Imidazole Transfer from 1,1′-Carbonyldimidazole and 1,1′-(Thiocarbonyl)diimidazole to Alcohols. A New Protocol for the Conversion of Alcohols to Alkylheterocycles

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The transfer of imidazole from 1,1′-carbonyldimidazole (CDI) and 1,1′-(thiocarbonyl)diimidazole in modest to excellent yields under mild conditions was observed with activated alcohols, unactivated alcohols generally providing the expected carbonylimidazole esters. Reasonable mechanisms for the transfer are proposed. 1,1′-Carbonyldi-1,2,4-triazole was found to work as well, providing a new heterocycle in good yield. Chemists should be aware of this reaction when treating benzylic, vinylogous benzylic, and benzhydryl alcohols with CDI-type reagents, expecting elimination of heterocycle rather than incorporation of heterocycle and elimination of CO_2.

Introduction

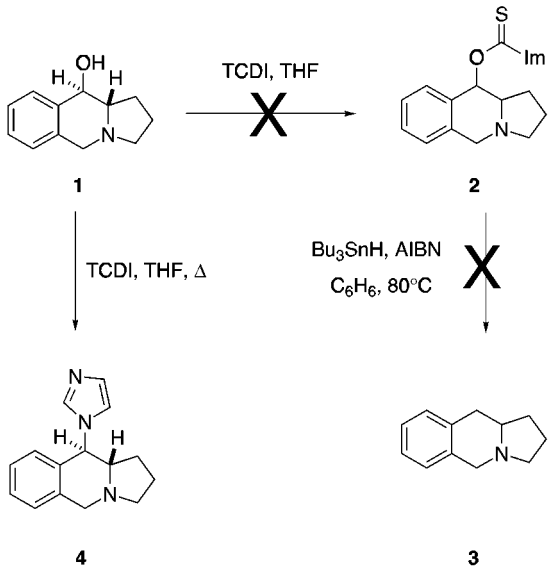
The imidazole group is a common functionality found in a number of biologically active and medicinally important molecules.[1] Examples of such imidazole-containing compounds include histidines, histamines, and antifungal agents such as miconazole, clotrimazole, and ketoconazole; histamine H_2-receptor antagonists such as cimetidine; and the hypnotic etomidate.[2]

New ways of preparing heterocycles are always of interest, especially if they employ mild methods which can tolerate many functional groups present in more complex molecules. During the course of our studies, we observed that (thiocarbonyl)diimidazole (TCDI) and carbonyldiimidazole (CDI)[3] transfer imidazole to benzylic, vinylogous benzylic, and benzhydryl carbinol carbons in modest to excellent yields.

Results and Discussion

In connection with other studies, we needed to prepare 1,2,3,5,10,10a-hexahydrobenz[*f*]indolizine, **3**, and decided to examine the deoxygenation of 10-hydroxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizine, **1**,[4] by Barton's method.[5a,b] We attempted to prepare the (thiocarbonyl)imidazole of **1** according to the literature[5b] by treatment of **1** with excess TCDI in refluxing THF (Scheme 1). The product of this reaction failed to react with tri-*n*-butyltin hydride/AIBN. Carbon NMR and FAB mass spectroscopy indicated that we did not obtain the (thiocarbonyl)imidazole **2** as expected, but rather the imidazole **4** in 54% yield. Interestingly, the transfer occurred with retention of stereochemistry! This assessment was based on the large coupling constants for the benzylic proton in **1** and **4**, which suggest an axial relationship between the benzylic and ring junction protons (see Experimental Section for spectroscopic evidence).

Scheme 1



To examine the generality of this reaction, we tested some representative substrates. The results are tabulated in Table 1. We also studied the use of CDI for this transformation in place of TCDI. As shown in Table 1, the more reactive CDI performs the transfer in higher yields. Other advantages of CDI are the higher purity of commercially available CDI, lower cost of the reagent, and cleaner products. (Combustion analysis of chromatographed **4** obtained from the reaction with TCDI showed the presence of 0.62% sulfur.) CDI thus is the preferred reagent.

α-Tetralol (entry 2) produced both the expected carbonylimidazole **6** in 55% yield (28% when TCDI used) and the imidazole **5**[6] in an unoptimized yield of 26% (13% with TCDI). Also isolated was an undetermined amount of 1,2-dihydronaphthalene, which likely resulted from elimination of the thiocarbonyl imidazole group.[7] An interesting case was provided by 4,4′-dimethoxybenzhy-

[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1997.

