(d, J = 6 hz, 2 H), 5.58-5.86 (m, 2 H), 5.90-6.27 (m, 2 H), 6.24 (d, J = 3 Hz, 1 H), 6.77 (d, J = 3 Hz, 1 H), 6.98-7.06 (br d, J = 8 Hz, 2 H), 7.10-7.35 (m, 5 H), 7.47 (d, J = 8 Hz, 1 H), 8.07 (d, J = 8 Hz, 1 H); IR (film) 3020, 1685, 1592, 1450, 1383, 985 cm^{-1}; MS m/e 81, 117, 182, 197, 292, 316; HRMS for $C_{21}H_{20}N_2O$ calcd 316.15757, measured 316.15727; R_f (3:1 H:EA) = 0.42.

***N*-(2,4-Hexadienyl)-*N*-phenyl-1-(3-(3-ethoxy-3-oxo-1-propenyl)indolyl)urea (14)**: tan oil, 76% yield; NMR ($CDCl_3$) δ 1.32 (t, J = 7 Hz, 3 H), 1.72 (d, J = 7 Hz, 3 H), 4.22 (q, J = 7 Hz, 2 H), 4.51 (d, J = 4 Hz, 2 H), 5.60-6.27 (m, 4 H), 6.32 (d, J = 15 Hz, 1 H), 7.00-7.42 (m, 8 H), 7.49 (d, J = 15 Hz, 1 H), 7.26 (d, J = 8 Hz, 1 H), 8.07 (d, J = 8 Hz, 1 H); IR ($CDCl_3$) 1695, 1680, 1520, 1295 cm^{-1}; R_f (3:1 H:EA) = 0.48.

***N*-(6-Ethoxy-6-oxo-2,4-hexadienyl)-*N*-phenyl-1-(3-formylindolyl)urea (15)**: oil, 76% yield; NMR ($CDCl_3$) δ 1.27 (t, J = 7 Hz, 3 H), 4.19 (q, J = 7 Hz, 2 H), 4.63 (d, J = 4 Hz, 2 H), 5.34-6.40 (m, 3 H), 7.05-7.60 (m, 8 H), 7.99 (d, J = 8 Hz, 1 H), 8.18 (d, J = 8 Hz, 1 H), 9.70 (s, 1 H); IR ($CDCl_3$) 1700, 1668, 1392, 1262, 1239 cm^{-1}; MS m/e 119, 167, 180, 194, 299, 373, 402; HRMS calcd 402.15796, measured 402.15766.

***N*-(2,4-Hexadienyl)-*N*-*tert*-butyl-1-(3-formylindolyl)urea (17)**: solid; mp 68-70 °C; 64% yield; NMR ($CDCl_3$) δ 1.32 (s, 9 H), 1.76 (d, J = 7 Hz, 3 H), 4.78 (d, J = 6 H, 2 H), 5.64-6.26 (m, 4 H), 7.30-7.42 (m, 3 H), 7.73 (s, 1 H), 8.29-8.33 (m, 1 H), 10.00 (s, 1 H); IR (CH_2Cl_2) 1650, 1645, 1520, 1373, 1155 cm^{-1}.

***N*-(2,4-Hexadienyl)-*N*-(2,6-dimethylphenyl)-1-(3-formylindolyl)urea (18)**: solid; mp 123 °C; 35% yield; 300-MHz NMR ($CDCl_3$) δ 1.74 (d, J = 7 Hz, 3 H), 2.21 (s, 6 H), 4.35 (d, J = 7 Hz, 2 H), 5.62-5.76 (m, 1 H), 5.78-5.92 (m, 1 H), 5.95-6.18 (m, 2 H), 6.96-7.43 (m, 6 H), 8.10 (d, J = 8 Hz, 1 H), 8.16 (d, J = 8 Hz, 1 H), 9.57 (s, 1 H); IR ($CDCl_3$) 1685, 1667, 1392, 1232 cm^{-1}; MS m/e 81, 343, 372; R_f (3:2 H:EA) = 0.40.

General Procedure for the Diels-Alder Reactions. A 0.1 M solution of urea in dry degassed toluene was heated in a sealed glass tube at the temperature specified in Table II for the time specified in Table II. The reaction was allowed to cool to ambient temperature and purified by silica gel flash chromatography using 1:1 to 5:1 H:EA. Isomers were separated by chromatography. Main isomer spectral data are given. All reactions were run on a 2-3-mmol scale.

(3aβ,6aβ,11aβ)-2,3,3a,6,6a,11a-Hexahydro-6a-formyl-6-methyl-2-phenyl-1*H*-pyrimidino[3,2,1-*jk*]carbazol-1-one (9): solid; mp 171 °C (from ethyl acetate); 93% yield; 6:1 exo:endo ratio; 300-MHz NMR ($CDCl_3$) δ 1.12 (d, J = 7 Hz, 3 H), 2.80-2.97 (m, 2 H), 3.79 (dd, J = 2.8, 12 Hz, 1 H), 4.12 (dd, J = 3.6, 12 Hz, 1 H), 4.98 (d, J = 4.4 Hz, 1 H), 5.72-5.88 (m, 2 H), 6.97-7.18 (m, 2 H), 7.23-7.55 (m, 6 H), 7.99 (d, J = 8 Hz, 1 H), 9.85 (s, 1 H); IR (film) 2715, 1722, 1650, 1480, 1430 cm^{-1}; MS m/e 81, 145, 193, 289, 315, 344; HRMS m/e for $C_{22}H_{20}N_2O_2$ calcd 344.15248, measured 344.15277. The X-ray data are summarized in ref 8. Anal. Calcd: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.63; H, 5.87; N, 8.16.

