = 6.1 Hz, CH_3 at C_{10}), 0.13 (s, 9 H, $Si(CH_3)_3$); high-resolution mass spectrum calcd for $C_{20}H_{27}NO_3Si$ 357.1761, found 357.1763.

3α,6α-3(*S)-(1(*R**)-Hydroxyethyl)-1,2-dicarbomethoxy-6-methyl-1,4-cyclohexdiene (adduct 23d) and 3β,6β-3(*R**)-(1(*R**)-hydroxyethyl)-1,2-dicarbomethoxy-6-methyl-1,4-cyclohexadiene (adduct 24d) from the reaction of diene 5d and DMAD (11)**: reaction time, 48 h (reflux); yield, 71.5%; ratio **25d**:**26d**, 1:2.7. The adduct mixture, a syrupy liquid, was not separable.

Hydrogenation of the Mixture 23d and 24d. A 59-mg (0.23-mmol) portion of adduct mixture **23d** and **24d** along with 15 mg of Pt/C catalyst in 10 mL of EtOAc was kept under hydrogen. After 6 h only one double bond equivalent of H_2 was taken up. Filtration of the catalyst and evaporation of the solvent gave a syrupy liquid (59 mg, yield 99%). The crude alcoholic mixture was separated by PLC (petroleum ether/ether, 3:1) to furnish 10.8 mg of alcohol **29** and 45.6 mg of alcohol **30**.

3α,6α-3(*S)-(1(*R**)-Hydroxyethyl)-1,2-dicarbomethoxy-6-methyl-1-cyclohexene (alcohol 29)**: colorless syrup; ^{1}H NMR (400 MHz) δ 3.80 (m, 1 H, C_7-*H*), 3.73 (s, 6 H, 2 OCH_3), 2.64–2.58 (br m, 2 H, C_3-*H* and C6-*H*), 1.75–1.63 (m, 4 H, CH_2CH_2), 1.20 (d, 3 H, $J_{Me,7}$ = 6.71 Hz, CH_3 at C_7), 1.10 (d, 3 H, $J_{Me,6}$ = 6.71 Hz, CH_3 at C6); high-resolution mass spectrum calcd for $C_{12}H_{16}O_4$ (M^+ – MeOH) 224.1048, found 224.1034.

3β,6β-3(*R)-(1(*R**)-Hydroxyethyl)-1,2-dicarbomethoxy-6-methyl-1-cyclohexene (alcohol 30)**: colorless syrup; ^{1}H NMR (400 MHz) δ 3.98 (dq, 1 H, C_7-*H*), 3.77 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 2.69–2.67 (br, m, 1 H, C_3-*H*), 2.49–2.45 (br, m, 1 H, C_6-*H*), 2.18 (br, 1 H, O*H*), 1.84–1.77 (m,1 H), 1.68–1.58 (m, 3 H, CH_2CH_2), 1.17 (d, 3 H, $J_{Me,7}$ = 6.10 Hz, CH_3 at C_7), 1.11 (d, 3 H, $J_{Me,6}$ = 7.32 Hz, CH_3 at C_6); high-resolution mass spectrum calcd for $C_{12}H_{16}O_4$ (M^+ – MeOH) 224.1048, found 224.1030.

General Procedure for the Diels–Alder Reaction of Dienes 5d and 5f with 4-Phenyl-1,2,4-triazoline-3,5-dione (10). To a cooled solution (−78 °C) of 175 mg (1 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione in 4 mL of THF/CH_2Cl_2 (1:1) was added dropwise 1.2 mmol of **5d** or **5f** in 3 mL of THF/CH_2Cl_2 (1:1). The color of the solution was slowly discharged, and after 15 min the cooling bath was removed. The solution was stirred for another 5 min, and excess solvent was evaporated. The product was purified by PLC.

2,3,5α,8α-Tetrahydro-5(*S)-(1(*R**)-hydroxyethyl)-1,3-dioxo-8-methyl-2-phenyl-1,2,4-triazolo[1,2-*a*]pyridazine (adduct 21d), 2,3,5β,8β-tetrahydro-5(*R**)-(1(*R**)-hydroxyethyl)-1,3-dioxo-8-methyl-2-phenyl-1,2,4-triazolo[1,2-*a*]pyridazine (adduct 22d), and the third isomer from the reaction of diene 5d and 4-phenyl-1,2,4-triazoline-3,5-dione (10)**: yield, 97%; ratio **21d**:**22d**:third compound, 1.8:4.8:1, separated by PLC (petroleum ether/EtOAc, 1.5:1, followed by petroleum ether/ether, 1:1).