(1) For a review of the chemistry of imidazoles, see: Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry*; Potts, K. T., Ed.; Pergamon: New York, 1984; Vol. 5, Part 4A, p 345, 373, 457.

(2) For a review of medicinally important imidazoles, see: Roth, H. J.; Kleeman, A. *Pharmaceutical Chemistry*; John Wiley: New York, 1988; p 218.

(3) For reviews of CDI and TCDI, see: (a) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351. (b) Staab, H. A.; Rohr, W. In *Newer Methods of Preparative Organic Chemistry*; Foerst, W., Ed.; Academic Press: New York, 1968; Vol. 5, p 61. (c) *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley: New York, 1995; Vol. 7, p 1006, 4862.

(4) Rigo, B.; Kolocouris, N. *J. Heterocycl. Chem.* **1983**, *20*, 893.

(5) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Barton, D. H. R.; Motherwell, W. B. *Pure Appl. Chem.* **1981**, *53*, 15 and references cited therein.

(6) Compound previously reported: Hirsch, K. S.; Jones, C. D.; Taylor, H. M. U.S. Patent 4 659 730, 1987.

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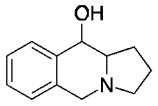
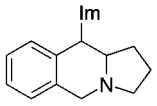
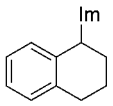
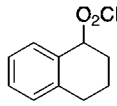
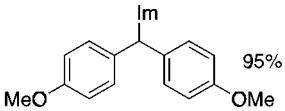
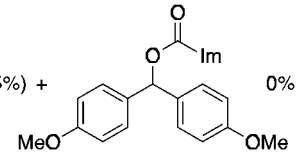
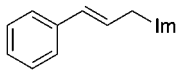
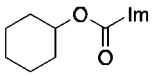
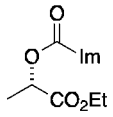
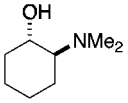
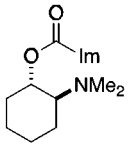
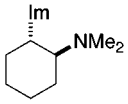
Table 1. Reactions of Alcohols with CDI and TCDI in Refluxing THF

Entry	Alcohol	Time (h)	Product(s)[a, b]
1	 **1**	7	 **4** 86% (54%)
2	α-tetralol	5	 **5** 26% (13%) +  **6** 55% (28%)
3	4, 4'-dimethoxybenzhydrol	6	 **7** 95% (35%) +  **8** 0%
4	cinnamyl alcohol	5.5	 **9** 69%
5	cyclohexanol	7	 **10** 88%
6	(*S*)-ethyl lactate	6	 **11** 75%
7		3.5	 **12**[c] 0%  **13** 0%

Im = imidazole. [a]Isolated yields of free bases. [b]Yields in parentheses are for TCDI. [c]Detected but not isolated.

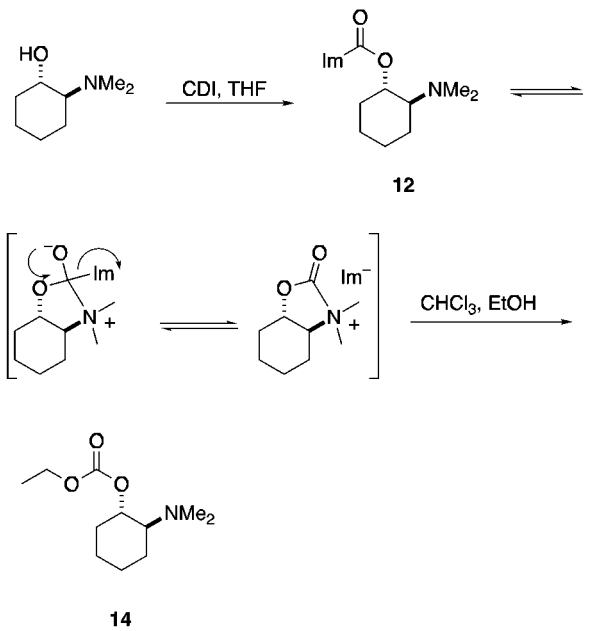
drol (entry 3). We obtained the benzhydrylimidazole **7** in a modest yield of 35% using TCDI in refluxing THF. Compound **7** was an oil, and the assigned structure was consistent with the spectral data. Also isolated was a mixture that appeared to contain some **8** and some other minor compounds that have not been clearly identified yet. A small amount of unreacted benzhydrol was detected, but was not isolated. In stark contrast, it has been reported that when the reaction is done with TCDI at room temperature in the solid state (grinding), the expected (thiocarbonyl)imidazole **8** was isolated as a solid in 85% yield.[8] As expected, the yield of **7** was substantially higher, 95%, when CDI was employed for the reaction.[9] Cinnamyl alcohol (entry 4) gave cinnamylimidazole (**9**)[10] in 69% yield as a yellow oil which solidified on standing after several days, along with what appeared to be a mixture of mainly cinnamyl alcohol plus unidentified impurities.