(3aβ,6aα,6aβ,11aβ)-2,3,3a,6,6a,11a-Hexahydro-6a-formyl-6-(ethoxycarbonyl)-2-phenyl-1*H*-pyrimidino[3,2,1-*jk*]carbazol-1-one (16): solid; mp 157-158 °C (from ethyl acetate); one isomer; 300-MHz NMR ($CDCl_3$) δ 1.19 (t, J = 7 Hz, 3 H), 2.84-3.92 (m, 1 H), 3.85 (dd, J = 3.2, 12 Hz, 1 H), 4.03-4.16 (m, 2 H), 4.91 (d, J = 4.5 Hz, 1 H), 5.91 (br d, J = 10 Hz, 1 H), 6.30 (dt, J = 10, 3 Hz, 1 H), 6.97 (t, J = 8 Hz, 1 H), 7.14 (d, J = 8 Hz, 1 H), 7.24-7.54 (m, 6 H), 7.96 (d, J = 8 Hz, 1 H), 10.04 (s, 1 H); IR (film) 1724, 1670, 1475, 1417 cm^{-1}; MS m/e 119, 139, 180, 299, 373, 402; HRMS m/e for $C_{24}H_{22}N_2O_4$ calcd 402.15796, measured 402.15790. Anal. Calcd: C, 71.63; H, 5.51; N, 6.85. Found: C, 71.03; H, 5.56; N, 6.96.

(3aβ,6aα,6aβ,11aβ)-2,3,3a,6,6a,11a-Hexahydro-6-methyl-2-phenyl-1*H*-pyrimidino[3,2,1-*jk*]carbazol-1-one (13): tan oil; 52% yield; one isomer; 300-MHz NMR ($CDCl_3$) δ 1.53 (d, J = 7 Hz, 3 H), 2.35-2.58 (m, 2 H), 3.23-3.33 (m, 1 H), 3.52-3.62 (m, 1 H), 3.96-4.10 (m, 2 H), 5.76 (dt, J = 7, 3 Hz, 1 H), 5.92 (dt, J = 7, 3 Hz, 1 H), 6.97 (t, J = 8 Hz, 1 H), 7.14-7.55 (m, 7 H), 7.94 (d, J = 8 Hz, 1 H); IR (film) 3030, 2920, 1650, 1590, 1475, 1280 cm^{-1}; MS m/e 81, 117, 182, 162, 316; HRMS m/e for $C_{21}H_{20}N_2O$ calcd 316.15757, measured 316.15785; R_f (4:1 H:EA) = 0.37.

(3aβ,6aα,6aβ,11aβ)-2,3,3a,6,6a,11a-Hexahydro-6-methyl-2-phenyl-6a-(phenylsulfinyl)-1*H*-pyrimidino[3,21-*jk*]carbazol-1-one (11): tan oil; 68% yield; 300-MHz NMR ($CDCl_3$) δ 1.53 (d, J = 7 Hz, 3 H), 3.56-3.76 (m, 1 H), 3.80-4.08 (m, 3 H), 5.75 (dt, J = 10, 3 Hz, 1 H), 5.98 (dt, J = 10, 3 Hz, 1 H), 7.18-7.53 (m, 7 H), 7.62 (br d, J = 8 Hz, 1 H), 8.33 (br d, J = 8 Hz, 1 H); IR (film) 2970, 1685, 1467, 1406, 1318, 1292 cm^{-1}; MS m/e 106, 180, 193, 299, 314; HRMS m/e for $C_{21}H_{18}N_2O$ calcd 314.14192, measured 314.14176; R_f (3:2 H:EA) = 0.59.

(3aβ,6aα,6aβ,11aβ)-2,3,3a,6,6a,11a-Hexahydro-6-formyl-6-methyl-2-(2,6-dimethylphenyl)-1*H*-pyrimidino[3,2,1-*jk*]-carbazol-1-one (19): oil; 67% yield; 5:1 ratio of isomers; 300-MHz NMR ($CDCl_3$) δ 1.64 (d, J = 7 Hz, 3 H), 2.20 (s, 3 H), 2.32 (s, 3 H), 2.56-2.69 (m, 1 H), 2.80-2.92 (m, 1 H), 3.42-3.73 (m, 2 H), 4.42 (d, J = 10 Hz, 1 H), 5.72-5.94 (m, 2 H), 6.95-7.40 (m, 5 H), 7.56 (d, J = 8 Hz, 1 H), 7.98 (d, J = 8 Hz, 1 H), 9.80 (s, 1 H); R_f (1:1 H:EA) = 0.33.

Supplementary Material Available: Crystal data, methods of data collection and structure solution and refinement, ORTEP drawings, tables of bond distances, bond angles, positional parameters, general displacement parameter expressions, and root-mean-square amplitudes of thermal variation for **9** (19 pages); table of observed and calculated structure factors for **9** (1 page). Ordering information is given on any current masthead page.

