Regiospecific and Stereospecific Palladium-Catalyzed Cycloaddition of Azetidines and Carbodiimides

Jin-Ook Baeg, Corinne Bensimon, and Howard Alper*

Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada K1N 6N5

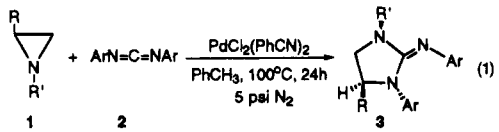
Received March 29, 1994[⊗]

Azetidines react with carbodiimides in the presence of bis(benzonitrile)palladium dichloride to form tetrahydropyrimidin-2-imines in 64–97% yields. The reaction is both regio- and stereospecific, the cycloaddition occurring with retention of configuration of the carbon centers bearing the substituent groups.

Introduction

Cycloaddition reactions of three-membered ring heterocycles with heterocumulenes is a useful method for the formation of five-membered ring heterocycles.[1-11] In principle, six-membered ring heterocycles can be synthesized by cycloaddition of four-membered ring heterocycles and heterocumulenes. Few publications have appeared on this subject. For example, reaction of oxetane and carbon dioxide catalyzed by organotin halides gave poly(trimethylene carbonate) and trimethylene carbonate.[12] Also, oxazinones were synthesized from oxetanes and isocyanates using organotin halides as catalysts. In spite of using an excess amount of oxetane (the ratio of oxetane/isocyanate is 3/1), the yields of oxazinones are relatively low.[13] There are no examples of the cycloaddition of azetidines and heterocumulenes. This may be due, in part, to the lower ring strain of the azetidine compared with that of the aziridine ring system. Consequently, ring cleavage of an azetidine occurs much less readily than that of an aziridine.[14]

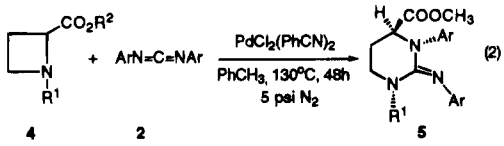
It was recently reported that bis(benzonitrile)palladium dichloride catalyzes the cycloaddition of aziridines **1** and carbodiimides **2** to form imidazolidinimines **3** in fine yields (eq 1).[15] We were gratified to observe that



tetrahydropyrimidin-2-imines **5** are isolated in excellent yields by the Pd(II)-catalyzed cycloaddition of **2** with azetidines. The stereoselectivity of the reaction, determined by the cycloaddition of *trans*-1-*n*-butyl-2-carbomethoxy-4-methylazetidine (**6**) with di-*p*-chlorophenylcarbodiimide (**2**), clearly shows that the cycloaddition reaction of 1,2,4-trisubstituted azetidine and carbodiimides is stereospecific.

Results and Discussion

When 1-*tert*-butyl-2-carbomethoxyazetidine (**4**, R^1 = $C(CH_3)_3$, R^2 = CH_3) was reacted with an equimolar amount of di-*p*-chlorophenylcarbodiimide (**2**) in toluene at 130 °C, using bis(benzonitrile)palladium dichloride (10 mol %) as the catalyst, the tetrahydropyrimidin-2-imine **5** (Ar = *p*-ClC_6H_4, R^1 = $C(CH_3)_3$, R^2 = CH_3) was formed in 95% yield (eq 2). No reaction ocurred if dichlorobis-



(triphenylphosphine)palladium(II) is used as the catalyst. Furthermore, addition of 2 equiv of triphenylphosphine to the $(PhCN)_2PdCl_2$-catalyzed system resulted in complete inhibition of the reaction. Finally use of acetonitrile as the nitrile ligand in the palladium catalyst (instead of PhCN) afforded **5** in only 36% yield.

