Alkylation of Ketene Silyl Acetals with Nitroolefins Mediated by Sterically Encumbered Lewis Acids

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The utility of nitroolefins as "$^{+}$C-C-NH_2" and "$^{+}$C(C═O)R" synthons is limited by their facile polymerization in the presence of nucleophiles. Although a number of procedures have been developed for the successful alkylation of *ketones* with nitroolefins, currently available procedures for the corresponding reaction of *esters* suffer from important limitations such as modest yields, lack of demonstrated generality, inconveniently low reaction temperatures, and/or the use of a large excess of one of the two reactants. In the present work, we examined the efficacy of a series of Lewis acid catalysts for the alkylation of ketene silyl acetals with nitroolefins. Previously reported conditions using diisopropoxytitanium dichloride failed to give satisfactory results with nitroolefins lacking a substituent α to the NO_2 group. In contrast, good to excellent results were obtained using sterically congested Lewis acids of the type pioneered by Yamamoto. The successful use of nitroethylene in this reaction represents a significant extension of the utility of this relatively unused "$^{+}CH_2CH_2NH_2$" synthon.

Nitroolefins are powerful Michael acceptors which can serve as synthons of the types "$^{+}$C-C-NH_2" and "$^{+}$C-(C═O)R".[1] Many nitroolefins are readily accessible via the Henry (nitroaldol) reaction, and others are easily prepared by a variety of more recently developed techniques.[2] In spite of their potential utility and ease of synthesis, the synthetic applications of nitroolefins have historically been limited by the great ease with which they polymerize in the presence of nucleophiles. This ease of polymerization can be understood in terms of the high reactivity of nitroolefins and their rather modest ability to discriminate between the intended nucleophile and nucleophile−nitroolefin adducts (nitronates) as reaction partners. As might be expected from this analysis, only a handful of reports exist concerning synthetically useful nucleophilic addition reactions of the most reactive simple nitroolefin, nitroethylene.[3]

Classically, the reactions of nitroolefins with carbon-centered nucleophiles have been limited to reactions carried out under mildly basic conditions using relatively acidic reaction partners such as malonate derivatives and 1,3-diketones.[4] In more recent years, Yoshikoshi,[5] Seebach,[6] Denmark,[7] and others[8] have reported a variety of procedures for the successful addition of simple ketones to nitroolefins via their lithium enolates, enol silanes, enol ethers, or enamines. Limited success has also been reported in the addition of simple esters to nitroolefins via their lithium enolates or ketene silyl acetals.[9] None of the previously reported procedures for the addition of esters to nitroolefins is completely satisfactory; however, as all suffer from modest yields, lack of demonstrated generality, inconveniently low reaction temperatures, and/or the use of a large excess of one of the two reactants. In the present work, we describe a procedure for the addition of esters to nitroolefins via their ketene silyl acetals which avoids many of the disadvantages of previously reported methods. A particularly significant aspect of this work is the successful extension of this procedure to the highly reactive substrate nitroethylene, which serves as a useful "$^{+}CH_2CH_2NH_2$" synthon in this procedure.

Our initial efforts in this area involved an examination of a procedure for the addition of ketene silyl acetals to nitroolefins reported previously by Yoshikoshi *et al.*[10] These workers found that a variety of ketene silyl acetals

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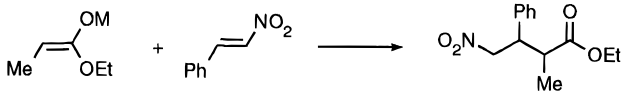
Table 1. Optimization of Reaction Conditions

