EtOAc, 20:1), to which is assigned the structure **ethyl 3,5,5-triethoxy-2-hexenoate (9)**: NMR (CCl_4) δ 1.1 (t, 6 H, J = 7 Hz), 1.24 (s, 3 H), 1.35 (t, 6 H, J = 7 Hz), 3.12 (s, 2 H), 3.43 (q, 4 H, J = 7 Hz), 3.9 (q, 2 H, J = 7 Hz), 4.04 (q, 2 H, J = 7 Hz), 4.9 (s, 1 H); IR (neat) 1715, 1625 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 63.83; H, 9.79. Because of the poor elemental analysis, the product was hydrolyzed (H_2SO_4, H_2O, glyme, 30 min, 25 °C) to give **ethyl 3-ethoxy-5-oxo-2-hexenoate**: bp 71-72 °C (0.005 mm); NMR (CCl_4) δ 1.2 (t, 3 H), 1.33 (t, 3 H), 2.1 (s, 3 H), 3.7 (s, 2 H), 3.5-4 (m, 4 H), 5.0 (s, 1 H); IR (neat) 1730, 1710, 1630 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 59.79; H, 8.12.

Registry No. 1, 1478-41-7; 2, 108-94-1; 3, 77070-73-6; 4, 77070-74-7; 5, 58995-69-0; 6, 6065-82-3; 7, 15839-65-3; 8, 21872-75-3; 9, 77070-75-8; 2,6-bis(diethoxymethyl)cyclohexanone, 77070-76-9; 2-(diethoxymethyl)cyclopentanone, 77070-77-0; 2,5-bis(diethoxymethyl)cyclopentanone, 77070-78-1; 1,1,5,5-tetraethoxy-3-pentanone, 77070-79-2; 4,4-diethoxy-2-butanone, 20082-91-1; 1,1-diethoxy-3-pentanone, 31086-94-9; 4,4-diethoxy-3-methyl-2-butanone, 64943-25-5; 2-methyl-1,1,5,5-tetraethoxy-3-pentanone, 77070-80-5; 6-(diethoxymethyl)-2-methylcyclohexanone, 15839-41-5; 2-(diethoxymethyl)-2-methylcyclohexanone, 77070-81-6; 3-(diethoxymethyl)-norcamphor, 77070-82-7; 1,1-diethoxy-5-methyl-4-hexen-3-one, 77070-83-8; 6-(diethoxymethyl)-2-cyclohexenone, 77070-84-9; 3,3-diethoxypropiophenone, 36234-10-3; 3,3-diethoxy-p-cyanopropiophenone, 77070-85-0; 1,1-diethoxy-6-hepten-3-one, 77070-86-1; 1,1-diethoxy-4-(diethoxymethyl)-6-hepten-3-one, 77070-87-2; 3-chloro-4,4-diethoxy-2-butanone, 77070-88-3; ethyl 6,6-diethoxy-4-oxohexanoate, 77070-89-4; ethyl 3-(diethoxymethyl)-4-oxopentanoate, 77070-90-7; 7,7-diethoxy-2,5-heptanedione, 66622-96-6; 3-(diethoxymethyl)-2,5-hexanedione, 77070-91-8; 7,7-diethoxy-3-(diethoxymethyl)-2,5-heptanedione, 77070-92-9; 1,1,8,8-tetraethoxy-3,6-octanedione, 77070-93-0; 2-(dimethoxymethyl)cyclohexanone, 15839-38-0; 3-(dimethoxymethyl)norcamphor, 77070-94-1; cyclopentanone, 120-92-3; acetone, 67-64-1; 2-butanone, 78-93-3; 2-methylcyclohexanone, 583-60-8; norcamphor, 497-38-1; 4-methyl-3-penten-2-one, 141-79-7; 2-cyclohexenone, 930-68-7; acetophenone, 98-86-2; p-cyanoacetophenone, 1443-80-7; 5-hexen-2-one, 109-49-9; chloroacetone, 78-95-5; ethyl 4-oxopentanoate, 539-88-8; 2,5-hexanedione, 110-13-4; dimethoxycarbenium fluoroborate, 18346-68-4; ethyl 3-ethoxy-5-oxo-2-hexenoate, 33663-70-6; triethyl orthoformate, 122-51-0.