These results can be rationalized by consideration of the bond strength between the palladium metal and its ligand. Triphenylphosphine in $(PPh_3)_2PdCl_2$ is firmly bound and benzonitrile in $(PhCN)_2PdCl_2$ is labile.[16] Indeed, even the IR spectrum of a freshly prepared bis(benzonitrile)palladium dichloride solution (irrespective of solvent) shows two bands ($\nu_{C\equiv N}$ at 2230 and 2290 cm^{-1}) due to both free and complexed PhCN and both are of comparable intensity.[17] The acetonitrile ligand in $(MeCN)_2PdCl_2$ is more basic than the benzonitrile ligand of $(PhCN)_2PdCl_2$.[16] Therefore, $(PhCN)_2PdCl_2$ should react in a more facile manner than $(MeCN)_2PdCl_2$ with aze-

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1994.

(1) Shibata, I.; Baba, A.; Iwasaki, H.; Matsuda, H. *J. Org. Chem.* **1986**, *51*, 2177.
(2) L'abbe, G.; Asch, A. V.; Toppet, S. *Bull. Soc. Chim. Belg.* **1978**, *87*, 929.
(3) Komatsu, M.; Ohshiro, Y.; Hoho, H.; Sato, M.; Toshio, A. *J. Org. Chem.* **1974**, *39*, 948.
(4) Herweh, J. E.; Kaffman, W. J. *Tetrahedron Lett.* **1971**, 809.
(5) Matsuda, H.; Ninagawa, A.; Hasegawa, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2717.
(6) Fujiwara, M.; Baba, A.; Matsuda, H. *J. Heterocycl. Chem.* **1988**, *25*, 135.
(7) Nair, V.; Kim, K. H. *J. Org. Chem.* **1974**, *39*, 3763.
(8) Nomura, R.; Nakano, T.; Nishio, Y.; Ogawa, S.; Ninagawa, A.; Matsuda, H. *Chem. Ber.* **1989**, *122*, 2409.
(9) Fujinami, T.; Suziki, T.; Kamiya, M. *Chem. Lett.* **1985**, 199.
(10) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792.
(11) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1988**, *110*, 7933.
(12) Baba, A.; Kashiwagi, H.; Matsuda, H. *Organometallics* **1987**, *6*, 137.
(13) Baba, A.; Shibata, I.; Masahiro, F.; Matsuda, H. *Tetrahedron Lett.* **1985**, *26*, 5167.
(14) Lwowski, W. *Comprehensive Heterocyclic Chemistry*; Pergamon Press: Oxford, 1984; Vol. 7, p 237.
(15) Baeg, J. O.; Alper, H. *J. Org. Chem.* **1992**, *57*, 157.
(16) Wilkinson, S. G.; Stone, F. G. A.; Abel, E. W. *Comprehensive Organometallic Chemistry;* Pergamon Press: Oxford, 1982; Vol. 6, p 238
(17) Dietl, H.; Reinheimer, H.; Moffat, J.; Maitlis, P. M. *J. Am. Chem. Soc.* **1970**, *92*, 2276.

0022-3263/95/1960-0253$09.00/0

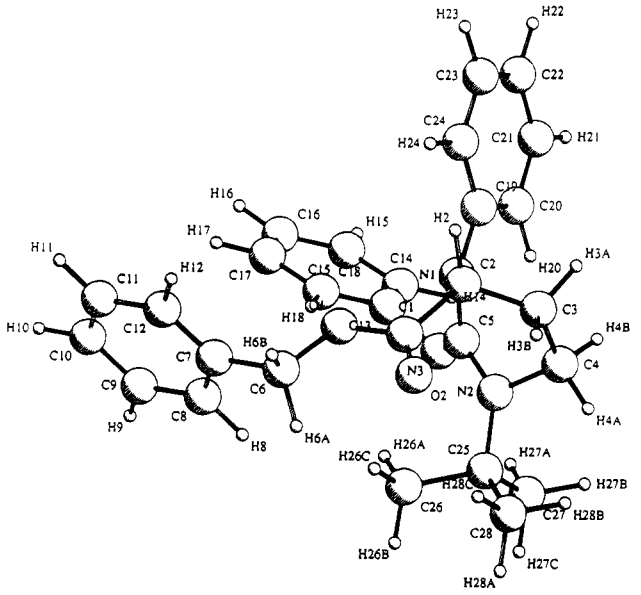


Figure 1. View of **5** ($R^1 = C(CH_3)_3$, $R^2 = CH_2C_6H_5$, Ar = Ph) showing the atom-numbering scheme.