Both cyclohexanol (entry 5) and ethyl (*S*)-lactate (entry 6) yielded the expected carbonylimidazolides **10** and **11**, respectively, in good yields. 2-(*N*,*N*-Dimethylamino)cyclohexan-1-ol (entry 7 and Scheme 2) gave none of the imidazole **13** but did give the ester **12** which proved to be unusually reactive. Thus, when the reaction was worked up with chloroform containing 0.75% ethanol stabilizer, ethyl 2-(*N*,*N*-dimethylamino)cyclohexyl carbonate, **14**, was obtained in 67% yield. When the workup is limited to solvent removal only, IR and FAB mass

(7) The material still contained impurities after chromatography. ^{1}H NMR spectrum matches Sadtler Standard Spectra 18210M (1974).
(8) Hagiwara, H.; Ohtsubo, S.; Kato, M. *Tetrahedron* **1997**, *53*, 2415.
(9) 4,4′-Dimethoxybenzhydrol (5%) was recovered.

(10) Compound previously reported: Baggaley, K. H.; Heald, M.; Hindley, R. M.; Morgan, B.; Tee, J. L.; Green, J. *J. Med. Chem.* **1975**, *18*, 833.

Scheme 2



spectroscopy of the crude mixture indicated that **12** and imidazole are the only products.[11]

A possible explanation for the reactivity of **12** is offered in Scheme 2. Compound **12** may form the ammonium salt shown. This salt should be very susceptible to nucleophilic attack by EtOH present in the $CHCl_3$, yielding the ethyl carbonate **14**. (The carbonate was also observed when the residue from THF removal was digested in CH_2Cl_2 and treated with absolute EtOH.)

From the data in Table 1, we note that the transfer of imidazole from CDI or TCDI occurs only with the benzylic or vinylogous benzylic alcohols. Simple alcohols such as cyclohexanol, or alcohols with adjacent electron-withdrawing groups, yield only the expected carbonylimidazole. This suggests that groups adjacent to the alcohol which stabilize positive charge allow the transfer to occur facilely (i. e., "activating" the alcohol carbon). A peripherally related example to our studies by Ford and Ley,[12] which showed the conversion of hemiketals to ketals in the presence of CDI and alcohols, offers some support for this suggestion as well.

We can propose four mechanisms to account for our observations (Scheme 3), using alcohol **1** as a model substrate. In mechanism A, **1** attacks CDI to give the tetrahedral intermediate **15**. Intermediate **15** would then collapse to the carbonylimidazole **16** and imidazole. The imidazole would then displace the carboxyimidazole group to give **4**, CO_2, and imidazole. The drawback to this mechanism is the observed retention of stereochemistry in **4**. If a purely S_N2 mechanism were in operation, we would expect inversion. However, the benzylic carbon of **16** may assume considerable cationic character. Mechanism B shows a more concerted pathway and is subject to the same above comment.

Mechanisms A and B may be operative in the case of entries 2, 3, and 4. In order to explain entry 1, in which retention of stereochemistry is observed, we propose mechanism C, and the intermediacy of aziridinium ion **17**. The aziridinium intermediate alone is not sufficient to explain this reaction, as demonstrated by the results of entry 7. However, the combination of the benzylic carbon coupled with the aziridinium intermediate allows us to explain the retention of stereochemistry noted in entry 1.

Another explanation for the retention of stereochemistry in 1 → 4 would be to invoke the S_Ni mechanism.[13]

We were curious about whether other carbonyl diheterocycles could transfer aromatic heterocyclic groups other than imidazole. To explore this possibility, we treated alcohol **1** with 1,1′-carbonyldi-1,2,4-triazole[14] in refluxing THF (Scheme 4). The reaction produced a gratifying 87% yield of *N*-alkyl-1,2,4-triazole **18**. This result demonstrates the potential of generating other heterocyclic compounds from activated alcohol under mild conditions.

