an effort to trap the acylium ion **2**. This was also unsuccessful. No ketones were formed in the reaction.

The formation of the two hydrolysis products **6** and **7** is rather intriguing. Although **6** probably results from direct nucleophilic attack of water on the carbonyl of **5d**, the formation of **7** by an S_N2 pathway seems unlikely due to the fact that backside attack is highly hindered. It seems most likely that **7** arises from the dipolar intermediate **3**, i.e., perhaps the diazetidinone **5** may be in equilibrium with trace amounts of the 1,4-dipole **3**.

Experimental Section

All melting and boiling points are uncorrected. The infrared spectra were recorded on a Perkin-Elmer 197 spectrophotometer. The ^1H NMR spectra were recorded on a Perkin-Elmer R32 (90 MHz) spectrometer. The ^{13}C NMR spectra were recorded on a Nicolet NT-200 FT-NMR spectrometer. Microanalysis were performed by Gailbraith Laboratories, Knoxville, TN.

The 4-substituted-1,2,4-triazoline-3,5-diones were prepared by oxidation of the corresponding urazoles with *N*-bromosuccinimide.[18] The 4-alkyl-TAD's were purified by sublimation prior to use and the phenyl-TAD was recrystallized from methylene chloride at −10 °C.

General Procedure. In 10 mL of spectroscopic grade methylene chloride was dissolved 0.002 mol of the R-TAD. This was added dropwise with stirring to a solution of 0.002 mol of diphenylketene in methylene chloride at 0–5 °C. In the case of phenyl-TAD, the reverse addition was used. After the addition was complete, the solvent was removed under vacuum. The reaction was essentially quantitative. Analytical samples were prepared by recrystallization with recovered yields in the range of 49–54%. The product from diphenylketene and *n*-butyl-TAD was a viscous oil. IR, ^1H NMR, melting points, recrystallization solvent, and ^{13}C NMR data are given below. Satisfactory elemental analyses were obtained for **5a**, **5b**, **5c**, and **5e**; **5d** was not analyzed.

Compound **5a**: IR (Nujol) 1852, 1785, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.96 (s), 7.3 (m); mp 155–156 °C (from nitroethane); ^{13}C NMR ($CDCl_3$) δ 149.8 (C_1), 94.5 (C_2), 164.5 (C_3), 158.3 (C_4), 133.0, 130.1, 129.0, 127.3 (aryls), 26.6 (CH_3).

Compound **5b**: IR (Nujol) 1860, 1789, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (t), 3.48 (q), 7.41 (m); mp 114–115 °C (from ether); ^{13}C NMR ($CDCl_3$) δ 149.7 (C_1), 94.8 (C_2), 164.9 (C_3), 158.2 (C_4), 133.0, 130.1, 129.0, 127.4 (aryls), 13.0 (CH_3), 36.3 (CH_2).

Compound **5c**: IR (Nujol) 1855, 1785, 1725 cm^{-1}; ^1H NMR δ 0.65 (t), 1.47 (m), 3.37 (t), 7.42 (m); mp 101–102 °C (from ether); ^{13}C NMR ($CDCl_3$) δ 149.8 (C_1), 94.7 (C_2), 164.8 (C_3), 158.4 (C_4), 133.1, 130.0, 129.1, 127.1 (aryls), 11.1 (CH_3), 20.8 (CH_2), 42.8 (CH_2N).

Compound **5d**: IR (neat) 1852, 1780, 1732 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 0.84 (t), 1.4 (m), 3.41 (t), 7.40 (m); viscous ligand.

Compound **5e**: IR (Nujol) 1860, 1782, 1730 cm^{-1}; ^1H NMR ($CHCl_3$) δ 7.45 (m); mp 170–172 °C dec (from ethyl acetate); ^{13}C NMR ($CHCl_3$) δ 148.7 (C_1), 95.8 (C_2), 164.7 (C_3), 157.1 (C_4), 133.5, 132.7, 130.3, 128.3, 128.0, 127.2, 125.6 (aryls).