Table 1. Reaction of Azetidines with Carbodiimides Catalyzed by $(PhCN)_2PdCl_2$[a]

Ar	R^1	R^2	yield of **5**[b] (%)
Ph	$C(CH_3)_3$	CH_3	92
Ph	$C(CH_3)_3$	$C_6H_5CH_2$	94
p-tolyl	$C(CH_3)_3$	$C_6H_5CH_2$	64
p-ClC_6H_4	C_6H_{11}	CH_3	88
p-ClC_6H_4	$C(CH_3)_3$	CH_3	95
p-ClC_6H_4	$C(CH_3)_3$	$C_6H_5CH_2$	97

[a] Reaction conditions: azetidine (1.0 mmol), carbodiimide (1.0 mmol), $(PhCN)_2PdCl_2$ (0.1 mmol), $PhCH_3$ (3.0 mL), 130 °C, 48 h, 5 psi N_2. [b] Isolated yields of pure materials.

tidines to give N-donor ligand complexes which are active species for the cycloaddition reaction.[15,18]

The bis(benzonitrile)palladium dichloride catalyzed cycloaddition reaction was effected using a variety of azetidines and carbodiimides, producing tetrahydropyrimidin-2-imines **5** in 64–97% yield (see Table 1). In all of these reactions the azetidines undergo selective cleavage of the more substituted ring carbon–nitrogen bond.

The tetrahydropyrimidin-2-imines **5** were identified by means of spectral data (see Experimental Section) and an X-ray analysis of one product. The imine and carbonyl stretching absorption bands of **5** occurred in the infrared spectrum at 1606–1623 cm^{-1} and 1736–1744 cm^{-1}, respectively.[19] The signals for the imine and carbonyl carbon appeared at δ 150.84–151.69 and δ 172.22–172.91, respectively, in the ^{13}C NMR spectra, and molecular ion peaks were observed in the mass spectra of **5**.[20] An X-ray structure determination revealed that the phenyl substituent of **5** ($R^1 = C(CH_3)_3$, $R^2 = CH_2C_6H_5$, Ar = Ph) was *trans* to both of the substituents ($O_2CCH_2C_6H_5$, $C(CH_3)_3$). An ORTEP drawing is presented in Figure 1.

The stereochemistry of the cycloaddition reaction is important for understanding the reaction mechanism as

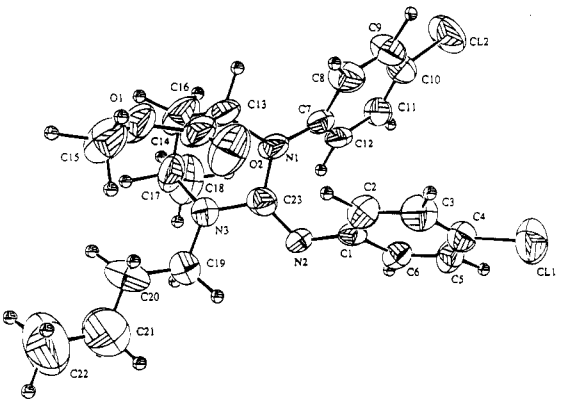
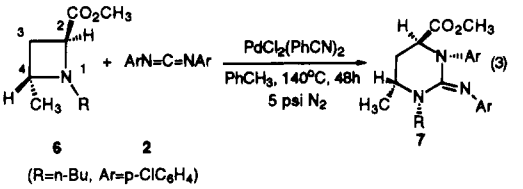


Figure 2. View of **7** ($R^1 = n\text{-}C_4H_9$, $R^2 = CH_3$, $R^3 = CH_3$, Ar = *p*-ClC_6H_4) showing the atom-numbering scheme.