Diels-Alder Reactions of Chiral Acrylylurea Derivatives and Resolution of the Adducts. Convenient Synthesis of Optically Pure Methyl (3*R*,4*R*,6*R*)-Bicyclo[2.2.1]heptene-4-carboxylate

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A new method to obtain optically pure methyl *endo*-bicyclo[2.2.1]heptene-4-carboxylates has been developed by using Diels-Alder reactions of chiral acrylylurea **3a** with cyclopentadiene and other dienes. The Diels-Alder adducts are easily separated by conventional column chromatography, and the chiral auxiliary is removed by methanolysis to give the methyl ester and the chiral urea **1**. The recovered urea can be converted to the acrylylurea **3** in two steps. Accordingly, the commercially available chiral source (both ((*S*)-1-phenylethyl)- and ((*R*)-1-phenylethyl)amine) can be recycled efficiently. The reaction has been investigated in the presence of various Lewis acids. Also studied were the reactions of acrylylurea **3a** with other dienes (1,3-cyclohexadiene and isoprene) and crotonylurea **3b** with cyclopentadiene. The excellent separability of the diastereomers is discussed based on conformational differences studied by ^1H NMR spectroscopy.

The asymmetric Diels-Alder reaction is becoming one of the most important synthetic tools in natural product synthesis,[1] and a spate of reports have appeared in recent years underlining its importance and presenting further

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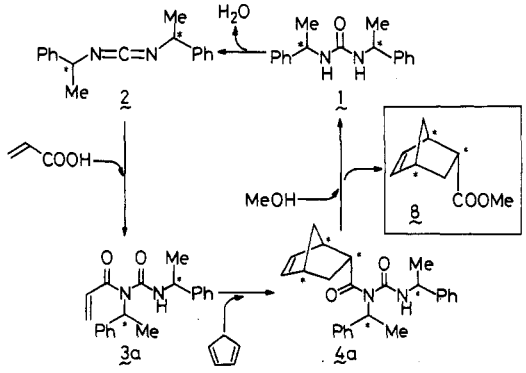
Table I. Diels–Alder Reaction[a] of Chiral Acylureas 3a and 3b

no.	dienophile	diene	Lewis acid	temp, °C	yield,[b] %	endo/exo[c]	4/5[c]
1	**3a**		no cat.	100	71	77:23	52:48
2			$BF_3{\cdot}OEt_2$	−78	24	96:4	62:38
3			$SnCl_4$	−78	87	97:3	64:36
4			Et_2AlCl	−78	95	99:1	57:43
5				−115	60	97:3	68:32
6			$Ti(Oi\text{-}Pr)_4$	−78	0	–	–
7			$Ti(Oi\text{-}Pr)_2Cl_2$	−78	16	96:4	75:25
8			$TiCl_4$	−78	97	97:2	83:17
9				−115	93	98:2	74:26
10	**3b**		$TiCl_4$	−40	16	98:2	45:55[d]
11				−78	9	97:3	52:48[d]
12	**3a**		$TiCl_4$	−40	20	99:1	78:22[d]
13				−78	10	99:1	82:18[d]
14	**3a**		$TiCl_4$	−40	34	–	60:40[d]
15				−78	14	–	64:36[d]

[a] The Diels–Alder reaction of acrylylurea **3** (1 equiv) with diene (1 equiv) was carried out in the presence of Lewis acid (1.5 equiv) in toluene at 100 °C (3 h), in CH_2Cl_2 at −40 and −78 °C (1 h), or in EtCl at −115 °C (1 h). [b] All yields are based on purified product isolated by chromatography (SiO_2). [c] Diastereomer analysis of *endo*-acylureas, **4** and **5** and these exo isomers were carried out by HPLC (Merck Lichrosorb Si 60, 4.6 × 150, hexane/ethyl acetate (4:1)) or ^1H NMR (270 MHz, $CDCl_3$) spectroscopy. [d] The ratio of 4*R* form and 4*S* form. The configuration was estimated from ^1H NMR (270 MHz) analysis.

Scheme I



improvements.[2] Conceptually, a Lewis acid assisted Diels–Alder reaction at low temperature gives high stereoselectivity because of the rigid Lewis acid–dienophile complex.[3] Some Lewis acid catalysts have been employed,[4] including some chiral alkyloxy-substituted ones,[5] to promote the high enantioselectivity of the reaction. However, perfect control to obtain optically pure products (100% ee), as a general method, has not been achieved yet. An alternative solution is to develop an easy separation of diastereomeric adducts and a simple removal of the chiral auxiliary. However, only a few successful examples[6]

Scheme II

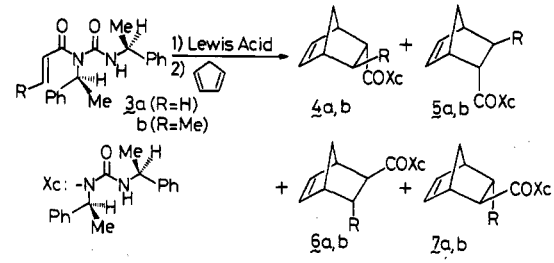
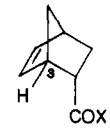
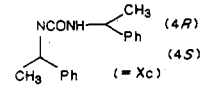
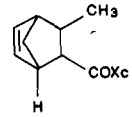
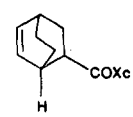
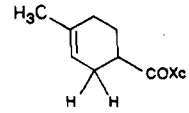


Table II. Chemical Shift of Proton at C3 of Adducts



X	chemical shift, δ
OH	3.25
OCH_3	3.20
$NH(CH_2)_3CH_3$	3.13
 (4*R*)	3.18
(4*S*)	2.78