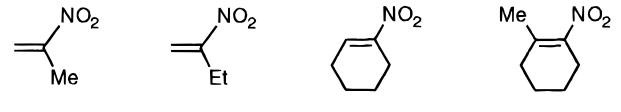


8 **6** **9**

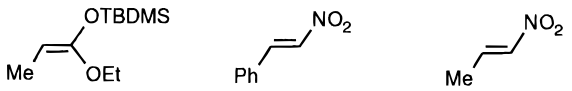
entry	Lewis acid[a]	solvent	M	temp	yield, %	diastereomer ratio
1	$TiCl_2(OiPr)_2$	CH_2Cl_2	TBS	−78 °C	<25	5:1
2	none	xylenes	TBS	100 °C	<25	1:1
3	none	THF	$SnMe_3$	−30 °C to −15 °C	80	1:1
4	$MgBr_2{\cdot}OEt_2$	Et_2O	TMS	25 °C	90	2.2:1
5	$MgBr_2$ (s)	Et_2O	TMS	−78 to 25 °C	slow/stops[b]	2:1
6	$Mg(OTf)_2$	CH_2Cl_2	TBS	−78 to 25 °C	slow/stops[b]	not det
7	$Eu(fod)_3$	$THF/CHCl_3$	TMS	25 °C	slow/stops[b]	not det
8	TMSOTf	CH_2Cl_2	TMS	−78 to 25 °C	slow/stops[b]	not det
9	$BF_3{\cdot}OEt_2$	CH_2Cl_2	TMS	−78 to 25 °C	slow/stops[b]	not det
10	ZnI_2	CH_2Cl_2	TMS	−20 to 25 °C	slow/stops[b]	3:1
11	$EtAlCl_2$	toluene	TMS	−78 to 25 °C	slow/stops[b]	not det
12	**MAD**	**toluene**	**TBS**	**−78 °C**	**90% (very fast)**	**6.3:1**
13	MAD (0.2 eq.)	toluene	TBS	−78 to 25 °C	slow/stops[b]	not det

[a] 1−1.5 equivalent of Lewis Acid was used except where noted. [b] Analysis by ^{1}H-NMR and/or thin layer chromatography indicated very modest conversions which were not improved upon extended stirring at 25 °C.

can be successfully added to the α-substituted nitroolefins **1**−**4** using diisopropoxytitanium dichloride as catalyst.

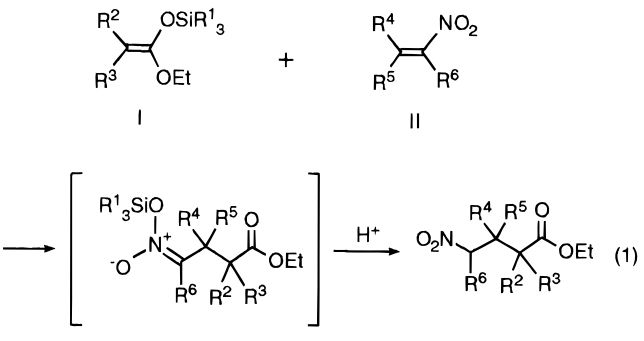


1 **2** **3** **4**



5 **6** **7**

The use of tin tetrachloride as catalyst was reported to give poorer results. In order to determine whether this procedure could be extended to the reactions of nitroolefins lacking an α substituent, we examined the diisopropoxytitanium dichloride-catalyzed reaction of ketene silyl acetal **5** with the nitroolefins *β*-nitrostyrene **6** and 1-nitropropene **7**. In each case highly colored, complex mixtures were obtained which contained little or none of the desired 4-nitrobutyrate product. The salutory effect of an α substituent (R^6) on the nitroolefin in this reaction can be understood in terms of the relative nucleophilicities of the intermediate silyl nitronates III (eq 1). Presumably the greater steric hinderance associated with nitronates in which $R^6 \neq H$ decreases their ability to compete with the ketene silyl acetal for addition to the unreacted nitroolefin.



I II III IV

In order to discover alternative reaction conditions which would permit the use of a wider range of nitroolefin substrates, we have examined a variety of catalysts for the addition of ketene silyl acetals to *β*-nitrostyrene **6**. The results of these studies are summarized in Table 1. The very modest reaction rates which were observed in most of these reactions may result from an insufficient affinity of the very weakly coordinating nitro group for the Lewis acid employed. As described previously, the use of diisopropoxytitanium dichloride as catalyst (entry 1) gave highly colored mixtures of apparently oligomeric products. The reaction of ethylene bromide with magnesium turnings in ether as solvent gave a two-phase mixture of ether and magnesium bromide etherate which exhibited good catalytic activity at 25 °C (entry 4). An attempt to perform this reaction at lower temperatures led to the precipitation of magnesium bromide as a solid. This latter material was not an effective catalyst for the reaction (entry 5). The trimethylstannyl enolate prepared *in situ* from the lithium enolate of ethyl propanoate and trimethylstannyl chloride reacted cleanly with *β*-nitrostyrene **6** at relatively low temperatures (entry 3). The most effective procedure involved the use of Yamamoto's sterically encumbered Lewis acid MAD,[11] which gave a very rapid and clean reaction at −78 °C (entry 12).