well as for the design of biologically active tetrahydropyrimidine derivatives.[21] The reaction of *trans*-1-*n*-butyl-2-carbomethoxy-4-methylazetidine (**6**) with di-*p*-chlorophenylcarbodiimide (**2**) in toluene at 140 °C, for 48 h, using bis(benzonitrile)palladium dichloride as the catalyst, gave *trans*-1-*n*-butyl-3-(*p*-chlorophenyl)-4-carbomethoxy-6-methyl-3,4,5,6-tetrahydropyrimidine-2(1*H*)-*p*-chlorophenylimine (**7**) in 55% yield (eq 3). Compound

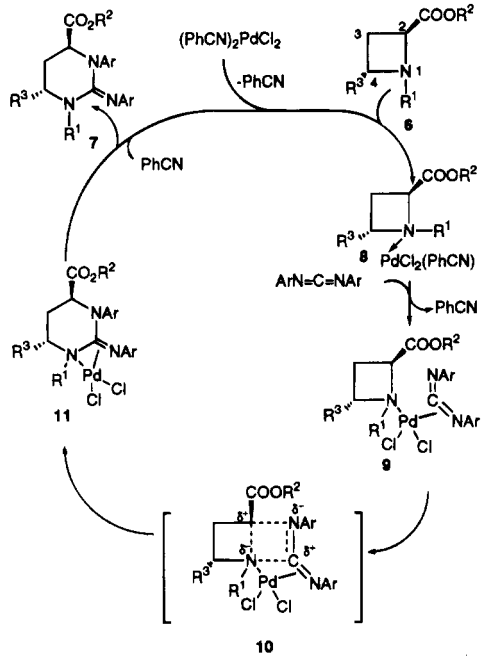


7 was identified by means of spectral data (see Experimental Section) as well as X-ray analysis. An ORTEP drawing is presented in Figure 2. As in the case of 1,2-disubstituted azetidine, the reaction proceeds by cleavage of only the N–C_2 bond (i.e. the N–C_4 bond is unaffected). The cycloaddition also occurs with retention of configuration. However, *trans*-1-*tert*-butyl-2-carbomethoxy-4-methylazetidine did not give any cycloaddition product under identical reaction conditions. This result can be explained by the probable slow rate of the formation of a palladium–azetidine N-donor ligand complex. Because of the steric hindrance caused by the bulky *N-tert*-butyl group, the formation of the N-donor ligand complex between the azetidine and $(PhCN)_2PdCl_2$ is much less efficient than in the case of *trans*-1-*n*-butyl-2-carbomethoxy-4-methylazetidine (**6**).

A possible pathway for the palladium-catalyzed cycloaddition reaction is outlined in Scheme 1. Reaction of $(PhCN)_2PdCl_2$ with the azetidine may afford the N-donor ligand complex **8**. Reaction of the latter with the carbodiimide can form **9**, in which there is π-complexation of one of the carbon–nitrogen double bonds to palladium.[22] The same intermediate **9** can result by complexation of the carbodiimide to Pd followed by the azetidine. It is also conceivable that the η-lone pair rather than π-electrons of the carbodiimide participate in bonding to palladium. Cycloaddition of the azetidine to the uncomplexed double bond of the carbodiimide ligand might be occurring via four-membered transition state **10** to give **11**. Therefore, the cycloaddition occurs with the retention of stereochemistry of the carbon

(18) Hassner, A.; Bunnel, C. A.; Haltiwanger, K. *J. Org. Chem.* **1978**, *43*, 57.
(19) Pretsch, E.; Seibl, J.; Simon, W.; Clerc, T. *Table of Spectral Data for Structure Determination of Organic Compounds;* Springer-Verlag: New York, 1983; pp I135, I190.
(20) Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy;* VCH: Weinheim, 1987; pp 226, 240.
(21) Adams, J. L.; Meek, T. D.; Mong, S. M.; Johnson, R. K.; Metcalf, B. W. *J. Med. Chem.* **1988**, *31*, 1355.
(22) Hoberg, H.; Korff, J. *J. Organomet. Chem.* **1978**, *150*, C20.