Hydrolysis of 5d. The viscous oil obtained from the above reaction between *n*-butyl-TAD and diphenylketene was allowed to stand open to the air for 4 months. Treatment of this oil with anhydrous ether gave a precipitate, mp 180–181 °C (5.7% yield). It was soluble in 5% sodium hydroxide but insoluble in 5% sodium bicarbonate. It was identified as 1-[2,2-diphenyl-2-(hydroxyacetyl)]-4-*n*-butylurazole: IR (Nujol, cm^{-1}) 3295, 1810, 1785, 1712; ^1H NMR ($CDCl_3$) δ 0.77 (3 H, t), 1.2 (4 H, m), 3.26 (3 H, t) NH and OH too broad to observe, 7.26 (10 H, m).

Anal. Calcd for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 66.01; H, 5.75; N, 11.20.

Removal of the ether from the above filtrate gave an oil. Treatment of this oil with nitromethane gave a second solid. It was dissolved in 5% sodium bicarbonate. The solution was filtered and the filtrate was acidified to give a 25% yield of 2-[1-(4-*n*-butylurazolyl)]-2,2-diphenylacetic acid: mp 170–182 °C dec; IR (Nujol, cm^{-1}) 3150, 1770, 1728, 1711, 1664; ^1H NMR ($CDCl_3$) 0.81 (3 H, t), 1.0–1.5 (4 H, m), 3.32 (2 H, t), 7.2–7.6 (10 H, m), 8.9 (1 H, v br), 10.2 (1 H, v br).

Anal. Calcd for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.44; H, 5.79; N, 11.36.

Registry No. **1a**, 13274-43-6; **1b**, 40609-72-1; **1c**, 90046-99-4; **1d**, 13482-57-0; **1e**, 4233-33-4; **4**, 525-06-4; **5a**, 90047-00-0; **5b**, 90047-01-1; **5c**, 90047-02-2; **5d**, 90047-03-3; **5e**, 90047-04-4; **6**, 90047-05-5; **7**, 90047-06-6.

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Synthesis of 1-(*p*-Carbomethoxyphenyl)-3-pyrrolidinone by a Diels–Alder Route[1]

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In connection with studies directed toward the synthesis of various annulated methotrexate and aminopterin derivatives as potential antimitotic agents, we required a convenient synthesis of 1-(*p*-carbomethoxyphenyl)-3-pyrrolidinone (**1**). This compound had previously been prepared in our laboratory either by Dieckmann cyclization of methyl *p*-[*N*-(carbomethoxymethyl)-*N*-(carbomethoxyethyl)amino]benzoate, followed by decarbomethoxylation, or by arylation of 3-pyrrolidinol with methyl *p*-fluorobenzoate, followed by oxidation.[3] We now describe a third synthesis of this key intermediate that represents a novel exploitation of our recently described conversion of primary amino groups to nitroso compounds.[4]

Treatment of methyl *p*-aminobenzoate with dimethyl sulfide, followed immediately by the addition of *N*-chlorosuccinimide in CH_2Cl_2 at −25 °C, gave a white slurry, which, upon extraction with 5% sodium hydroxide, gave a solution of the sulfilimine **2** (Scheme I). Oxidation of **2** in situ at 0 °C to methyl *p*-nitrosobenzoate (**3**) was accomplished by addition of 1.2 equiv of *m*-chloroperbenzoic acid. Diels–Alder reaction of **3** with 2-methoxy-1,3-butadiene at 0 °C then led to separation of the dihydro-2*H*-1,2-oxazine **4** in 76% yield.

Initial attempts to effect hydrogenolysis of the N–O bond in **4** were disappointing. Zinc in acetic acid, which has been used successfully to cleave the N–O bond in many related dihydrooxazines,[5] failed to give the desired amino alcohol **5**. Aluminum amalgam, reputed to be the most effective of available reducing agents for such N–O bond cleavages,[6] gave **5** in very low yield, and the product proved to be both difficult to purify and resistant to cyclization to the pyrroline **6**. The dihydro-2*H*-1,2-oxazine enol ether **4** was therefore hydrolyzed in 1 N hydrochloric acid at room temperature to the tetrahydro-2*H*-1,2-oxazinone **7**. Although neither zinc in acetic acid nor aluminum amal-