		
4*R* δ 3.07 (**4b**)	2.78 (**9**)	2.26, 2.10 (**11**)
4*S* δ 2.85 (**5b**)	2.33 (**10**)	2.13, 1.95 (**12**)

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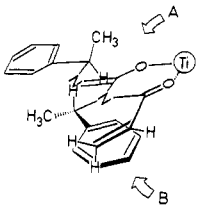

Figure 1.

have been reported. Moreover, in many cases, chiral auxiliaries are not readily available and their recycling is inefficient. To cope with these difficulties, we devised a new chiral auxiliary, *N*,*N*′-bis((*S*)-1-phenylethyl)urea,[7] which reasonably satisfies the above requisites. In this paper, we present its application to the synthesis of optically pure methyl (3*R*,4*R*,6*R*)-bicyclo[2.2.1]heptene-4-carboxylate (**8**)[8] by the route depicted in Scheme I.

N-Acrylyl-*N*,*N*′-bis((*S*)-1-phenylethyl)urea (**3a**) and *N*-crotonyl-*N*,*N*′-bis((*S*)-1-phenylethyl)urea (**3b**) were synthesized from the corresponding acids (acrylic acid and crotonic acid) and the carbodiimide **2**,[9] which was prepared from the chiral urea **1**.[10]

Diels–Alder reactions of dienophiles **3a** and **3b** with dienes (cyclopentadiene, isoprene, and 1,3-cyclohexadiene) were investigated in the presence of several Lewis acids (Table I). For comparison, all four possible Diels–Alder adducts were prepared as authentic samples from the corresponding acid[11] (bicyclo[2.2.1]heptene-4-carboxylic acid, bicyclo[2.2.2]octene-4-carboxylic acid, 5-methylbicyclo[2.2.1]heptene-4-carboxylic acid, and 1-methylcyclohexene-4-carboxylic acid) and the chiral carbodiimide **2**.[9] The ratio of diastereomers was determined by ^{1}H NMR and HPLC analysis.[12]

The reaction of dienophile **3a** with cyclopentadiene was investigated first (Scheme I, Table II). An uncatalyzed reaction[13] afforded the products in good yield with poor stereoselectivity. To increase the selectivity, the reaction was examined with Lewis acids at low temperature. The endo selectivity was significantly improved (>96%) together with a conspicuous increase in the diastereomeric ratio of endo-bicyclic acylureas (**4**/**5**). Out of the Lewis acids examined (Table I), titanium tetrachloride, at −78 °C, was found to give the highest diastereoselectivity (**4**/**5**) of 83:17 (entry no. 8). Tetrafluoroborate diethyl etherate gave a low yield with moderate selectivity. Tin(IV) chloride and diethylaluminum chloride significantly promoted the reaction, but the selectivity was moderate to poor. Dienophile **3b** was quite unreactive. Also, dienophile **3a** has poor reactivity toward dienes due to the steric interactions involved in the transition state.

The observed stereoselectivity can be rationalized by considering the complex depicted in Figure 1. The π–π interactions of the pendant vinyl group with the phenyl group[14] can occur on either the upper face (A) or lower face (B). In the former case, the proton–proton repulsions between the olefin and the methyl group of the phenethyl moiety will make for an unstable conformation. The interactions from the lower face (B) therefore seem to be more serious, and the Diels–Alder reaction should occur stereoselectivity from the upper face (A), giving the bicyclic acylurea **4a** as a major product.

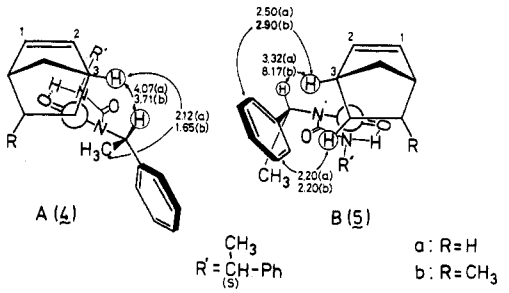

Figure 2.

The ^{1}H NMR spectra of **4a** show a characteristic upfield shift of 0.4 ppm for the H-C3 proton as compared to the analogous proton in **5a** (comparison of chemical shifts of various bicyclo[2.2.1]heptene-4-carboxylic acid derivatives[15] was carried out, as shown in Table II). A similar tendency was also observed for the other 4*R*-series adducts, which show upfield H-C3 signals compared to those in the 4*S*-series.

Inspection of two conformational models A and B in Figure 2, for adducts **4** and **5**, respectively, suggests that the bridgehead proton at C3 should be shielded by the phenyl group in **5** (model B), while the one in **4** (model A) is too far to experience such an effect. This explains the upfield shift of H-C3 in **4**.

The conformations for the adducts (**4** and **5**) can be also deduced from analysis of NOE enhancements (Figure 2) in the 500-MHz ^{1}H NMR spectra.