Scheme 1



centers bearing the substituent groups. If the cycloaddition of azetidine occurred by nucleophilic attack of the nitrogen of the carbodiimide at the C_2-carbon of the azetidine, then inversion of configuration would take place. Reaction of the latter with additional benzonitrile (dissociated from $(PhCN)_2PdCl_2$) and azetidine could afford the tetrahydropyrimidin-2-imine **7** and regenerate **8**.

In conclusion, bis(benzonitrile)palladium dichloride is an excellent catalyst for the stereospecific and regiospecific cycloaddition of azetidines and carbodiimides.

Experimental Section

General Methods. A Fisher-Johns apparatus was used for melting point determinations. The following spectrometers were used to obtain spectral data: Bomem MB 100-C15 (FT-IR); Bruker AMX 500, Varian XL-300, and Gemini 200 (NMR); VG 7070 E (MS). The azetidines, carbodiimides, and palladium catalysts were either purchased or prepared according to literature procedures.[23-27] The organic solvents were dried and distilled prior to use. Elemental analyses were carried out by MHW Laboratories, Phoenix, AZ. All reactions were conducted under a dry nitrogen atmosphere.

General Procedure for the Palladium-Catalyzed Cycloaddition Reaction of Azetidines and Carbodiimides. A mixture of azetidine (1.0 mmol), carbodiimide (1.0 mmol), and bis(benzonitrile)palladium dichloride (0.038 g, 0.10 mmol) in toluene (3.0 mL) was heated with stirring in a glass autoclave for 48 h, at 130 °C (oil bath temperature) under a slight pressure of nitrogen (5 psi). After being cooled to room temperature, the autoclave was opened and the red-brown homogeneous solution was filtered through Celite. The filtrate was concentrated by rotary evaporation, and the crude product was purified by silica gel thin-layer chromatography using 1:1 chloroform/acetonitrile as the developer. Melting points, IR, NMR, MS and analytical data for **5** are as follows:

(a) $R^1 = C(CH_3)_3$, $R^2 = CH_3$, Ar = Ph: viscous oil; IR $\nu_{C=N}$ 1619, $\nu_{C=O}$ 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 9H, $C(CH_3)_3$), 2.26 (m, 1H, CH_2), 2.57 (m, 1H, CH_2), 3.08 (m, 1H, CH_2N), 3.52 (m, 1H, CH_2N), 3.81 (s, 3H, CH_3), 4.07 (dd, 1H, $CHCO_2$, J = 2.3 and 7.7 Hz), 6.39–6.62 (m, 1H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 28.40 (CH_3), 29.84 (CH_2), 38.56 (CH_2N), 52.47 (CH_3), 56.11 ($C(CH_3)_3$), 61.44 ($CHCO_2$), 119.37, 121.66, 123.60, 124.44, 127.71, 128.33 (CH-aromatic), 145.03, 149.53, (quaternary aromatic carbons), 150.84 (C=N), 172.77 (C=O); MS m/e 365 [M^+]. Anal. Calcd for $C_{22}H_{27}N_3O_2$: C, 72.29; H, 7.45; N, 11.50. Found: C, 71.90; H, 7.55; N, 11.24.

(b) $R^1 = C(CH_3)_3$, $R^2 = CH_2Ph$, Ar = C_6H_5: mp 69–70 °C; IR $\nu_{C=N}$ 1619, $\nu_{C=O}$ 1736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9H, $C(CH_3)_3$), 2.23 (m, 1H, CH_2), 2.69 (m, 1H, CH_2), 3.17 (m, 1H, CH_2), 3.61 (m, 1H, CH_2), 4.17 (dd, 1H, $CHCO_2$, J = 2.4 and 7.6 Hz), 5.32 (dd, 2H, CH_2Ph, J = 12.0 and 35.6 Hz), 6.58–7.48 (m, 15H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 29.07 (CH_3), 30.25 (CH_2), 39.28 (CH_2N), 56.77 ($C(CH_3)_3$), 62.37 ($CHCO_2$), 68.34 (CH_2Ph), 119.89, 122.45, 124.30, 125.27, 128.31, 129.01, 129.35, 129.43, 129.64 (CH-aromatic), 135.98, 145.91 150.30 (quaternary aromatic carbons), 151.35 (C=N), 172.70 (C=O); MS m/e 441 [M^+]. Anal. Calcd for $C_{28}H_{31}N_3O_2$: C, 76.16; H, 7.08; N, 9.52. Found: C, 76.56; H, 7.31; N, 9.10.