Adduct 21d: colorless pastry syrup; IR ($CHCl_3$) 3400, 1690 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.48–7.19 (m, 5 H, Ar *H*), 5.97 (ddd, 1 H, *J* = 10.38, 4.88 and 2.44 Hz, C_7-*H*), 5.67 (ddd, 1 H, *J* = 10.38, 2.44 and 1.83 Hz, C_6-*H*), 4.78 (d, 1 H, *J* = 10.99 Hz, O*H*), 4.55 (m, 1 H, C_8-*H*), 4.48 (m, 1 H, C_5-*H*), 4.05 (m, 1 H, C_{10}-*H*), 1.34 (d, 3 H, $J_{Me,8}$ = 6.1 Hz, CH_3, CH_3 at C_8), 1.19 (d, 3 H, $J_{Me,10}$ = 6.72 Hz, CH_3 at C_{10}); high-resolution mass spectrum calcd for $C_{15}H_{17}N_3O_3$ 287.1271, found 287.1278.

Adduct 22d: colorless syrup; ^{1}H NMR (400 MHz) δ 7.45–7.19 (m, 5 H, Ar *H*), 5.86 (m, 2 H, C_6-*H* and C_7-*H*), 4.44 (m, 1 H, C_8-*H*), 4.38 (m, 1 H, C_5-*H*), 4.22 (m, 1 H, C_{10}-*H*), 3.18 (br s, 1 H, O*H*), 1.45 (d, $J_{Me,8}$ = 6.71 Hz, CH_3 at C_8), 1.18 (d, 3 H, $J_{Me,10}$ = 6.72 Hz, CH_3 at C_{10}); high-resolution mass spectrum calcd for $C_{15}H_{17}N_3O_3$ 287.1271, found 287.1275.

Third isomer: syrup; ^{1}H NMR (400 MHz) δ 7.52–7.23 (m, 5 H, Ar *H*), 6.02 (m, 1 H, C_7-*H*), 5.83 (ddd, 1 H, *J* = 10.38, 3.66, and 1.83 Hz, C_6-*H*), 4.69 (m, 1 H, C_8-*H*), 4.57 (m, 1 H, C_5-*H*), 4.24 (m, 1 H, C_{10}-*H*), 3.2 (br, 1 H, O*H*), 1.37 (dd, 3 H, *J* = 6.71 and 6.10 Hz, CH_3 at C_8), 1.20 (dd, 3 H, *J* = 6.71 and 6.10 Hz, CH_3 at C_{10}); high-resolution mass spectrum calcd for $C_{15}H_{17}N_3O_3$ 287.1271, found 287.1272.

2,3,5α,8α-Tetrahydro-5(*S)-[1(*R**)-(trimethylsiloxy)ethyl]-1,3-dioxo-8-methyl-2-phenyl-1,2,4-triazolo[1,2-*a*]pyridazine (adduct 21f) and 2,3,5β,8β-tetrahydro-5(*R**)-[(*R**)-(trimethylsiloxy)ethyl]-1,3-dioxo-8-methyl-2-phenyl-1,2,4-triazolo[1,2-*a*]pyridazine (adduct 22f) from the reaction of diene 5f with 4-phenyl-1,2,4-triazoline-3,5-dione (10)**: yield, 92%; ratio **21f**:**22f**, 1:5.5 separated by PLC (petroleum ether/EtOAc, 4:1).

Adduct 21f: pasty mass; ^{1}H NMR (400 MHz) δ 7.52–7.24 (m, 5 H, Ar *H*), 6.00–5.91 (m, 2 H, C_7-*H* and C_6-*H*), 4.69 (m, 1 H, C_{10}-*H*), 4.49 (m, 1 H, C_8-*H*), 4.37 (m, 1 H, C_5-*H*), 1.47 (d, 3 H, $J_{Me,8}$ = 6.59 Hz, CH_3 at C_8), 1.11 (d, 3 H, $J_{Me,10}$ = 6.59 Hz, CH_3 at C_{10}), 0.13 (s, 9 H, $Si(CH_3)_3$); high-resolution mass spectrum calcd for $C_{17}H_{22}N_3O_3Si$ (M^+ – Me) 344.1431, found 344.1437.