The Diels–Alder adducts were easily separated by column chromatography on silica gel,[16] using hexane–ethyl acetate as an eluant (**4a** and **5a** (α = 1.56),[17] **4b** and **5b** (α = 1.51), **9** and **10** (α = 1.42), **11** and **12** (α = 1.08)). The excellent separability of the Diels–Alder adducts can be explained on the basis of the conformational differences protrayed in model A and B. The attractive interactions of silica gel oxygen (adsorbent) with the N–H seem to be hindered by the bicyclic skeleton in **4** (model A) as compared to the one in **5** (model B) in which the interaction site is relatively accessive. Accordingly adduct **5** (model B, 4*S*-form) was observed to be more polar than **4** (model A, 4*R*-form).[18]

The absolute configuration of **4** and **5** was determined by low-temperature (0 °C, 8 h) methanolysis (NaOMe/MeOH) of **4a** (Scheme I) to methyl ester **8** (94%) and urea **1** (83%). Polarimetric analysis showed that ester **8** was optically pure ($[\alpha]^{22}_D$ +144.6°).[19]

The demonstrated advantageous features of our chiral auxiliary *N*,*N*′-bis((*S*)-1-phenylethyl)urea are (i) formation

(7) *N*,*N*′-Bis((*S*)-1-phenylethyl)urea is a known product (ref 8); however, this is first example that the reagent is used as a chiral auxiliary of a carboxylic acid.

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of easily separable adducts, (ii) simple removal of the chiral urea by methanolysis to optically pure methyl (3R,4R,6R)-bicyclo[2.2.1]heptene-4-carboxylate, (iii) its commercial availability, and (iv) its efficient recycling. The above methodology can also be extended to the 3S,4S,6S enantiomer starting from N,N'-bis((R)-1-phenylethyl)urea.

Experimental Section

The purity of all title compounds was judged to be >95% by ^{1}H NMR spectral determinations. Melting points are uncorrected. Silica gel (Fujigel BW 820 MH) was used for column chromatography, and analytical TLC was performed on silica gel (Merck 7731).

N-((S)-1-Phenylethyl)-N-((((S)-1-phenylethyl)amino)carbonyl)acrylamide (3a). To a solution of acrylic acid (347 mg, 4.82 mmol) in 40 mL of acetonitrile was added triethylamine (404 mg, 4.00 mmol) at 0 °C. To the resulting solution was added dropwise a solution of N,N'-bis((S)-1-phenylethyl)carbodiimide (1.00 g, 3.97 mmol) in 10 mL of acetonitrile. After complete addition the temperature was raised to room temperature, and the solution was further stirred for 24 h. The solvent was removed in vacuo, and the products were separated by column chromatography on silica gel (hexane/ethyl acetate, 4:1) to give the acrylamide **3a** (937 mg, 73%): R_f 0.15 (hexane/ethyl acetate, 4:1); mp 71–72 °C (CCl_4); IR (CCl_4) 3300, 3000, 1700, 1660, 1520–1500 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.50 (d, J = 7.0 Hz, 1 H), 1.72 (d, J = 7.0 Hz, 1 H, 5.01 (qi, J = 7.0 Hz, 1 H), 5.60 (dd, J = 7.7, 4.5 Hz, 1 H), 6.13 (q, J = 7.0 Hz, 1 H), 6.33 (d, J = 7.7 Hz, 1 H), 6.33 (d, J = 4.5 Hz, 1 H), 7.4–7.2 (m, 10 H), 8.65 (s, 1 H); HRMS calcd for $C_{20}H_{22}N_2O_2$ 322.1680, found 322.1687. Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.41; H, 6.89; N, 8.74.

3b: R_f 0.40 (hexane/ethyl acetate, 2:1); mp 76–77 °C (hexane/carbon tetrachloride, 4:1); IR ($CHCl_3$) 3420, 3280, 3000, 1690, 1620, 1510, 1445, 1400, 1175, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.49 (d, J = 7.0 Hz, 3 H), 1.73 (d, J = 7.0 Hz, 3 H), 1.75 (dd, J = 7.0, 1.8 Hz, 3 H), 5.01 (qi, J = 7.0 Hz, 1 H), 6.03 (dd, J = 14.5, 1.8 Hz, 1 H), 6.07 (q, J = 7.0 Hz, 1 H), 6.91 (dq, J = 14.5, 7.0 Hz, 1 H), 7.21–7.35 (m, 10 H), 8.7 (broad, 1 H). Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.94; H, 7.18; N, 8.35.

Diels–Alder Reaction of Acrylylurea 3a with Cyclopentadiene in the Absence of a Catalyst. A solution of acrylylurea **3a** (315 mg, 0.9789 mmol) and cyclopentadiene (0.1 mL, 80 mg, 1.2 mmol) in 6 mL of toluene was heated in a sealed tube at 100 °C for 3 h. The products were chromatographed on silica gel to give exo adducts (**6a + 7a**) (60 mg, 16%), endo adduct **4a** (110 mg, 29%), endo adduct **5a** (101 mg, 27%), and recovered acrylylurea **3a** (28 mg, 9%).

Exo Adducts (6a + 7a): R_f 0.26 (hexane/ethyl acetate, 4:1); IR (neat) 3300, 3000, 2950, 1700, 1670–1650, 1540–1500, 1460 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) (**6a**) δ 1.2–1.5 (m, 2 H), 1.47 (d, J = 6.7 Hz, 3 H), 1.69 (d, J = 7.0 Hz, 3 H), 1.9–1.6 (m, 2 H), 2.36 (dd, J = 9.0, 4.6 Hz, 1 H), 2.90 (s, 1 H), 4.97 (qi, J = 7.0 Hz, 1 H), 5.69 (dd, J = 5.8, 2.8 Hz, 1 H), 5.98 (q, J = 7.0 Hz, 1 H), 6.09 (m, 1 H), 7.3–7.1 (m, 10 H), (**7a**) δ 1.2–1.5 (m, 2 H), 1.43 (d, J = 7.0 Hz, 3 H), 1.73 (d, J = 7.0 Hz, 3 H), 1.9–1.6 (m, 2 H), 2.43 (dd, J = 8.4, 4.8 Hz, 1 H), 2.90 (s, 1 H), 3.01 (s, 1 H), 4.94 (qi, J = 7.0 Hz, 1 H), 5.87 (q, J = 6.7 Hz, 1 H), 6.06 (dd, J = 5.3, 2.9 Hz, 1 H), 6.09 (m, 1 H), 7.3–7.1 (m, 10 H); HRMS calcd for $C_{25}H_{28}N_2O_2$ 388.2149, found 388.2149.