(c) $R^1 = C(CH_3)_3$, $R^2 = CH_2Ph$, Ar = p-$CH_3C_6H_4$: mp 77–78 °C; IR $\nu_{C=N}$ 1623, $\nu_{C=O}$ 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9H, $C(CH_3)_3$), 2.10 (s, 3H, p-$CH_3C_6H_4$), 2.16 (s, 3H, p-$CH_3C_6H_4$), 2.35 (m, 1H, CH_2), 2.66 (m, 1H, CH_2), 3.15 (m, 1H, CH_2), 3.62 (m, 1H, CH_2), 4.16 (dd, 1H, $CHCO_2$, J = 2.2 and 7.4 Hz), 5.35 (dd, 2H, CH_2Ph, J = 12.0 and 35.6 Hz), 6.56–7.54, (m, 13H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 21.31, 21.36 (p-$CH_3C_6H_4$), 29.07 (CH_3), 30.08 (CH_2), 39.20 (CH_2N) 56.63 ($C(CH_3)_3$), 62.58 ($CHCO_2$), 68.22 (CH_2Ph), 122.15, 125.04, 128.85, 129.27, 129.39, 129.51, 129.58 (CH-aromatic), 128.70, 133.69, 136.06, 143.48, 147.69 (quaternary aromatic carbons), 151.37 (C=N), 172.82 (C=O); MS m/e 469 [M^+]. Anal. Calcd for $C_{30}H_{35}N_3O_2$: C, 76.73; H, 7.51; N, 8.95. Found: C, 76.40; H, 7.51; N, 8.86.

(d) $R^1 = C(CH_3)_3$, $R^2 = CH_2Ph$, Ar = p-ClC_6H_4: mp 123–124 °C; IR $\nu_{C=N}$ 1613, $\nu_{C=O}$ 1739 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (s, 9H, $C(CH_3)_3$), 2.31 (m, 1H, CH_2), 2.64 (m, 1H, CH_2), 3.11 (m, 1H, CH_2), 3.56 (m, 1H, CH_2), 4.08 (dd, 1H, $CHCO_2$, J = 2.5 and 7.7 Hz), 5.27 (dd, 2H, CH_2Ph, J = 30.0 Hz), 6.46–7.47 (m, 13H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 28.96 (CH_3), 30.17 (CH_2), 39.29 (CH_2N), 57.08 ($C(CH_3)_3$), 62.17 ($CHCO_2$), 68.50 (CH_2Ph), 123.43, 126.27, 128.33, 129.18, 129.45, 129.47, 129.65 (CH-aromatic), 124.95, 129.78, 135.60, 144.26, 148.56 (quaternary aromatic carbons), 151.69 (C=N), 172.22 (C=O); MS (*m/e*) 509 [M^+], 511 [$M^+ + 2$], 513 [$M^+ + 4$]. Anal. Calcd for $C_{28}H_{29}Cl_2N_3O_2$: C, 65.88; H, 5.73; N, 8.23. Found: C, 65.87; H, 5.62; N, 7.98.

(e) $R^1 = C_6H_{11}$, $R^2 = CH_3$, Ar = p-ClC_6H_4: mp 181–182 °C; IR $\nu_{C=N}$ 1606, $\nu_{C=O}$ 1744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92–2.11 (m, 10H, CH_2 of cyclohexyl), 2.31 (m, 2H, CH_2 ring), 3.25 (m, 2H, CH_2N), 4.10 (dd, 1H, $CHCO_2$, J = 4.8 and 6.5 Hz), 4.42 (m, 1H, CHN), 6.50–6.98 (m, 8H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 26.36, 28.12, 30.64 (CH_2 of cyclohexyl), 30.87 (CH_2 ring), 37.77 (CH_2N), 53.19 (CH_3), 55.98 (CHN), 61.89 (CH), 124.18, 125.85, 128.32, 129.12 (CH-aromatic), 124.85, 129.65, 144.94, 149.91 (quaternary aromatic carbons), 151.24 (C=N), 172.55 (C=O); MS m/e 459 [M^+], 461 [$M^+ + 2$], 463 [$M^+ + 4$]. Anal. Calcd for $C_{24}H_{27}N_3O_2Cl_2$: C, 62.61; H, 5.91; N, 9.13. Found: C, 62.41; H, 6.91; N, 8.93.