Adduct 22f: white solid; mp 109 °C, ^{1}H NMR (400 MHz) δ 7.5–7.24 (m, 5 H, Ar *H*), 5.94 (m, 2 H, C_6-*H* and C_7-*H*), 4.58 (m, 1 H, C_{10}-*H*), 4.47 (m, 1 H, C_8-*H*), 4.37 (m, 1 H, C_5-*H*), 1.55 (dd, 3 H, J = 6.71 and 6.71 Hz, C*H*$_3$ at C_8), 1.23 (dd, 3 H, J = 6.71 and 6.10 Hz, C*H*$_3$ at C_{10}), 0.07 (s, 9 H, Si(C*H*$_3$)$_3$). Anal. Calcd for $C_{18}H_{25}N_3O_3Si$: C, 60.16; H, 6.96; N, 11.69. Found: C, 60.22; H, 6.98; N, 11.71.

General Procedure for Hydrolysis and/or Lactonization of the Adducts 15b, 15f, 16b, 16d, 16f, 21f, 22f, 29, and 30. A 1-mmol portion of the adduct in 3 mL of MeOH along with 2–3 drops of a saturated oxalic acid solution was refluxed for 0.5–4 h. The course of the reaction was followed by TLC. The reaction mixture was cooled, excess methanol was removed by rotary evaporator, and the remaining pasty mass was dissolved in EtOAc and passed through a short column of Florisil. The column was eluted with EtOAc, and concentration of the eluent gave the crude lactone, which was further purified by PLC (petroleum ether/EtOAc, 4:1) and crystallization.

Hydrolysis and lactonization of the silyl adduct 15b: time, 0.5 h; yield, 93.8%. Crystallization from EtOAc gave 1β,3,3aα,4α,5,7aα-hexahydro-1-methyl-3-oxo-*N*-phenyl-4-isobenzofurancarboxamide (lactone **27c**) as colorless needles: mp 220 °C; IR ($CHCl_3$) 1745, 1670 cm^{-1}; ^{1}H NMR (400 MHz) δ 9.83 (br, 1 H, N*H* Ar), 7.59–7.06 (m, 5 H, Ar *H*), 5.95 (ddd, 1 H, J = 9.77, 3.05, 2.44 Hz, C_5-*H*), 5.65 (d, 1 H, J = 10.38 Hz, C_4-*H*), 4.47 (dq, 1 H, $J_{Me,3}$ = 6.10 Hz, $J_{3,9}$ = 1.71 Hz C_3-*H*), 3.52 (dd, 1 H, J = 7.33 and 6.72 Hz, C_8-*H*), 2.9–2.85 (m, 2 H, C_7-*H* and C_9-*H*), 2.47–2.39 (m, 2 H, C*H*$_2$), 1.44 (d, 3 H, $J_{Me,3}$ = 6.10 Hz, C*H*$_3$ at C_3). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.84; H, 6.27; N, 5.16. Found: C, 70.75; H, 6.23; N, 5.11.

Hydrolysis and lactonization of the silyl adduct 16b: time, 3 h; yield, 79.9%; 1β,3,3aβ,4β,5,7aβ-hexahydro-1-methyl-3-oxo-*N*-phenyl-4-isobenzofurancarboxamide (lactone **28c**) crystallized from MeOH; mp 205 °C; IR ($CHCl_3$) 1745, 1670 cm^{-1}; ^{1}H NMR (300 MHz) δ 10.03 (br, 1 H, N*H* Ar), 7.66–7.11 (m, 5 H, Ar *H*), 6.12 (m, 1 H, C_5-*H*), 5.72 (dd, 1 H, J = 10.24 and 2.11 Hz, C_4-*H*), 4.77 (dq, 1 H, $J_{Me,3}$ = 6.51 Hz, $J_{3,9}$ = 4.85 Hz, C_3-*H*), 3.54 (dd, 1 H, J = 6.68 and 2.85 Hz, C_8-*H*), 3.19 (m, 1 H, C_9-*H*), 2.94 (ddd, 1 H, J = 5.70, 2.88, and 0.78 Hz, C_7-*H*), 2.56–2.49 (m, 2 H, C*H*$_2$), 1.49 (d, 3 H, $J_{Me,3}$ = 6.51 Hz, C*H*$_3$ at C_3). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.84; H, 6.27; N, 5.16. Found: C, 71.00; H, 6.09; N, 5.08.

Hydrolysis and lactonization of the silyl adduct 15f: reaction time, 3 h; yield, 98%. The product **27d** is identical with the major adduct (**27d**) of the reaction of alcohol **5d** with **7**.