Endo Adduct 4a: R_f 0.21 (hexane/ethyl acetate, 4:1); IR (neat) 3340, 3000, 1710, 1660, 1510–1500, 1450, 1230–1210 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.2–1.8 (m, 4 H), 1.37 (d, J = 7.0 Hz, 3 H), 1.69 (d, J = 7.0 Hz, 3 H), 2.87 (s, 1 H), 3.18 (s, 1 H), 3.31 (qi, J = 7.0 Hz, 1 H), 5.88 (q, J = 7.0 Hz, 1 H), 6.08 (dd, J = 5.6, 3.0 Hz, 1 H), 6.24 (dd, J = 5.5, 3.0 Hz, 1 H), 7.3–7.1 (m, 10 H); HRMA calcd for $C_{25}H_{28}N_2O_2$ 388.2149, found 388.2157.

Endo Adduct 5a: R_f 0.18 (hexane/ethyl acetate, 4:1); IR (CCl_4) 3420, 3280, 2990, 1700, 1510, 1500, 1450, 1220–1200 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.2–1.6 (m, 3 H), 1.41 (d, J = 7.0 Hz, 3 H), 1.66 (d, J = 7.0 Hz, 3 H), 1.88 (ddd, J = 11.5, 9.1, 3.6 Hz, 1 H), 2.78 (s, 1 H), 2.89 (s, 1 H), 3.37 (qi, J = 4.2 Hz, 1 H), 4.94 (qi, J = 7.0 Hz, 1 H), 5.90 (dd, J = 5.8, 2.8 Hz, 1 H), 5.95 (q, J = 7.0 Hz, 1 H), 6.26 (dd, J = 5.5, 3.0 Hz, 1 H), 7.3–7.1 (m, 10 H); HRMS calcd for $C_{25}H_{28}N_2O_2$ 388.2149, found 388.2153.

An Example of Diels–Alder Reaction (at −78 °C) in the Presence of a Lewis Acid (BF_3·OEt_2). To a solution of acrylylurea **3a** (441 mg, 1.37 mmol) in 10 mL of CH_2Cl_2 was added dropwise, within 40 min, under an N_2 atmosphere, at −78 °C a solution of BF_3·OEt_2 (339 mg, 2.39 mmol) in 11 mL of CH_2Cl_2. The solution was stirred for 1 h at −78 °C. To this solution was added, within 40 min, a solution of cyclopentadiene (138 mg, 2.09 mmol) in 10 mL of CH_2Cl_2. After the addition, the solution was stirred for 1 h at −78 °C. Water (20 mL) was added to quench the reaction. The organic phase was separated, and the aqueous layer was extracted with two 20-mL portions of CH_2Cl_2. The combined organic fraction was dried ($MgSO_4$) and concentrated in vacuo. The oily products were chromatographed to give **6a + 7a** (5 mg, 1%), **4a** (76 mg, 14%), **5a** (47 mg, 9%), and recovered **3a** (331 mg, 75%).

Adduct 4b: R_f 0.34 (hexane/ethyl acetate, 4:1); IR (neat) 3325, 3060, 2970, 1700, 1650, 1500, 1200, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.78 (d, J = 6.6 Hz, 3 H), 1.41 (d, J = 7.0 Hz, 3 H), 1.41 (m, 1 H), 1.50 (m, 1 H), 1.74 (d, J = 7.0 Hz, 3 H), 1.85 (m, J = 6.3 Hz, 1 H), 2.45 (s, 1 H), 2.63 (dd, J = 4.1, 3.3 Hz, 1 H), 3.07 (s, 1 H), 4.93 (qi, J = 7.0 Hz, 1 H), 5.93 (dd, J = 5.5, 2.8 Hz, 1 H), 5.98 (q, J = 7.0 Hz, 1 H), 6.36 (dd, J = 5.5, 3.3 Hz, 1 H), 7.14–7.36 (m, 10 H), 7.9 (broad, 1 H); HRMS calcd for $C_{26}H_{30}N_2O_2$ 402.2305, found 402.2303.

Adduct 5b: R_f 0.26 (hexane/ethyl acetate, 4:1); IR (neat) 3325, 3060, 2975, 1700, 1650, 1510, 1220, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.13 (d, J = 7.2 Hz, 3 H), 1.31 (dd, J = 8.8, 1.7 Hz, 1 H), 1.42 (d, J = 7.0 Hz, 3 H), 1.42 (m, 1 H), 1.64 (d, J = 7.0 Hz, 3 H), 2.04 (m, 1 H), 2.46 (d, J = 1.4 Hz, 1 H), 2.51 (s, 1 H), 2.85 (s, 1 H), 2.85 (s, 1 H), 4.96 (qi, J = 7.0 Hz, 1 H), 5.80 (dd, J = 5.8, 2.7 Hz, 1 H), 6.02 (q, J = 7.0 Hz, 1 H), 6.36 (dd, J = 5.8, 3.2 Hz, 1 H), 7.17–7.32 (m, 10 H), 7.3 (broad, 1 H); HRMS calcd for $C_{26}H_{30}N_2O_2$ 402.2305, found 402.2304.