(f) $R^1 = C(CH_3)_3$, $R^2 = CH_3$, Ar = p-ClC_6H_4: mp 116–117 °C; IR $\nu_{C=N}$ 1614, $\nu_{C=O}$ 1741 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H, $C(CH_3)_3$), 2.27 (m, 1H, CH_2), 2.60 (m, 1H, CH_2), 3.09 (m, 1H, CH_2N), 3.54 (m, 1H, CH_2N), 3.84 (s, 3H, CH_3), 4.05 (dd, 1H, $CHCO_2$, J = 2.6 and 7.8 Hz), 6.55–6.90 (m, 8H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 28.95 (CH_3), 30.38 (CH_2), 39.23 (CH_2N), 53.14 (CH_3), 56.91 ($C(CH_3)_3$), 61.89 ($CHCO_2$), 123.38, 126.05, 128.38, 129.14 (CH-aromatic), 124.93, 129.52, 144.22, 148.83 (quaternary aromatic carbons), 151.53 (C=N), 172.91 (C=O); MS m/e 433 [M^+], 435 [$M^+ + 2$], 437 [$M^+ + 4$].

(23) Campbell, T. W.; Monagle, J. J.; Foldi, V. S. *J. Am. Chem. Soc.* **1962**, *84*, 3673.
(24) Doyle, J. R.; Slade, P. E.; Jonassen, H. B. *Inorg. Synth.* **1960**, *6*, 218.
(25) Cromwell, N. H.; Rodebaugh, R. M. *J. Heterocycl. Chem.* **1968**, *5*, 309.
(26) Cromwell, N. H.; Rodebaugh, R. M. *J. Heterocycl. Chem.* **1969**, *6*, 435.
(27) Cromwell, N. H.; Rodebaugh, R. M. *J. Heterocycl. Chem.* **1971**, *8*, 421.

Anal. Calcd for $C_{22}H_{25}Cl_2N_3O_2$: C, 60.83; H, 5.80; N, 9.67. Found: C, 60.58; H, 5.77; N; 9.50.

Synthesis of *trans*-1-*n*-Butyl-2-carbomethoxy-4-methylazetidine (6). A solution of 27.5g (0.1 mol) of methyl α,γ-dibromovalerate and 21.9 g (0.3 mol) of *n*-butylamine in 300 mL of acetonitrile was refluxed for 15 h. The mixture was diluted with ether (150 mL) and filtered and the solvent evaporated. The residue was extracted with ether (250 mL) and the extract exposed to a stream of hydrogen chloride gas for 5 min. The ether was decanted, and the residual syrup was dissolved in 25 mL of water. The aqueous solution was washed twice with ether (discarded), 150 mL of ether was added, and solid sodium bicarbonate was added to neutrality. The ether layer was separated, the aqueous layer was washed with three 50-mL portions of ether, and the combined extracts were dried over magnesium sulfate. Careful vacuum fractional distillation of the crude product through a 30-cm Vigreaux column gave 5.49 g (30%) of **6** as a colorless oil: bp 45–50 °C (0.5 mmHg); IR ($CDCl_3$) $\nu_{C=O}$ 1743 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (t, 3H, CH_3, J = 7.0 Hz), 1.14 (d, 3H, CH_3, J = 6.0 Hz), 1.28 (m, 4H, CH_2CH_2), 1.82 (m, 1H, CH_2 ring), 2.30 (m, 1H, CH_2 ring), 2.45 (m, 2H, CH_2N), 2.95 (m, 1H, CH), 3.34 (t, 1H, $CHCO_2$, J = 8.4 Hz), 3.65 (s, 3H, methoxy); ^{13}C NMR ($CDCl_3$) δ 14.48 (CH_3), 21.19 (CH_2), 22.83 (CH_3), 29.79 (CH_2 ring), 30.16 (CH_2), 52.32 (CO_2CH_3), 58.98 (CH_2N), 59.48 (CH), 62.75 ($CHCO_2$), 174.02 (C=O); MS m/e 185 [M^+]. Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34; N, 7.56. Found: C, 65.04; H, 10.34; N, 8.04.