Subsequent to this study, we became aware that this direct conversion of alcohols to alkylimidazoles had been observed previously albeit in poor yields after long reaction times[15a] or treatment at elevated temperature.[15b]

Conclusion

A new route to *N*-alkyl aromatic heterocycles has been explored. The transfer of imidazole and 1,2,4-triazole to activated alcohols was accomplished under mild conditions under 6 h, in moderate to excellent yields, and apparent retention of stereochemistry. The process employs a relatively inexpensive, commercially available reagent and produces fairly innocuous byproducts. Efforts to extend the generality, scope, and mechanism of the reaction will be conducted in due course.

Experimental Section

General. 1,1′-Carbonyldiimidazole (CDI, Aldrich), 90% 1,1′-(thiocarbonyl)diimidazole (TCDI, Aldrich), 1,1′-carbonyldi-1,2,4-triazole (CDT, Fluka), 4,4′-dimethoxybenzhydrol (Fluka), cinnamyl alcohol (Aldrich), cyclohexanol (Aldrich), and 1,2,3,4-tetrahydro-1-naphthol (Aldrich) were commercially available and used without further purification. 2-(*N*,*N*-Dimethylamino)cyclohexanol was prepared by literature methods.[16] 10-Hydroxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine, **1**, was obtained from the $LiAlH_4$ reduction of 1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine-3,10-dione according to the literature.[4] THF was tested for peroxides (aqueous KI) prior to use and used without further purification or drying. All reactions were performed under a nitrogen atmosphere in oven- or flame-dried glassware unless otherwise noted.

^1H and ^{13}C NMR spectra were recorded on a Varian spectrometer at 300 MHz for proton and 75 MHz for carbon. The predicted carbon spectra were obtained from the ACD Labs CNMR program. Flash column chromatography was done on silica gel (E. M. Merck silica gel 60, 230−400 mesh) in the stated solvents. Melting points were obtained on a Thomas-Hoover apparatus and are uncorrected.

General Procedure for Imidazole Transfer: The alcohol (1 equiv) was dissolved in THF (0.36 M) in a 2-neck flask equipped with a magnetic stir bar and reflux condenser. CDI or TCDI (2.1 equiv) was added all at once under a stream of nitrogen. The reaction was then stirred at reflux (bath temperature = 75 °C) for 3.5−7 h (TLC indicated the reactions

(11) A peak at *m*/*z* 323 (64%) in the FAB mass spectrum correlates with the M + H of the 4-nitrobenzyl carbonate resulting from reaction of the carbonylimidazole **12** with 4-nitrobenzyl alcohol used as the FAB matrix.

(12) Ford, M. J.; Ley, S. V. *Synlett* **1990**, 255.

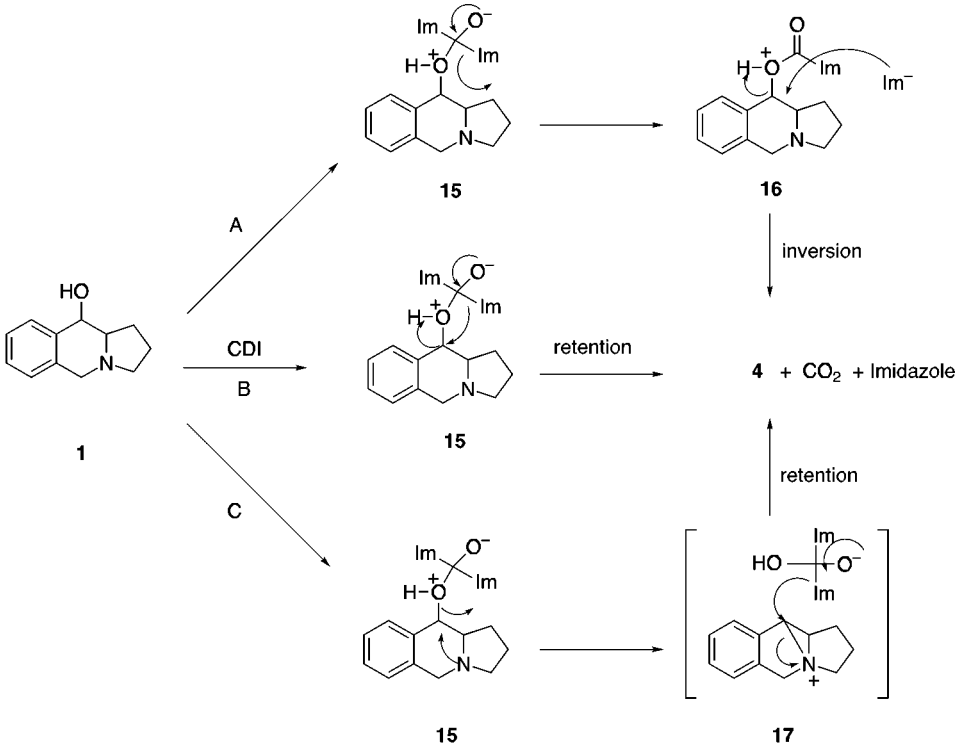
(13) March, J. *Advanced Organic Chemistry*, 2nd ed.; McGraw Hill: New York, 1977; p 302.