Palladium-Assisted Functionalization of Olefins: A New Amination of Electron-Deficient Olefins

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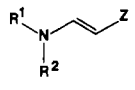
Palladium chloride catalyzed the reaction of substituted anilines with methyl vinyl ketone, methyl acrylate, and acrylonitrile to produce vinylogous arylamino ketones, esters, and nitriles. *N*-Methylaniline gave the highest yields. Aniline and benzylamine failed to react in the desired fashion. The reaction was restricted to enones lacking α and β substitution.

Introduction

Vinylogous arylamino ketones, esters, and nitriles (**1a-c**)



1a R^1 or R^2 = Ar; Z = COR_3
1b R^1 or R^2 = Ar; Z = $COOR_3$
1c R^1 or R^2 = Ar; Z = CN

are useful synthetic intermediates, particularly in the construction of heterocyclic compounds. Vinylogous arylamino ketones (**1a**) have been prepared by the reaction of substituted anilines with β-chloro-[1] and β-(acetylmethyl)acrylate.[2] The addition of aniline to acetylacetone gives a derivative of **1a** substituted in the 4-position.[3] Synthesis of vinylogous arylamino esters (**1b**) has been accomplished by the reaction of aniline with methyl propiolate and other conjugated alkynes.[4] Vinylogous arylamino nitriles (**1c**, R = Ph, R = H) are available from the reaction of $NaNH_2$ with 1-phenylimidazole in xylene at reflux.[5] Heating 1-phenyl-4-cyanotriazole at 80 °C in 1% Et_3N/C_6H_6 also gives the same product.[6] Vinylogous arylamino nitriles substituted with a methyl group in the 3-position have been prepared by the reaction of aniline and 3-methyl-3-aminoacrylonitrile in H_2O[7] and by the action of aniline on 3-cyanoallene.[8]

In connection with efforts toward the total synthesis of ergot alkaloids by means of our previously developed indole synthesis,[9] the reaction shown in eq 1 was investigated. Compound **2** had been shown to undergo palladium-catalyzed closure to 4-bromoindole, presumably via the σ-alkylpalladium intermediate **3**.[10] Since the methodology necessary to trap σ-alkylpalladium intermediates by insertion processes was well established,[11] it was anticipated that subjection of compound **2** to catalytic indole-formation conditions in the presence of methyl acrylate would yield the insertion product **4**. However, none of compound

(1) (a) M. L. Filleux-Blanchard, H. Durand, M. T. Bergeon, F. Clesse, H. Quinious, and G. J. Martin, *J. Mol. Struct.*, **3**, 351 (1969); (b) G. Inouye, *Nippon Kagaku Zasshi*, **75**, 732 (1954).
(2) (a) A. N. Nesmeyanov and M. I. Rybinskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1764 (1966); (b) C. Jutz, *Chem. Ber.*, **91**, 1867 (1958).
(3) (a) C. Kashima, H. Aoyama, Y. Yamamoto, T. Nishio, and K. Yamada, *J. Chem. Soc., Perkin Trans. 2*, 665 (1975). (b) E. Roberts and E. Turner, *J. Chem. Soc.*, 1832 (1927).
(4) (a) N. D. Heindel, P. D. Kennewell, and V. B. Fish, *J. Heterocycl. Chem.*, **6**, 77 (1969); (b) R. Huisgen, K. Herbig, A. Siegl, and H. Huber, *Chem. Ber.*, **99**, 2526 (1966); (c) L. A. Miller, U.S. Patent 3 093 679, 1963; *Chem. Abstr.*, **59**, 11331*b* (1963).
(5) I. I. Grandberg and N. I. Bobrova, *Kim. Geterotsikl. Soedin. Akad. Nauk Latv. SSR*, 566 (1965).
(6) R. Huisgen, G. Szeimies, and L. Mobius, *Chem. Ber.*, **99**, 475 (1966).
(7) J. K. Coward and T. C. Bruice, *J. Am. Chem. Soc.*, **91**, 5329 (1969).
(8) P. Kurtz, H. Gold, and H. Disselnkotter, *Justus Liebigs Ann. Chem.*, **624**, 1 (1959).
(9) L. S. Hegedus, G. F. Allen, J. J. Bozell, and E. L. Waterman, *J. Am. Chem. Soc.*, **100**, 5800 (1978).
(10) J. Bozell, unpublished results.
(11) L. S. Hegedus, G. F. Allen, and D. J. Olsen, *J. Am. Chem. Soc.*, **102**, 3584 (1980).