As part of preliminary efforts to determine the scope of the MAD-catalyzed addition of ketene silyl acetals to nitroolefins, we examined the reaction of ketene silyl acetal **5** with 1-nitropropene **7**. Unexpectedly, the sole product isolated from this reaction was the ligand−nitroolefin adduct **10** (Scheme 1). Reasoning that an increase in steric hinderance about the nucleophilic 4-position of the phenolate ligand would reduce the rate of this side reaction, we prepared the modified catalyst "MABu" from trimethylaluminum and commercially available 2,4,6- tri-*tert*-butylphenol. As seen in Scheme 1, the use of this modified catalyst eliminated the formation of ligand−nitroolefin adducts as side-products.

The results of a series of experiments designed to probe the generality of MAD- and MABu-catalyzed additions of ketene silyl acetals to nitroolefins are summarized in

(11) (a) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573. (b) Maruoka, K.; Araki, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 2650. Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1992**, *114*, 1089.

Scheme 1. Modification of the Catalyst for Use with More Reactive Nitroolefins

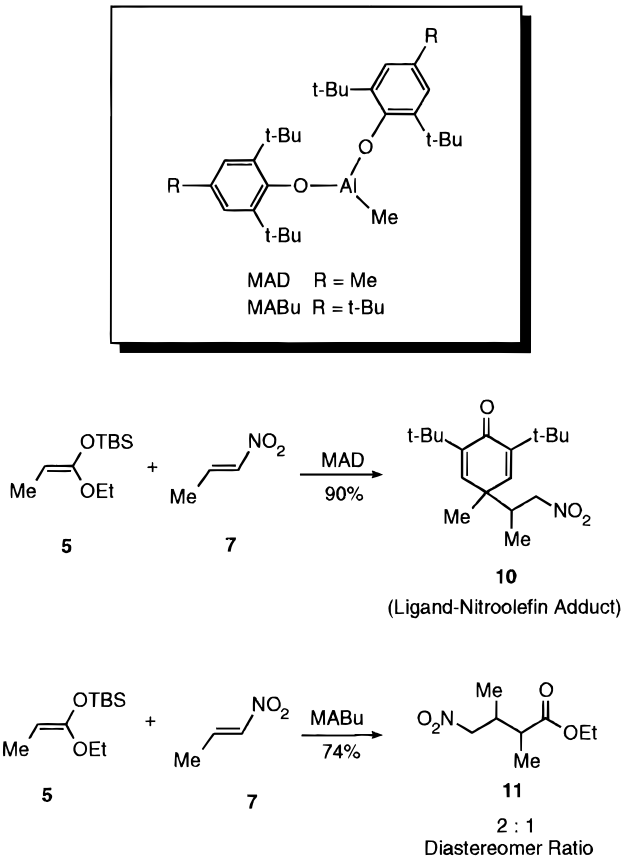
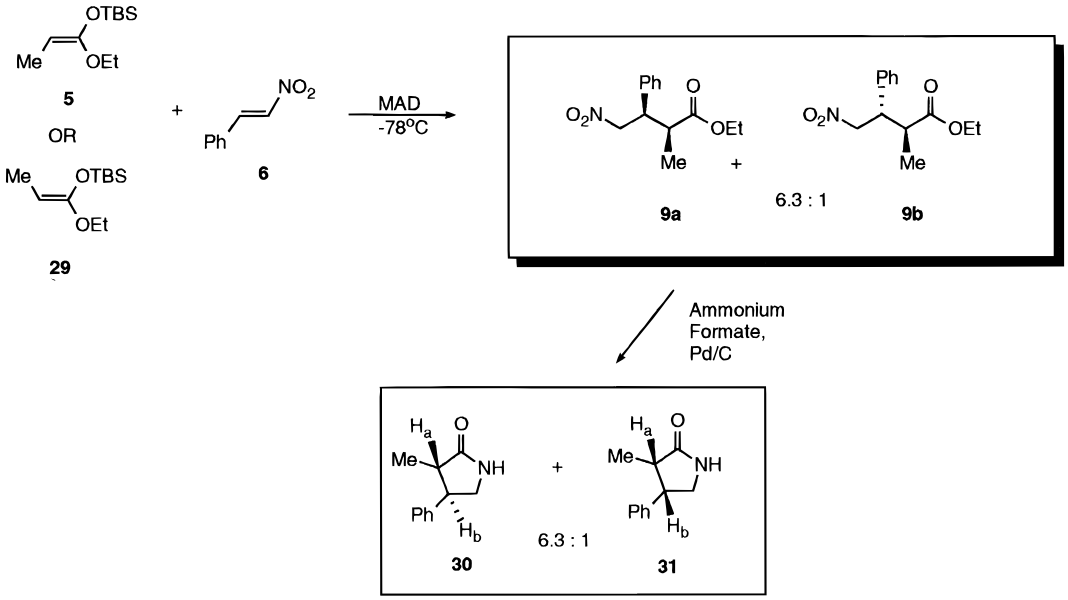