(14) For a review of 1,1′-carbonyldi-1,2,4-triazole, see ref 3c, p 1010.

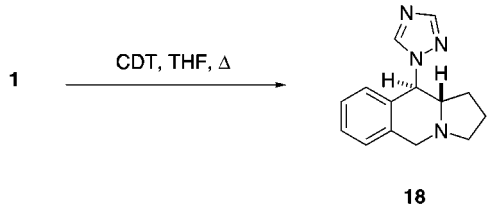
(15) (a) Jones, C. D.; Winter, M. A.; Hirsch, K. S.; Stamm, N.; Taylor, H. M.; Holden, H. E.; Davenport, J. D.; Krumkalns, E. V.; Suhr, R. G. *J. Med. Chem.* **1990**, *33*, 416. (b) Staab, H. A.; Mannschreck, A. *Chem. Ber.* **1962**, *95*, 1284.

(16) Mandrou, A. M.; Potin, P.; Wylde-Lachazette, R. *Bull. Soc. Chim. Fr.* **1962**, 1546.

Scheme 3



Scheme 4



were usually done after 3 h). The reaction was cooled to room temperature and the THF removed on a rotary evaporator. The residue was partitioned between 5% NaOH (20 mL) and an appropriate solvent (ether or ethyl acetate, 20 mL). The layers were separated, and the aqueous layer was extracted with solvent (3 × 10 mL). The organic layers were combined, washed with brine (25 mL), dried over Na_2SO_4, filtered, and concentrated.

1,2,3,5,10,10a-Hexahydro-10-imidazolobenz[*f*]indolizidine (4). Alcohol **1** (101 mg, 0.53 mmol) gave 115 mg of crude product. Flash chromatography in $CHCl_3$/MeOH (11.5:1) + 1% NH_4OH provided 110 mg (86%) of an orange brown solid, mp 98.5−110.5 °C. ^{1}H NMR ($CDCl_3$): δ 7.59 (s, 1H), 7.20 (d, J = 6.98 Hz, 1H), 7.09 (s, 1H), 6.81 (s, 1H), 6.74 (d, J = 7.66 Hz, 1H), 5.07 (d, J = 9.67 Hz, 1H), 4.18 (d, J = 15.91 Hz, 1H), 3.60 (d, J = 14.90 Hz, 1H), 3.30 (t, J = 8.19, 16.68 Hz, 1H), 2.58 (m, 1H), 2.38 (m, 1H), 1.89 − 1.79 (m, 3H), 1.63 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 137.16, 135.27, 133.97, 129.53, 127.47, 126.73, 126.31, 126.23, 117.73, 66.08, 62.33, 55.34, 54.62, 29.01, 21.00. IR (neat film): 3128, 2980, 2815, 1668, 1518, 1304, 1248, 1095, 920, 906, 755 cm^{-1}. MS (FAB): m/z 240 (M + H, 71), 172 (M + H − imidazole, 100), 143 (11), 115 (6.5). HRMS (FAB): calcd 240.1500 for $C_{15}H_{18}N_3$ (M + H), obsd 240.1491.