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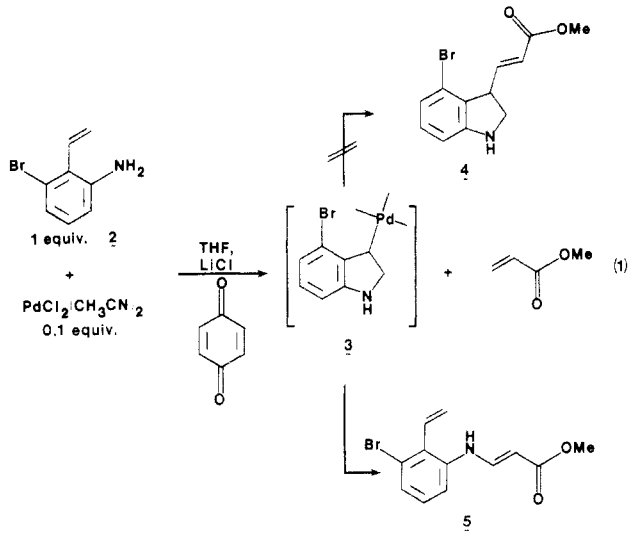
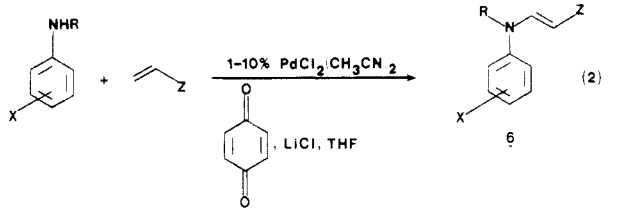


4 was observed. Instead, the only product isolated was compound **5**, resulting from amination of the methyl acrylate by **2**. We report herein the results of the study of this new process.

Results and Discussion

The general process for the palladium assisted amination is shown in eq 2, and the results are summarized in Table I.



The method affords moderate to very good yields of a number of aminated olefins, **6**. The reactions with methyl vinyl ketone and acrylonitrile (entries 2 and 3) give aminated product in yields comparable to or better than those of previously reported methods.[1,2,5-8]

The reaction is quite dependent upon the nature of the amine. Although *N*-methylaniline reacts cleanly, aniline itself fails to aminate conjugated enones. Instead, a heavy yellow precipitate (presumably the bis amino palladium dichloride complex) forms, and no reaction ensues. This behavior parallels that observed in the palladium-assisted aminations of simple olefins, in which secondary amines react in high yield, but primary amines instead produce intractable precipitates.[12] With the exception of *o*-bromoaniline, other primary aromatic amines also react poorly, if at all, with conjugated enones. Benzylamine also fails because it reacts quickly with the benzoquinone used to oxidize the Pd(0).

Alkyl-substituted conjugated enones (methyl crotonate, cyclohexenone, cyclopentenone) also fail to undergo this amination. Increasing substitution on olefins decreases their ability to coordinate to palladium.[13] Interaction of conjugated enones with palladium appears to be particularly sensitive to substitution since insertion reactions of these substrates into σ-alkylpalladium complexes failed completely if the enone was substituted in either the α or β position.[14]

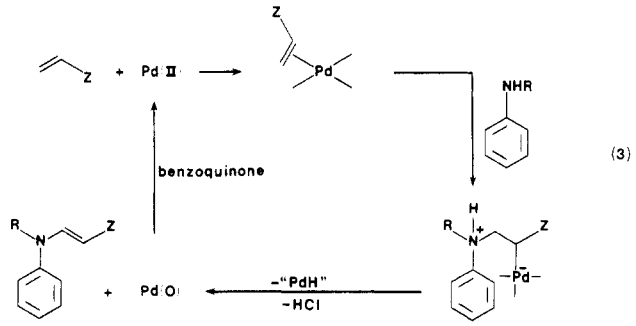
(12) B. Akermark, J. E. Backvall, L. S. Hegedus, K. Zetterberg, K. Siirala-Hansen, and K. Sjoberg, *J. Organomet. Chem.*, **72**, 124 (1974).
(13) F. R. Hartley, "The Chemistry of Platinum and Palladium", Halsted Press, New York, 1973, p 365.