Procedure for the Palladium-Catalyzed Cycloaddition Reaction of *trans*-1-*n*-Butyl-2-carbomethoxy-4-methylazetidine and 1,3-Di-*p*-chlorophenylcarbodiimide. A mixture of azetidine (1.0 mmol), carbodiimide (1.0 mmol), and bis(benzonitrile)palladium dichloride (0.076 g, 0.20 mmol) in toluene (3.0 mL) was heated with stirring in a glass autoclave for 48 h, 140 °C (oil bath temperature) under a slight pressure of nitrogen (5 psi). The workup procedure was the same as that described in the general procedure for the palladium-catalyzed cycloaddition reaction of azetidines and carbodiimides. The isolated yield of **7** was 0.25 g: 55% yield; mp 98–99 °C; IR $\nu_{C=N}$ 1607, $\nu_{C=O}$ 1744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, CH_3), 1.25 (m, 2H, CH_2), 1.30 (d, 3H, CH_3, J = 6.4 Hz), 1.45 (m, 2H, CH_2), 1.98 (m, 1H, CH_2), 2.65 (m, 1H, CH_2), 2.68 (m, 1H, CH_2, ring), 3.61 (m, 1H, CH), 3.84 (s, 3H, CH_3), 3.95 (m, 1H, CH_2 ring), 4.04 (dd, 1H, $CHCO_2$, J = 3.7 and 5.7 Hz), 6.55–6.98 (m, 8H, aromatic protons); ^{13}C NMR ($CDCl_3$) δ 14.56 (CH_3), 20.60 (CH_2), 22.03 (CH_3), 30.49 (CH_2), 35.06 (CH_2N), 47.56 (CH_2 ring), 49.69 (CH), 53.26 (CH_3), 61.77 ($CHCO_2$), 123.87, 126.02, 128.46, 129.27 (CH-aromatic), 125.09, 129.90, 144.17, 149.58 (quaternary aromatic carbons), 150.79 (C=N), 172.36 (C=O); MS m/e 447 [M^+], 449 [M^+ + 2], 451 [M^++ 4]. Anal. Calcd for $C_{23}H_{27}Cl_2N_3O_2$: C,61.61; H, 6.07; N, 9.37. Found: C, 61.41; H, 6.55; N, 9.29.

X-ray Analysis. A plate crystal of $C_{23}H_{27}Cl_2N_3O_2$ was mounted on glass capillary, and all measurements were made on a Rigaku diffractometer obtained from least-squares refinement using the setting angles of 25 reflections in the range $40° < 2\theta < 50°$ corresponding to a monoclinic cell.[30] For Z = 4 and FW = 451.35, the calculated density is 1.252 g/cm^3. The space group was determined to be $P21/n$. The data were collected at 20 °C using the $\omega-2\theta$ scan technique to a maximum 2θ value 49.9, and the data were corrected for Lorentz and polarization effects.[28]

The structure was solved by direct methods. All of the atoms with the exception of hydrogen were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 2069 observed reflections ($I > 2.5\sigma(I)$) and 272 variable parameters. All calculations were performed using the NRC VAX crystallographic software package.[29]

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council for support of this research.

(28) Grant, D. F.; Gabe, E. J. *J. Appl. Crystallogr.* **1978**, *11*, 114.
(29) Gabe, E. J.; Lee, A. L.; Lepage, Y. *J. Appl. Crystallogr.* **1987**, *22*, 384.
(30) The author has deposited atomic coordinates for structures **5** and **7** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.