Lactonization of the alcoholic adduct 16d: time, 2 h; yield, 85%. The 1β,3,3aβ,4β,5β,7aβ-hexahydro-1,5-dimethyl-3-oxo-*N*-phenyl-4-isobenzofurancarboxamide (lactone **28d**) was separated by PLC (CH_2Cl_2/acetone, 19:1). The minor product was unlactonized free alcohol (7.4%). Crystallization of **28d** from EtOAc gave white needles: mp 188 °C; IR ($CHCl_3$) 3300, 3260, 1745, 1660 cm^{-1}; ^{1}H NMR (400 MHz) δ 10.77 (br, 1 H, N*H* Ar), 7.64–7.08 (m, 5 H, Ar *H*), 6.08 (dd, 1 H, J = 10.38, 3.05 Hz, C_5-*H*), 5.57 (br d, 1 H, J = 10.38 Hz, C_4-*H*), 4.71 (dq, 1 H, $J_{Me,3}$ = 6.11 Hz, $J_{3,9}$ = 3.66 Hz, C_3-*H*), 3.43 (dd, 1 H, $J_{8,9}$ = 7.33 Hz, $J_{8,7}$ = 3.66 Hz, C_8-*H*), 3.15 (dd, 1 H, $J_{7,6}$ = 6.10 Hz, $J_{7,8}$ = 3.66 Hz, C_7-*H*), 3.10 (m, 1 H, C_9-*H*), 2.86 (m, 1 H, C_6-*H*), 1.47 (d, 3 H, $J_{Me,3}$ = 6.71 Hz, C*H*$_3$ at C_3), 1.11 (d, 3 H, $J_{Me,6}$ = 7.32 Hz, CH_3 at C_6). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.57; H, 6.66; N, 4.9. Found: C, 71.39; H, 6.95; N, 4.89.

Hydrolysis and lactonization of the silyl adduct 16f: time, 4 h; yield, 49.2%. PLC (petroleum ether/EtOAc, 4:1) gave the pure product, which was identical in all respects with the lactone **28d** obtained from the lactonization of minor adduct **16d**. Recovered *N*-phenylmalemide was also isolated, which had contaminated adduct **16f**.

Hydrolysis of the silyl adduct 21f: time, 2 h; yield, 84.5%. The product was purified by PLC (petroleum ether/EtOAc, 1.5:1). This product was identical with the adduct **21d** obtained from the reaction of diene **5d** and **10**. Adduct **21d** did not cyclize to lactone under the reaction conditions.

Hydrolysis of the silyl adduct 21f: time, 2 h; yield, 89.4%. The product did not cyclize to the lactone; IR and NMR data proved its identity to **22d** obtained from reaction of **5f** and **10**. Hydroxy compound **22d** also did not cyclize under the reaction conditions.

Lactonization of the alcoholic adduct 29: time, 1.5 h; yield, 73.1%. 1β,3,5α,7aα-Tetrahydro-1,5-dimethyl-3-oxo-4-carbomethoxyisobenzofuran (lactone **31**) was purified by crystallization from petroleum ether/EtOAc: colorless crystals; mp 97 °C; IR ($CHCl_3$) 1755, 1725 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.10 (dq, 1 H, $J_{3,9}$ = 9.15 Hz, $J_{Me,3}$ = 6.1 Hz, C_3-*H*), 3.81 (s, 3 H, COOC*H*$_3$), 2.77 (ddd, 1 H, J = 9.15, 4.27 and 3.05 Hz, C_9-*H*), 2.45 (m, 1 H, C_6-*H*), 1.90–1.84 (m, 1 H, C*H*$_2$CH$_2$), 1.76–1.55 (m, 2 H, C*H*$_2$CH$_2$), 1.46 (d, 3 H, $J_{Me,3}$ = 6.1 Hz, C*H*$_3$ at C_3), 1.35–1.10 (m, 1 H, C*H*$_2$CH$_2$), 1.07 (d, 3 H, $J_{Me,6}$ = 6.71 Hz, C*H*$_3$ at C_6). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 64.28; H, 7.14. Found: C, 64.36; H, 7.28.