Table I. Amination of Conjugated Enones

entry	R	X	Z	% yield[a]	stereochemistry
1	Me	H	COOMe	73	trans
2	Me	H	COMe	63	trans
3	Me	H	CN	53	trans
4	H	*o*-Br	COOMe	76	cis
5	H	*o*-NO_2	COOMe	16[b]	cis
6	H	*o*-NO_2, *p*-OMe	COOMe	19[c,d]	2:1 cis/trans[e]
7	H	*p*-Me	COOMe	16	cis

[a] Yields are of isolated purified product. [b] Yield increases to 33% with a 10× excess of olefin. [c] Yield increases to 35% with a 10× excess of olefin. [d] 50% starting material recovered. [e] Stereochemistry cleanly cis with a 10× excess of olefin.

A possible course of the reaction is shown in eq 3. Although this route has not been experimentally verified, it is based on analogy to other well-established amination procedures.[9,12]



The catalytic palladium(II) species (probably $PdCl_4^{2-}$) coordinates the olefin which undergoes nucleophilic attack by the amine to generate the σ-alkylpalladium comlex **7**. This species then decomposes by β-elimination to give an unstable palladium hydride complex and the observed product. The palladium complex ultimately forms palladium(0) which is reoxidized to palladium(II) by benzoquinone to carry the catalytic cycle.

Experimental Section

Materials. All solvents were freshly distilled before use. Tetrahydrofuran (THF, Baker, reagent grade) was distilled from Na/benzophenone at atmospheric pressure. Aniline and *N*-methylaniline were distilled at atmospheric pressure from powdered zinc. All other materials are commercially available and were used without further purification. NMR spectra are reported with tetramethylsilane as an internal standard.

General Procedure for Amination of α,β-Unsaturated Olefins. In a 25-mL round-bottomed flask equipped with a magnetic stirring bar were placed benzoquinone (1 equiv), $PdCl_2(CH_3CN)_2$ (0.1 equiv), and LiCl (10 equiv). Freshly distilled THF (4 mL/mmol of substrate) was added followed by the olefin (1 equiv). The mixture was stirred for 10 min and the amine (1 equiv) was added. The mixture was stirred for 24 h and the solvent was removed under reduced pressure. The residue was stirred with Et_2O (10 mL) and filtered and the ether solution washed once with 0.5 N NaOH (10 mL). The organic layer was dried over $MgSO_4$ and filtered and the solvent was removed to give the crude product which was purified by medium-pressure liquid chromatography using a variety of solvent systems.

Preparation of Methyl 3-(Methylphenylamino)-2-propenoate. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (25 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and methyl acrylate (86 mg, 1 mmol, 90 μL) were mixed in THF (5 mL) in the usual manner. Isolation after 24 h followed by medium-pressure liquid chromatography (5:1 hexane/Et_2O, silica gel) gave 140 mg (73%)

(14) R. A. Holton, *Tetrahedron Lett.*, 355 (1977).

of methyl 3-(methylphenylamino)-2-propenoate as a light amber oil: NMR ($CDCl_3$) δ 3.21 (s, 3, NMe), 3.71 (s, 3, OMe), 4.92 (d, 1, J=13 Hz, C=CHCO), 6.91-7.58 (m, 5, aromatic), 7.92 (d, 1, J = 13 Hz, CH=CHCO); IR (film) 1675 (C=O), 1620, 1585, 1495, 1460 cm^{-1}. Anal. ($C_{11}H_{13}NO_2$) C, H, N.