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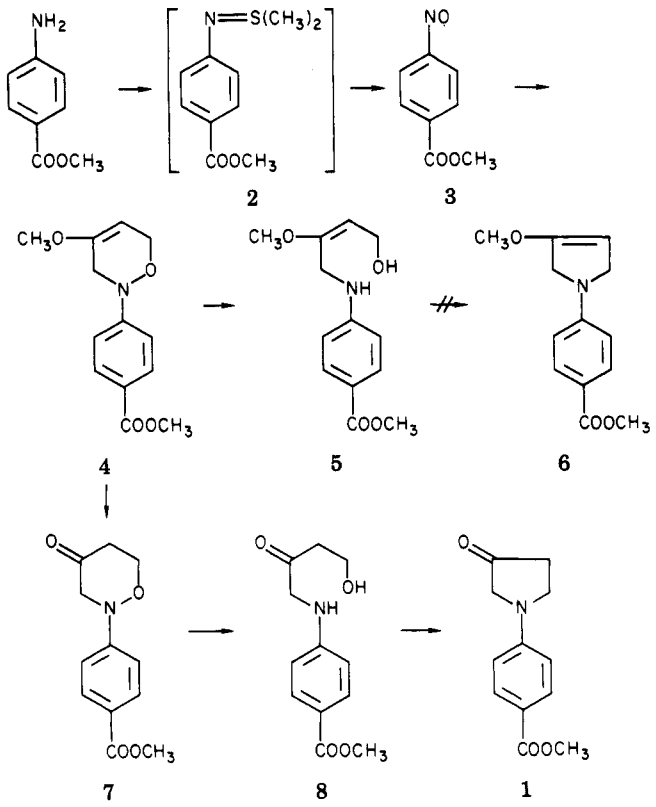
Scheme I



gam successfully effected N–O bond cleavage with **7**, hydrogenation over Pd/C led in 75% yield to the desired amino alcohol **8**.

Dehydrative ring closure of **8** to the target 3-pyrrolidinone **1** failed both with triphenylphosphine/diethyl azodicarboxylate/toluene[7] and with triphenylphosphine/triethylamine/CCl_4/acetonitrile,[8] but this key conversion could be successfully effected in moderate yield (53%) with 2 equiv of *p*-toluenesulfonyl chloride at 0 °C in the presence of pyridine.[9]

Given the wide structural variations possible with both Diels–Alder partners, the above cycloaddition route to **1** should prove to be generally useful for the preparation of 1-aryl(or hetaryl)-3-pyrrolidinones.

Experimental Section

Methyl *p*-Nitrosobenzoate (3). To a solution of 8.05 g (0.053 mol) of methyl *p*-aminobenzoate in 150 mL of CH_2Cl_2 at −25 °C was added 4.0 mL (3.37 g, 0.054 mol) of dimethyl sulfide, followed immediately by dropwise addition of 7.82 g (0.055 mol) of *N*-chlorosuccinimide in 400 mL of CH_2Cl_2. After the addition was complete, the reaction mixture was stirred for 1 h at −25 °C and then extracted with 400 mL of 5% aqueous sodium hydroxide. The organic layer was separated, dried over anhydrous sodium sulfate, and filtered, and the filtrate was added in one portion to 11.63 g (0.067 mol) of *m*-chloroperbenzoic acid in 200 mL of CH_2Cl_2 at 0 °C. The reaction mixture immediately turned green. It was stirred for 30 min and extracted with 200 mL of saturated aqueous sodium carbonate, and the organic layer was separated, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. Recrystallization of the residual brown solid from hot methanol then gave 4.60 g (52%) of **3** as yellow needles, mp 126–127 °C (lit.[10] mp 128–129.5 °C).

Anal. Calcd for $C_8H_7NO_3$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.07; H 4.29; N, 8.39.

2-(*p*-Carbomethoxyphenyl)-4-methoxy-3,6-dihydro-2*H*-1,2-oxazine (4). To a slurry of 3.99 g (0.024 mol) of methyl *p*-nitrosobenzoate in 30 mL of $HCCl_3$ at 0 °C was added dropwise 8.13 g (0.097 mol) of 2-methoxy-1,3-butadiene. The reaction mixture was stirred for 1 h, during which time the color of the solution became orange. The solution was warmed to room temperature and unreacted diene and solvent removed by evaporation under reduced pressure. The residual orange solid was triturated in hot methanol and filtered. Cooling of the filtrate then resulted in separation of 4.56 g (76%) of **4**: mp 95 °C; NMR ($CDCl_3$) δ 7.98 (d, 2 H, J = 9 Hz), 7.08 (d, 2 H, J = 9 Hz), 4.82 (m, 1 H), 4.54 (m, 2 H), 3.89 (s, 3 H), 3.85 (d, 2 H, J = 1.3 Hz), 3.64 (s, 3 H).