Adduct 9: R_f 0.22 (hexane/ethyl acetate, 4:1); IR (neat) 3300, 3050, 2940, 1700, 1640, 1500, 1445, 780, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.22 (m, 2 H), 1.33 (m, 3 H), 1.41 (d, J = 7.0 Hz, 3 H), 1.48 (m, 1 H), 1.68 (d, J = 7.0 Hz, 3 H), 2.51 (d, J = 2.8 Hz, 1 H), 2.78 (s, 1 H), 2.95 (t, J = 7.4 Hz, 1 H), 4.93 (qi, J = 7.0 Hz, 1 H), 5.96 (q, J = 7.0 Hz, 1 H), 6.30 (m, 2 H), 7.15–7.36 (m, 10 H); HRMS calcd for $C_{26}H_{30}N_2O_2$ 402.2305, found 402.2315.

Adduct 10: R_f 0.14 (hexane/ethyl acetate, 4:1); IR (neat) 3300, 3050, 2950, 1700, 1650, 1510, 1445, 790, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.05 (m, 2 H), 1.18 (tq, J = 12.2, 3.3 Hz, 1 H), 1.35 (m, 1 H), 1.43 (d, J = 7.0 Hz, 3 H), 1.58 (dt, J = 9.4, 3.0 Hz, 1 H), 1.67 (d, J = 7.0 Hz, 3 H), 1.75 (ddd, J = 12.2, 6.7, 3.0 Hz, 1 H), 2.33 (s, 1 H), 2.58 (t, J = 3.2 Hz, 1 H), 2.92 (t, J = 7.4 Hz, 1 H), 4.95 (qi, J = 7.0 Hz, 1 H), 6.01 (q, J = 7.0 Hz, 1 H), 6.18 (t, J = 7.0 Hz, 1 H), 7.17–7.33 (m, 10 H), 8.0 (broad, 1 H); HRMS calcd for $C_{26}H_{30}N_2O_2$ 402.2305, found 402.2302.

Adduct 11: R_f 0.24 (hexane/ethyl acetate, 4:1); mp 145.5–147.0 °C (hexane/benzene, 9:1); IR ($CHCl_3$) 3300, 2950, 1695, 1510, 1450, 1405, 1165, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.25 (m, 1 H), 1.48 (d, J = 7.0 Hz, 3 H), 1.58 (s, 3 H), 1.67 (d, J = 7.0 Hz, 3 H), 1.5–1.7 (m, 3 H), 2.10 (m, 1 H), 2.26 (m, 1 H), 2.60 (m, 1 H), 5.00 (qi, J = 7.0 Hz, 1 H), 5.33 (d, J = 1.9 Hz, 1 H), 6.17 (q, J = 7.0 Hz, 1 H), 7.23–7.34 (m, 10 H), 8.6 (broad, 1 H); MS (relative intensity) 390 (9), 285 (7), 243 (17), 181 (21), 120 (28), 105 (100). Anal. Calcd for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17. Found: C, 77.10; H, 7.78; N, 7.18.

Adduct 12: R_f 0.22 (hexane/ethyl acetate, 4:1); mp 132.5–133.5 °C (hexane/benzene, 9:1); IR ($CHCl_3$) 3275, 2925, 1695, 1505, 1445, 1400, 1165, 905, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.44 (d, J = 7.0 Hz, 3 H), 1.45–1.6 (m, 1 H), 1.61 (s, 3 H), 1.67 (d, J = 7.0 Hz, 3 H), 1.73 (m, 1 H), 1.90–1.95 (m, 3 H), 2.13 (t, J = 13.5 Hz, 1 H), 2.67 (m, 1 H), 4.96 (qi, J = 7.0 Hz, 1 H), 5.22 (s, 1 H), 6.06 (q, 1 H), 7.18–7.32 (m, 10 H), 8.0 (broad, 1 H); MS (relative intensity) 390 (9), 285 (6), 243 (20), 181 (20), 120 (26), 105 (100). Anal. Calcd for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17. Found: C, 76.96; H, 7.78; N, 7.15.

An Example of Diels–Alder Reaction (at −115 °C) in the Presence of a Lewis Acid (Et_2AlCl). To a solution of acrylylurea **3a** (475 mg, 1.47 mmol) in 10 mL of EtCl was added dropwise within 25 min a solution of Et_2AlCl (2.2 mmol) in 10 mL of EtCl under N_2 atmosphere at −115 °C. The solution was stirred for 1 h. Then a solution of cyclopentadiene (0.18 mL, 145

mg, 2.2 mmol) in 10 mL of EtCl was added within 25 min, and the solution was stirred for 1 h at −115 °C. Water (20 mL) was added to quench the reaction. The organic phase was separated, and the aqueous layer was extracted with two 20-mL portions of CH_2Cl_2. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The oily products were chromatographed to give **6a** + **7a** (9 mg, 2%), **4a** (228 mg, 40%), **5a** (108 mg, 19%), and recovered **3a** (171 mg, 36%).