The imidazole (50 mg, 0.21 mmol) was dissolved in MeOH and filtered to remove particulate. The solution was treated with 1:1 concentrated HNO_3/H_2O (about 20 drops, pH ≪ 2).[17] The solvents were removed under reduced pressure to give a dark orange residue. The residue was dissolved in a minimal amount of MeOH with swirling; then ether was slowly added to produce a precipitate. The suspension was allowed to stand overnight; then the supernatant liquid was carefully removed by pipette and the solid washed with ether. This procedure was repeated twice. The material was dried under a stream of N_2 and then in vacuo for 24 h. The yield of a golden-brown solid was 40 mg (52%), mp 190−192 °C dec. Anal. Calcd for $C_{15}H_{17}N_3 \cdot 2HNO_3 \cdot CH_3OH$: C, 48.36; H, 5.83; N, 17.62. Found: C, 48.74; H, 5.15; N, 17.46.

1-Imidazolo-1,2,3,4-tetrahydronaphthalene (5).[6] 1,2,3,4-Tetrahydro-1-naphthol (250 mg, 1.7 mmol) provided 450 mg of a crude mixture. The mixture was flash chromatographed first in EtOAc/hexane (4:1) to give α-tetrahydronaphthyl carbonylimidazole **6**, 228 mg (55%) of a white solid, mp 88−90 °C, then $CHCl_3$/MeOH (15.66:1) + 1% NEt_3 to give **5**, 87 mg (26%) of a pale yellow solid, mp 114−115 °C.

For **5**. ^{1}H NMR ($CDCl_3$): δ 7.45 (s, 1H), 7.23−7.11 (m, 3H), 7.05 (s, 1H), 6.87 (d, J = 7.58 Hz, 1H), 6.82 (t, J = 1.18, 2.37 Hz, 1H), 5.34 (t, J = 6.87, 12.56 Hz, 1H), 2.89 (m, 2H), 2.21 (m, 1H), 2.12 (m, 1H), 1.88 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 137.57, 137.28, 134.20, 129.42, 128.61, 128.17, 126.55, 118.47, 56.08, 32.38, 28.99, 20.05. IR (Nujol): 2723, 1227, 1151, 1077, 934, 905, 823, 806, 722 cm^{-1}. MS (FAB): m/z 199 (M + H, 100%), 154 (21%), 131 (M + H − imidazole, 86%). HRMS (FAB): for $C_{13}H_{15}N_2$ (M + H), calcd 199.1235, obsd 199.1211. Anal. Calcd for $C_{13}H_{14}N_2 \cdot 0.11H_2O$: C, 77.97; H, 7.16; N, 13.99. Found: C, 77.91; H, 7.24; N, 13.88.

For **6**. ^{1}H NMR ($CDCl_3$): δ 8.12 (s, 1H), 7.40 (s, 1H), 7.39 (d, J = 7.93 Hz, 1H), 7.25 (d, J = 7.25 Hz, 1H), 7.19 (m, 2H), 7.02 (s, 1H), 6.18 (t, J = 3.90, 8.06 Hz, 1H), 2.95−2.79 (broad m, 2H), 2.25−1.88 (broad m, 4H). ^{13}C NMR ($CDCl_3$): δ 148.48, 138.13, 137.13, 132.56, 130.54, 129.79, 129.32, 128.97, 117.14, 75.06, 28.93, 28.75, 18.59. IR (Nujol): 2728, 1759, 1738, 1286, 1238, 1172, 1059, 999, 892, 763 720 cm^{-1}. MS (FAB): m/z 243 (M + H, 4.4), 199 (46), 154 (10), 131 (100), 115 (35). HRMS (FAB): calcd 243.1133 for $C_{14}H_{15}N_2O_2$ (M + H), obsd 243.1147. Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.82; N, 11.56. Found: C, 69.21; H, 5.82; N, 11.48.

4,4′-Dimethoxybenzhydryl)imidazole (7).[15] 4,4′-Dimethoxybenzhydrol (250 mg, 1 mmol) provided 337 mg of crude material. Flash chromatography in $CHCl_3$/MeOH (49:1) + 0.5% NH_4OH afforded 281 mg (95%) of the imidazole as a viscous, pale yellow residue. About 14 mg (5%) of starting material was recovered. The ^{13}C spectrum closely matches the

(17) The salts from reaction of **4** with ethereal HCl, maleic, methanesulfonic, and oxalic acids gave only oils or noncrystalline solids.