Table 2. The generality of the reaction is fairly good, acceptable yields being obtained with ketene silyl acetals and nitroolefins of a variety of substitution patterns. Most notable is the successful application of nitroethylene in this procedure (entries 6, 7, and 11). One major limitation was observed in the reactions of the sterically hindered ketene silyl acetal **23** (entries 8 and 9). In these cases only very modest yields of difficultly purified product were obtained. Satisfactory yields were obtained, however, with the more reactive disubstituted ketene silyl acetal **26** (entries 10 and 11).

In order to examine the stereoselectivity of this transformation, the experiments described in Scheme 2 were carried out. The MAD-catalyzed reactions of the *E*- and *Z*-ketene silyl acetals of ethyl propionate each gave a 6.3:1 ratio of stereoisomeric 4-nitrobutyrates **9**, with the same stereoisomer of the product predominating in both reactions. Hydrogenation of this mixture of stereoisomers gave a 6.3:1 mixture of stereoisomeric lactams. The close match between observed and predicted (MM2/Karplus) coupling constants and the upfield chemical shift of the methyl hydrogens of the minor isomer led us to tentatively assign the *trans* and *cis* arrangements to the major and minor isomers respectively. This tentative assignment was later confirmed in an equilibration experiment in which a 64:36 mixture of **30** and **31** was converted to a 90:10 mixture by stirring three days in tetrahydrofuran solution in the presence of 3.0 equiv of potassium *tert*-butoxide. Overall, these experiments demonstrate that the alkylation of the *E*- and *Z*-ketene silyl acetals **5** and **29** with β-nitrostyrene **6** is stereoconvergent and the major 4-nitrobutyrate product in each case has the *syn* geometry.

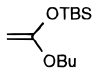
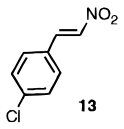
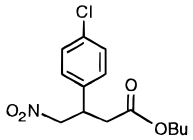
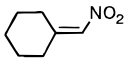
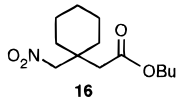
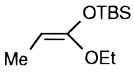
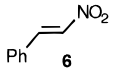
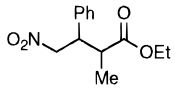
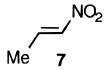
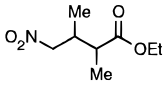
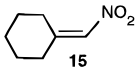
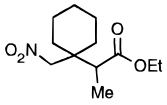
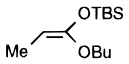
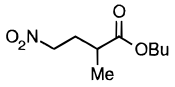
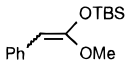
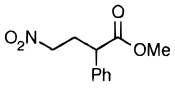
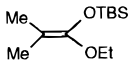
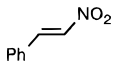
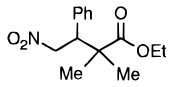
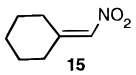
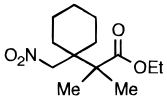
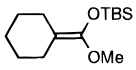
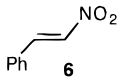
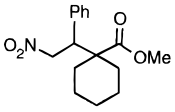
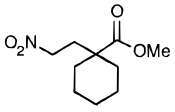
Overall, the research described in this paper demonstrates that synthetically useful yields can be obtained in the alkylation of ketene silyl acetals with nitroolefins of widely varying structure including nitroethylene. The success of this procedure is based on the use of a Lewis acid catalyst prepared by the reaction of trimethylaluminum with 2 equiv of commercially available 2,4,6-tri-*tert*-butylphenol. This catalyst is structurally related to Lewis acids which have been reported previously by Yamamoto,[11] but incorporates greater steric hinderance