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.46; H, 6.00; N, 5.46.

2-(*p*-Carbomethoxyphenyl)tetrahydro-2*H*-1,2-oxazin-4-one (7). A slurry of 9.75 g (0.039 mol) of 2-(*p*-carbomethoxyphenyl)-4-methoxy-3,6-dihydro-2*H*-1,2-oxazine in 200 mL of 15% aqueous hydrochloric acid was stirred at room temperature for 48 h. Chloroform (50 mL) was then added, the aqueous phase neutralized with saturated sodium bicarbonate solution, and the organic layer separated. The aqueous layer was extracted twice with 100-mL portions of chloroform, and the combined chloroform extracts were dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. Recrystallization of the residual yellow solid from 2-propanol gave 7.6 g (84%) of **7** as colorless needles: mp 124–126 °C; NMR ($CDCl_3$) δ 8.03 (d, 2 H, J = 9 Hz), 7.09 (d, 2 H, J = 9 Hz), 4.48 (t, 2 H, J = 7 Hz), 4.01 (s, 2 H), 3.91 (s, 3 H), 2.77 (t, 2 H, J = 7 Hz).

Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.11; H, 5.56; N, 6.19.

1-(*p*-Carbomethoxyanilino)-4-hydroxy-2-butanone (8). A mixture of 5.0 g (0.021 mol) of 2-(*p*-carbomethoxyphenyl)tetrahydro-2*H*-1,2-oxazin-4-one and 0.75 g of 5% Pd/C in 100 mL of ethanol was hydrogenated under 45 atm of hydrogen for 11 h. The reaction mixture was then filtered through Celite, the filtrate evaporated under reduced pressure, and the residual solid recrystallized from ethanol to give 3.88 g (78%) of **8** as light pink needles: mp 106 °C; NMR ($CDCl_3$) δ 7.87 (d, 2 H, J = 9 Hz), 6.54 (d, 2 H, J = 9 Hz), 5.00 (br s, 1 H, OH), 4.08 (s, 2 H), 3.96 (t, 2 H, J = 5.6 Hz), 3.85 (s, 3 H), 2.76 (t, 2 H, J = 5.6 Hz), 2.12 (br s, 1 H, NH).

Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.59; H, 6.15; N, 6.14.

1-(*p*-Carbomethoxyphenyl)-3-pyrrolidinone (1). To a solution of 0.47 g (2 mmol) of 1-(*p*-carbomethoxyanilino)-4-hydroxy-2-butanone in 4 mL of pyridine at −5 °C was added a solution of 0.762 g (4 mmol) of *p*-toluenesulfonyl chloride in 1 mL of pyridine. After 24 h of stirring, the reaction mixture was diluted with 10 mL of water and the mixture extracted three times with 30-mL portions of ether. The combined ether extracts were washed with 25 mL of water, 4 × 25 mL portions of saturated cupric sulfate solution, 25 mL of water, and 30 mL of saturated aqueous sodium chloride solution. The organic layer was separated, dried over anhydrous sodium sulfate, and filtered, and the filtrate was evaporated under reduced pressure. The residual solid was dissolved in 3 mL of toluene and filtered rapidly through a short column of Florisil. The Florisil was then washed with 20 mL of 1:1 ether/petroleum ether, and the combined filtrates were evaporated under reduced pressure to give 0.208 g (53%) of **1** as colorless crystals: mp 162–164 °C; NMR ($CDCl_3$) δ 7.98 (d, 2 H, J = 9 Hz), 6.93 (d, 2 H, J = 9 Hz), 3.89 (s, 3 H), 3.7–3.9 (superimposed s and t, 4 H, NCH_2CO and NCH_2CH_2CO), 2.79 (t, 2 H, NCH_2CH_2CO, J = 8 Hz).

Anal. Calcd for $C_{12}H_{13}NO_4$: C, 65.75; H, 5.94; N, 6.39. Found: C, 65.60; H, 5.96; N, 6.41.

Registry No. **1**, 90030-20-9; **3**, 13170-28-0; **4**, 90030-17-4; **7**, 90030-18-5; **8**, 90030-19-6; *p*-$NH_2C_6H_4C(O)OMe$, 619-45-4; $CH_2{=}C(OMe)CH{=}CH_2$, 3588-30-5.

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