A Preparative-Scale Procedure of a Diels–Alder Reaction of Acrylylurea 3a with Cyclopentadiene in the Presence of $TiCl_4$ (−78 °C). To a solution of acrylylurea **3a** (2.101 g, 6.52 mmol) in 100 mL of CH_2Cl_2 was added dropwise, within 30 min under N_2 atmosphere at −78 °C, a solution of $TiCl_4$ (0.807 mL, 1.39 g, 7.34 mmol) in 20 mL of CH_2Cl_2. To the solution was added, within 15 min, a solution of cyclopentadiene (0.786 mL, 616 mg, 9.32 mmol) in 10 mL of CH_2Cl_2. Water (30 mL) was added to quench the reaction. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic fraction was dried ($MgSO_4$) and concentrated in vacuo. The oily products were chromatographed on silica gel, by eluting with hexane/ethyl acetate (4:1) to give Diels–Alder products **4a** + **5a** + **6a** + **7a** 2.454 g (97%) and recovered **3a** (66 mg, 3%). Then the Diels–Alder adducts were separated by flash column chromatography on silica gel, eluting with hexane/ethyl acetate (9:1), to give exo adducts **6a** + **7a** (29 mg, 1%), endo adduct **4a** (1.860 g, 74%), and endo adduct **5a** (381 mg, 15%).

Methanolysis of Diels–Alder Adduct 4a. The acylurea **4a** (498 mg, 1.28 mmol) in 10 mL of methanol was added to a solution of sodium methoxide (prepared from sodium (304 mg, 13.2 mmol)) in 20 mL of methanol at 0 °C and stirred further for 8 h at 0 °C. The solution was acidified with 1 N hydrochloric acid (50 mL) and extracted with five 20-mL portions of dichloromethane. The combined organic solution was dried ($MgSO_4$) and concentrated in vacuo. The products were separated by column chromatography on silica gel, eluting with benzene–ethyl acetate (9:1), to give methyl bicyclo[2.2.1]heptene-4-carboxylate (**8**) (183 mg, 94%), recovered starting material **4a** (30 mg, 6%), and the removed urea **1** (285 mg, 83%). **8**: $[\alpha]^{22}_D$ +144.6° (c = 0.329, EtOH).[5]

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Registry No. **3a**, 119908-37-1; **3b**, 119908-38-2; **4a**, 119945-16-3; **4b**, 119908-40-6; **5a**, 119945-17-4; **5b**, 119945-18-5; **6a**, 119908-39-3; **7a**, 119945-15-2; **8**, 72203-34-0; **9**, 119908-41-7; **11**, 119908-42-8; **12**, 119945-19-6; $SnCl_4$, 7646-78-8; Et_2AlCl, 96-10-6; $TiCl_4$, 7550-45-0; $H_3CC(=CH_2)C(=CH_2)CH_3$, 513-81-5; 1,3-cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 29797-09-9; crotonic acid, 3724-65-0; acrylic acid, 79-10-7; *N,N'*-bis((*S*)-1-phenylethyl)carbodiimide, 57122-22-2.

Isolation of Stable 1:1 and 2:1 Salts of Nitrosamines with Protic Acids

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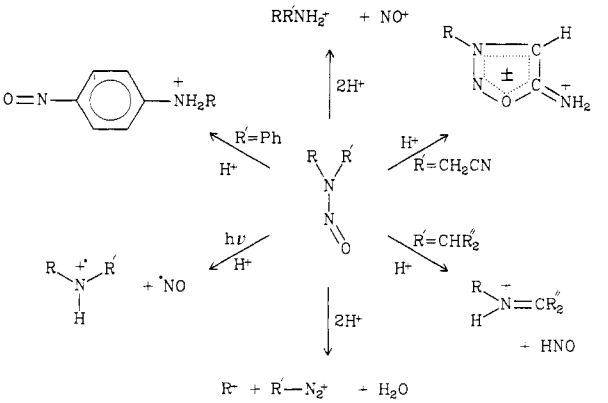
Several well-defined salts of *N*-nitroso compounds with Brønsted acids have been prepared. Both 1:1 and 2:1 adducts of nitrosamine to acid have been characterized. The former were isolated after reacting the nitrosamines with perchloric or trifluoromethanesulfonic acid and are of the form $R_2N{=}NOH^+X^-$ (X^- = ClO_4^- or $CF_3SO_3^-$). The 2:1 adducts were isolated from nitrosamine–hexafluorophosphoric acid mixtures; they have the structure $(R_2N{=}NO{---}H{---}ON{=}NR_2)^+PF_6^-$, in which two nitrosamine molecules are associated with each proton in a very strong, symmetrical hydrogen bond. The surprising stability of the salts reported here may be attributed to the use of nonnucleophilic counterions and solvents, as well as of polar media that increase the double-bond character of the N–N linkage. The practical application of these findings to the formation of crystalline derivatives of liquid nitrosamines and to the suppression of their volatility in certain synthetic and analytical procedures is discussed.

The literature to date suggests that nitrosamines are moderately to highly unstable in the presence of protic acids. While numerous N,N-disubstituted *N'*-hydroxydiazenium ions have been characterized in solution,[1-3] protonated nitrosamines are known to decompose by a variety of mechanisms (Scheme I). These include heterolysis of the N–N bond to produce ammonium ions,[3-7] cyclization of α-nitrosamino nitriles to sydnone imines,[8]

Scheme I. Some Pathways of Nitrosamine Decomposition under Protonating Conditions (see ref 3–11)



disproportionation to iminium ions and nitroxyl,[3] dissociation of the C–N linkage to yield carbocations,[3] photolysis

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