Scheme 2. Stereoselectivity and Structural Assignments



δ (CH_3) :	1.12 ppm	0.75 ppm
$J_{a,b}$:	10.7 Hz	7.0 Hz
Predicted $J_{a,b}$ (MM2/Karplus) :	11.7 Hz	7.2 Hz
Equilibrium Ratio (t-BuOK, THF):	9.0 :	1

Table 2. Representative MAD- and MABu-Catalyzed Transformations

Entry	Silyl acetal	Nitroolefin	Lewis Acid	Adduct	Yield
1	 **12**	 **13**	MAD	 **14**	78%
2		 **15**	MABu	 **16**	76%
3	 **5**	 **6**	MAD	 **9** *d.r. = 6.3 : 1*	90%
4		 **7**	MABu	 **11** *d.r. = 2 : 1*	74%
5		 **15**	MABu	 **17**	82%
6	 **18**	 **19**	MABu	 **20**	81%
7	 **21**	 **19**	MABu	 **22**	60%
8	 **23**	 **19**	MABu	 **24**	<25%
9		 **15**	MABu	 **25**	<25%
10	 **26**	 **6**	MABu	 **27**	95%
11		 **19**	MABu	 **28**	76%

in the 4-position of the ligand to inhibit reaction of the ligand with the nitroolefin substrate.

Experimental Section

General Experimental. All reactions were performed in oven-dried (200 °C, 2 h) glassware which was flushed with nitrogen prior to cooling. It was found particularly important to rigorously remove the air from reaction vessels in which trimethylaluminum was to be used. Methylene chloride, toluene, and diisopropylamine were distilled from calcium hydride immediately prior to use. Tetrahydrofuran was distilled from sodium benzophenone ketyl immediately before use. The nitroolefins **7**, **13**, **15**, and **19** were prepared according to literature procedures[12] and stored neat in the dark at −15 °C until use. All of the nitroolefins used in this work, including nitroethylene, retained satisfactory purity after several months of storage under these conditions. Ketene silyl acetals were prepared according to reference 13 and purified by Kugelrohr distillation prior to use.

General Procedure for Alkylation of Ketene Silyl Acetals with Nitroolefins Other Than Nitroethylene. Procedure A. A solution of 1.57 g (6.00 mmol) of 2,4,6-tri-*tert*-butylphenol (Aldrich) in 4.5 mL of anhydrous methylene chloride was prepared in an oven-dried 15 mL round bottom flask. (When MAD is used as the catalyst, 2,6-di-*tert*-butyl-4-methylphenol is used in place of 2,4,6-tri-*tert*-butylphenol, and toluene is used in place of methylene chloride as the reaction solvent.) The solution was deoxygenated with a stream of dry nitrogen and cooled to 0 °C. Neat trimethylaluminum (0.288 mL, 3.00 mmol, *extremely pyrophoric!*) was added to the solution dropwise over 2−3 min via syringe. When the gas evolution became slow (5 min), the solution was warmed to 25 °C and stirred for 1 h (solution A). In a separate 50 mL oven-dried round bottom flask, a solution of the ketene silyl acetal (3.0 mmol) in 6 mL of methylene chloride was cooled to −78 °C and treated with a solution of the nitroolefin (2.73 mmol) in 6 mL of methylene chloride. (In some cases precipitation of the nitroolefin was observed.) After stirring this solution 5 min at −78 °C, solution A was added dropwise over 2 min. The resulting mixture was stirred an additional 30 min at −78 °C, and then 0.32 g of anhydrous sodium sulfate was added followed by 0.32 g of sodium sulfate decahydrate. The mixture was allowed to warm to 25 °C and stirred 30 min at this temperature. The solution was diluted with 50 mL of chloroform (this is important in order to minimize solvent evaporation and consequent crystallization of the tri-*tert*-butylphenol within the frit during filtration) and filtered through Celite. Evaporation of the filtrate at reduced pressure gave a white solid which was chromatographed on 100 mL of silica gel eluting with 10% methylene chloride in pentanes until the tri-*tert*-butylphenol was completely removed from the column and then with a more polar mixture of methylene chloride/pentanes to elute the product. Yields are given in Table 2.