predicted spectrum. ^{1}H NMR ($CDCl_3$): δ 7.38 (s, 1H), 7.08 (s, 1H), 7.01 (d, J = 8.73 Hz, 4H), 6.88 (d, J = 8.32 Hz, 4H), 6.85 (s, 1H), 6.42 (s, 1H), 3.80 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 159.21, 137.07, 131.43, 128.95, 119.07, 113.93, 63.69, 55.06. IR (neat film): 2740, 1610, 1580, 1508, 1305, 1250, 1175, 1110, 1075, 1030, 905, 815, 790 cm^{-1}; MS (FAB): m/z 295 (M + H, 4.8), 227 (M + H − imidazole, 100), 154 (52), 136 (41), 106 (5.4). HRMS (FAB): calcd 295.1446420 for $C_{18}H_{19}N_2O_2$ (M + H), obsd 295.1400.

Cinnamylimidazole (9).[10] Cinnamyl alcohol (279 mg, 2.08 mmol) provided 469 mg of crude material. Flash chromatography in $CHCl_3$/MeOH (24:1) + 0.5% NH_4OH gave 265 mg (69%) of the imidazole as a light yellow-gold oil that solidifies on standing several days, mp 70−72 °C (lit. mp 46−48 °C, see ref 10). ^{1}H NMR ($CDCl_3$): δ 8.15 (s, 1H), 7.43−7.35 (m, 3H), 7.34−7.26 (m, 3H), 7.05 (s, 1H), 6.73 (d, J = 15.85 Hz, 1H), 6.35 (m, 1H), 4.98 (dd, J = 1.21, 6.71 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 137.03, 136.39, 135.44, 130.52, 128.62, 128.52, 126.71, 126.58, 120.90, 117.06, 68.62. IR (neat film): 3132, 1758 (absorption of CO_2 likely), 1474, 1400, 1285, 1096, 1000, 833, 747, 694, 649 cm^{-1}. MS (FAB): m/z 185 (M + H, 20), 154 (29), 136 (24), 117 (100), 115 (14), 106 (11). HRMS (FAB): calcd 185.1078 for $C_{12}H_{13}N_2$ (M + H), obsd 185.1116.

1-((Cyclohexyloxy)carbonyl)imidazole (10). Cyclohexanol (0.18 mL, 1.7 mmol) gave 317 mg of a colorless oil that crystallized on standing. Flash chromatography in $CHCl_3$/MeOH (49:1) yielded 290 mg (88%) of the expected carbamate as a faintly colored oil that crystallized on standing, mp 44−46 °C. ^{1}H NMR ($CDCl_3$): δ 8.14 (s, 1H), 7.43 (s, 1H), 7.05 (s, 1H), 4.99 (m, 1H), 1.98 (m, 2H), 1.78 (m, 2H), 1.61 (m, 3H), 1.44 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 147.87, 136.85, 130.25, 116.88, 77.23, 31.10, 24.91, 23.24. IR (Nujol): 1764, 1487, 1396, 1288, 1238, 1001, 826, 770 cm^{-1}. MS (FAB): m/z 195 (M + H, 100), 151 (14), 136 (5), 113 (93). HRMS (FAB): calcd 195.1133 for $C_{10}H_{15}N_2O_2$ (M + H), obsd 195.1152. Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.84; H, 7.27; N, 14.42. Found: C, 61.68; H, 7.28; N, 14.33.

Ethyl *O*-(Imidazolylcarbonyl)-(*S*)-lactate (11). The ester (0.20 mL, 1.76 mmol) gave 419 mg of crude material after washing with H_2O only (no aqueous NaOH). Flash chromatography in $CHCl_3$/MeOH (19:1) gave 265 mg (69%) of a white solid, mp 71−73 °C. ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 7.46 (t, J = 1.61, 2.96 Hz, 1H), 7.09 (s, 1H), 5.31 (q, J = 7.12, 14.23 Hz, 1H), 4.26 (q, J = 7.12, 14.23 Hz, 2H), 1.67 (d, J = 7.12 Hz, 3H), 1.30 (t, J = 7.12, 14.23 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 169.10, 147.83, 136.99, 130.56, 117.00, 71.74, 61.71, 16.61, 13.83. IR (Nujol): 3141, 3110, 1763 (broad, poor resolution), 1532, 1519, 1207, 1170, 1091, 1000, 898, 868, 834, 769, 745, 654 cm^{-1}. MS (FAB): m/z 213 (M + H, 100), 154 (39), 136 (32), 106 (13). HRMS (FAB): calcd 213.0875 for $C_9H_{13}N_2O_4$ (M + H), obsd 213.0882. Anal. Calcd for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found: C, 51.00; H, 5.60; N, 13.10.