Lactonization of the alcoholic adduct 30: time, 1.5 h; yield, 75.8%. 1β,3,5β,7aβ-Tetrahydro-1,5-dimethyl-3-oxo-4-carbomethoxyisobenzofuran (lactone **32**) was purified by crystallization from petroleum ether/EtOAc to furnish colorless crystals: mp 76 °C; IR ($CHCl_3$) 1755, 1725 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.80 (dq, 1 H, $J_{3,9}$ = 7.93 Hz, $J_{Me,3}$ = 6.11 Hz, C_3-*H*), 3.79 (s, 3 H, COOC*H*$_3$), 3.01 (ddd, 1 H, J = 7.93, 4.89, and 3.06 Hz, C_9-*H*), 2.76 (m, 1 H, C_6-*H*), 1.81–1.64 and 1.41–1.29 (m, 4 H, C*H*$_2$C*H*$_2$), 1.19 (d, 3 H, $J_{Me,3}$ = 6.11 Hz, C*H*$_3$ at C_3), 1.07 (d, 3 H, $J_{Me,6}$ = 6.71 Hz, C*H*$_3$ at C_6). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 64.28; H, 7.14. Found: C, 63.93; H, 7.15.

Hydrolysis of the Silyl Adduct 13c. A mixture of 175 mg (0.56 mmol) of **13c** and 50 mg of Dowex 50W-X-8 resin in 7 mL of MeOH was stirred for 48 h. The solution was filtered and evaporated to give a white crystalline solid. Crude NMR (300 MHz) showed the direct formation of lactone ester **27b** and a trace of lactonic acid **27a**. Lactone **27b** was purified by PLC (petroleum ether/EtOAc 1.5:1) to furnish 41 mg (34%) of a solid, which was crystallized from water to give colorless crystals, mp 142 °C. This product has identical IR and NMR spectra with the earlier sample of **27b**.

Lactonization of the Alcoholic adduct 22d: To an ice-cooled stirred suspension of NaH (from 10 mg of 50% dispersion in mineral oil, 0.2 mmol) in 3 mL of dry THF (kept under nitrogen) was added dropwise a solution of alcohol (30 mg, 0.10 mmol) in 3 mL of dry THF. After the addition, the cooling bath was removed, and after 1 h the reaction was quenched with a saturated solution of NH_4Cl. The solution was extracted with ether (2 × 15 mL) dried over Na_2SO_4. Evaporation of the solvent gave a pasty mass, which was subjected to PLC (petroleum ether/EtOAc, 1.5:1). A white crystalline solid (9 mg, 30%) was obtained, which was recrystallized from a petroleum ether/EtOAc mixture to give 1,2β,4aβ,5β-tetrahydro-2,5-dimethyl-7-oxo-7*H*-oxazolo[3,4-*b*]-pyridazine-1-carboxanilide (carbamate **28e**) as colorless crystals: mp 190 °C; IR ($CHCl_3$) 3420, 1785, 1685 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.46–7.02 (m, 5 H, Ar *H*), 6.09 (ddd, 1 H, J = 10.99, 3.66 and 1.83 Hz, C_5-*H*), 5.73 (br d, 1 H, C_4-*H*), 4.98 (m, 1 H, C_6-*H*), 4.86 (dq, 1 H, $J_{Me,3}$ = 6.71 Hz, $J_{3,9}$ = 7.32 Hz, C_3-*H*), 4.33 (ddd, 1 H, J = 7.32, 3.66 and 1.83 Hz, C_9-*H*), 1.48 (d, 3 H, $J_{Me,3}$ = 6.72 Hz, C*H*$_3$ at C_3), 1.38 (d, 3 H, $J_{Me,6}$ = 6.71 Hz, C*H*$_3$ at C-6). Anal. Calcd for $C_{15}H_{17}N_3O_3$: C, 62.71; H, 5.92; N, 14.63. Found: C, 62.63; H, 5.84; N, 14.59.

Crystal data: $C_{17}H_{19}NO_3$, M = 285.3, monoclinic, a = 9.072 (1) Å, b = 18.512 (5) Å, c = 9.838 (1) Å, β = 110.65 (1)°, U = 1546.1 (5) Å^3, Z = 4, D_{calcd} = 1.225 g/cm^3, $F(000)$ = 608, Cu Kα radiation (λ = 1.5418 Å), μ = 0.7 cm^{-1}, space group $P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2) from systematic absences: $0k0$ when $k \neq 2n$. Shown to be the former by refinement.

Details of data collection and structure determination are in the supplementary material.

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Supplementary Material Available: Tables of coordinates, thermal parameters, bond lengths, valency angles, and torsion angles as well as details of the X-ray analysis of **27d** (10 pages). Ordering information is given on any current masthead page.