Preparation of 4-(Methylphenylamino)-3-buten-2-one. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and methyl vinyl ketone (70 mg, 1 mmol, 81 μL) were mixed in THF (4 mL) as usual. Addition of N-methylaniline (107 mg, 1 mmol, 108 μL) and isolation after 24 h followed by medium-pressure liquid chromatography (5:1 hexane/ether) gave 111 mg (63%) of 4-(methylphenylamino)-3-buten-2-one as a light amber oil: NMR ($CDCl_3$) δ 2.19 (s, 3, $COCH_3$), 3.25 (s, 3, NMe), 5.41 (d, J = 13 Hz, C=CHCO), 6.99-7.59 (m, 5, aromatic), 7.90 (d, J = 13 Hz, CH=CHCO); IR (film) 1665 (s, C=O), 1610, 1590, 1550, 1500 cm^{-1}. Anal. ($C_{11}H_{13}NO$) C, H, N.

Preparation of 3-(Methylphenylamino)-2-propenonitrile. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and acrylonitrile (53 mg, 1 mmol, 66 μL) were mixed as usual. Addition of N-methylaniline (107 mg, 1 mmol, 108 μL) and isolation after 24 h followed by medium-pressure liquid chromatography (5:1 hexane/Et_2O, silica gel) gave 83 mg (53%) of 3-(methylphenylamino)-2-propenonitrile as a light amber oil: NMR ($CDCl_3$) δ 3.20 (s, 3, NMe), 4.15 (d, J = 15 Hz, C=CHCN), 6.90-7.58 (m, 6, aromatic and CH=CHCN); IR (film) 2200 (C≡N), 1620, 1590, 1500, 1460, 1430, 1360, 1345, 1325, 1310 cm^{-1}. Anal. ($C_{10}H_{10}N_2$) C, H, N.

Preparation of Methyl 3-[(2-Bromophenyl)amino]-2-propenoate. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and methyl acrylate (86 mg, 1 mmol, 90 μL) were combined in THF (4 mL) as usual. Addition of 2-bromoaniline (172 mg, 1 mmol), isolation after 24 h, and medium-pressure liquid chromatography (5:1 hexane/Et_2O) gave 194 mg (76%) of methyl-3-[(2-bromophenyl)amino]-2-propenoate as a light yellow oil: NMR ($CDCl_3$) δ 3.80 (s, 3, NMe), 4.92 (d, J = 8 Hz, C=CHCO), 6.18-7.63 (m, 5, aromatic and CH=CHCO), 10.30 (br s, 1, NH); IR (film) 3300 (m, NH), 1680 (C=O), 1630, 1600, 1580, 1520, 1460 cm^{-1}. Anal. ($C_{10}H_{10}NO_2$) C, H, N.

Preparation of Methyl 3-[(2-Nitro-4-methoxyphenyl)amino]-2-propenoate. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and methyl acrylate (860 mg, 10 mmol, 900 μL) were combined in THF (10 mL) as usual. Addition of 2-nitro-4-methoxyaniline (168 mg, 1 mmol), isolation after 24 h and medium-pressure liquid chromatography (5:1 hexane/Et_2O, silica gel) gave 87 mg (35%) of methyl-3-[(2-nitro-4-methoxyphenyl)amino]-2-propenoate as an orange solid, mp 100-104 °C. Running the reaction with an equimolar amount of methyl acrylate gave 47 mg (19%) of the product as a 2:1 mixture of cis and trans isomers: NMR ($CDCl_3$) δ 3.83 and 3.86 (s, 6, p-OMe and COOMe), 5.09 (d, J = 9 Hz, 1, C=CHCO), 6.10 (br s, 1, NH), 6.72-7.79 (m, 4, aromatic and CH=CHCO); IR (KBr) 1680 (C=O), 1635, 1600, 1570, 1530, 1515, 1460 cm^{-1}. Anal. ($C_{11}H_{12}N_2O_5$) C, H, N.