***O*−(Imidazolylcarbonyl)-2-(*N*,*N*-dimethylamino)cyclohexanol (12).** A 2-(*N*,*N*-dimethylamino)cyclohexanol (270 mg, 1.88 mmol) reaction mixture was evaporated to give a crude material as a near white solid. No aqueous workup was performed. IR (Nujol, crude product): 1755, 1313, 1280, 1173, 1090, 1050, 1000, 820, 735 cm^{-1}. MS (FAB, crude product): m/z 238 (M + H, 12), 202 (62), 170 (11), 137 (30), 126 (100).[11]

Ethyl (2-(*N*,*N*-Dimethylamino)cyclohexyl Carbonate (14). 2-(*N*,*N*−Dimethylamino)cyclohexanol (258 mg, 1.8 mmol) provided 477 mg of crude product as a moist looking, soft solid after aqueous workup as described in the general procedure (used ether for extraction). $CHCl_3$ (containing EtOH) was used to dissolve the solid, and the resulting solution was chromatographed in $CHCl_3$/MeOH (11.5:1) to give 270 mg (67%) of a light colored oil. The carbon spectrum closely matches the calculated spectrum. ^{1}H NMR ($CDCl_3$): δ 4.63 (dt, J = 4.44, 9.94, 20.01 Hz, 1H), 4.17 (q, J = 7.12, 14.23 Hz, 2H), 2.48 (m, 1H), 2.29 (s, 6H), 2.06 (m, 1H), 1.84 (m, 1H), 1.71 (m, 2H), 1.41 (m, 1H), 1.29 (t, J = 7.12, 14.23 Hz, 4H), 1.20 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 154.35, 75.78, 65.66, 63.02, 40.56, 31.23, 24.27, 23.83, 23.46, 13.86. IR (neat film): 2920, 2840, 2812, 2760, 1730, 1443, 1370, 1249, 1005, 870 cm^{-1}; MS (FAB): m/z 216 (M + H, 100), 154 (11), 142 (22), 126 (99). HRMS (FAB): calcd 216.1599 for $C_{11}H_{22}NO_3$ (M + H), obsd 216.1603.

1,2,3,5,10,10a-Hexahydro-10-(1,2,4)triazolobenz[*f*]indolizidine (18). Alcohol (250 mg, 2.8 mmol) afforded 301 mg of crude material. Flash chromatography in $CHCl_3$/MeOH (19:1) + 0.25% NH_4OH gave 277 mg (86%) of a very pale orange solid. The product was further purified by crystallization from CH_2Cl_2/*n*-heptane to give lightly colored plates, mp 176.5−178 °C dec. ^{1}H NMR ($CDCl_3$): δ 8.09 (s, 1H), 7.89 (s, 1H), 7.12 (d, J = 7.05 Hz, 1H), 7.04 (m, 2H), 6.57 (d, J = 8.33, 16.41 Hz, 1H), 5.30 (d, J = 9.61 Hz, 1H), 4.09 (d, J = 14.61 Hz, 1H), 3.53 (d, J = 14.87 Hz, 1H), 3.21 (t, J = 8.33, 16.41 Hz, 1H), 2.74 (q, J = 8.84, 15.25 Hz, 1H), 2.30 (q, J = 8.21, 16.67 Hz, 1H), 1.90−1.45 (broad m, 4H). ^{13}C NMR ($CDCl_3$): δ 151.96, 143.31, 127.76, 126.86, 126.60, 126.18, 65.18, 64.85, 55.38, 54.62. IR (nujol): 2988, 2824, 1474, 1441, 1372, 1278, 1136, 1011, 990, 961, 940, 723 cm^{-1}. MS (FAB): m/z 241 (M + H, 69, 239 (M − H, 33), 173 (94), 170 (100), 143 (14), 117 (14), 115 (14). HRMS (FAB): calcd 241.1453 for $C_{14}H_{17}N_4$ (M + H), obsd 241.1478. Anal. Calcd for $C_{14}H_{16}N_4$: C, 69.97; H, 6.71; N, 23.31. Found: C, 70.22; H, 6.70; N, 23.44.

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