Preparation of Methyl 3-[(2-Nitrophenyl)amino]-2-propenoate. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol) and methyl acrylate (86 mg, 1 mmol, 90 μL) were combined in THF (4 mL) as usual. Addition of 2-nitroaniline (138 mg, 1 mmol), isolation after 24 h, and medium-pressure liquid chromatography (10:1 hexane/Et_2O, silica gel) gave 35 mg (16%) of methyl-3-[(2-nitrophenyl)amino]-2-propenoate as an orange solid: NMR ($CDCl_3$) δ 3.80 (s, 3, NMe), 5.10 (d, J = 8 Hz, C=CHCO), 6.69-7.77 (m, 4, aromatic), 8.20 (dd, J = 8 Hz, CH=CHCO); IR (KBr) 3220 (NH), 1675 (C=O), 1600, 1570,1505, 1445, 1380,1330,1315 cm^{-1}. Anal. ($C_{10}H_{10}N_2O_4$) C, H, N.

Preparation of Methyl 3-[(4-Methylphenyl)amino]-2-propenoate. Benzoquinone (108 mg, 1 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), LiCl (420 mg, 10 mmol), and methyl acrylate (860 mg, 10 mmol, 900 μL) were combined as usual. Addition of p-toluidine (107 mg, 1 mmol), isolation after 24 h, and medium-pressure liquid chromatography (5:1 hexane/ether) gave 31 mg (16%) of methyl 3-[(4-methylphenyl)amino]-2-propenoate as a white solid: mp 49-52 °C; NMR ($CDCl_3$) δ 2.55 (s, 3, p-Me), 4.00 (s, 3, OMe), 5.00 (d, J = 8 Hz, C=CHCO), 6.97-7.65 (m, 5, aromatic and CH=CHCO); IR (KBr) 3300 (m, NH), 1670 (C=O), 1620, 1580, 1520, 1500, 1480, 1460 cm^{-1}. Anal. ($C_{11}H_{13}NO_2$) C, H, N.

Acknowledgment. We thank the Public Health Service (Grant 1R01 GM 26178) for financial support of this work. Technical assistance by Mr. Keith McCarthy is also gratefully acknowledged.

Registry No. (*E*)-6 (R = Me; X = H; Z = COOMe), 7542-92-9; (*E*)-6 (R = Me; X = H; Z = COMe), 76946-78-6; (*E*)-6 (R = Me; X = H; Z = CN), 76946-79-7; (*Z*)-6 (R = H; X = o-Br; Z = COOMe), 76946-80-0; (*Z*)-6 (R = H; X = o-NO_2; Z = COOMe), 76946-81-1; (*Z*)-6 (R = H; X = o-NO_2), 76946-82-2; (*E*)-6 (R = H; X = o-NO_2, p-OMe; Z = COOMe), 76946-83-3; (*Z*)-6 (R = H; X = p-Me; Z = COOMe), 7542-87-2; methyl acrylate, 96-33-3; methyl vinyl ketone, 78-94-4; N-methylaniline, 100-61-8; acrylonitrile, 107-13-1; 2-nitro-4-methoxyaniline, 96-96-8; 2-nitroaniline, 88-74-4; p-toluidine, 106-49-0; $PdCl_2(CH_3CN)_2$, 14592-56-4.

Dimethylaluminum Chloride Catalyzed Reactions of Methyl α-Cyanoacrylate with Alkenes

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The methyl α-cyanoacrylate–Me_2AlCl complex reacts with alkenes to give zwitterion **2**. Ring closure on carbon gives the cyclobutane **3** with ~90% retention of alkene stereochemistry, ring closure on oxygen gives dihydropyran **5**, and a 1,5-hydrogen shift gives the ene adduct **4**. Reaction of the zwitterion **2** with another molecule of methyl α-cyanoacrylate gives 2:1 adducts.

Introduction

We have found that methyl acrylate undergoes aluminum chloride catalyzed ene reactions at 25 °C with reactive alkenes.[2,3] Introduction of an electron-withdrawing group in the α-position of the acrylate ester should increase its reactivity and extend the reaction to less reactive alkenes. We have recently reported that methyl α-chloro- or -bromoacrylate is roughly an order of magnitude more reactive than methyl acrylate in Lewis acid catalyzed ene reactions.[4]

(1) Fellow of the Alfred P. Sloan Foundation, 1979-81.
(2) Snider, B. B. *J. Org. Chem.* **1974**, *39*, 255.
(3) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426.

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