Ethyl 2-Methyl-4-nitro-3-phenylbutyrate (9). R_f 0.29 (7% MTBE in dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.14 (m, 3 H, both diastereomers), 7.10 (dd, J = 1.7, 8.1 Hz, 2 H, both diastereomers), 4.78 (dd, J = 5.8, 12.9 Hz, 1 H, minor diastereoisomer), 4.67 (dd, J = 9.3, 12.9 Hz, 1 H, minor diastereomer), 4.63 (d, J = 7.4 Hz, 2 H, major diastereomer), 4.11 (q, J = 7.1 Hz, 2 H, major diastereomer), 3.91 (q, J = 7.1 Hz, 2 H, minor diastereomer), 3.63 (dt, J = 9.8, 7.4 Hz, 1 H, both diastereomers), 2.79 (dq, J = 7.1, 7.1 Hz, 1 H, minor diastereomer), 2.68 (dq, J = 9.8, 7.1 Hz, 1 H, major diastereomer), 1.21 (t, J = 7.1 Hz, 3 H, major diastereomer), 1.16 (d, J = 7.1 Hz, 3H, minor diastereomer), 1.00 (t, J = 7.1 Hz, 3H, minor diastereomer), 0.96 (d, J = 7.1 Hz, 3 H, major diastereomer). ^{13}C-NMR (75 MHz, $CDCl_3$): The major isomer (in full): δ 174.34, 136.99, 128.90, 128.80, 127.84, 78.43, 60.86, 46.59, 42.63, 15.84, 13.97. The minor isomer (in part): δ 173.40, 136.99, 128.90, 128.80, 127.84, 77.53, 60.54, 46.42, 42.95, 14.62, 13.74. IR (neat) 2983, 2464 (w), 1957 (w), 1729 (s), 1556 (s), 1497, 1455, 1434, 1380, 1344, 1248, 1180 (s), 1130, 1097, 702, cm^{-1}. MS (EI) m/z (rel intensity) 251 (M +, 1), 206 (24), 205 (25), 204 (55), 189 (98), 132 (29), 131 (95), 117 (33), 104 (91), 103 (23), 91 (100). Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.11; H, 6.86; N, 5.60.

Ethyl 2,3-Dimethyl-4-nitrobutyrate (11). R_f 0.35 (1:1 dichloromethane/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (dd, J = 12.3, 5.3 Hz, 1 H, major diastereomer), 4.43 (dd, J = 12.1, 5.5 Hz, 1 H, minor diastereomer), 4.29 (dd, J = 12.1, 8.4 Hz, 1 H, major diastereomer), 4.28 (dd, J = 12.3, 8.2 Hz, 1 H, minor diastereomer), 4.15 (overlapping q, J = 7.1 Hz, 2 H, both diastereomers), 2.70−2.40 (m, 2 H, both diastereomers), 1.21 (overlapping t, J = 7.1 Hz, 3 H, both diastereomers), 1.14 (d, J = 7.1 Hz, 3 H, minor diastereomer), 1.13 (d, J = 7.1 Hz, 3 H, major diastereomer), 0.98 (d, J = 7.1 Hz, 3 H, minor diastereomer), 0.97 (d, J = 7.1 Hz, 3 H, major diastereomer). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.29, 173.90, 79.19, 79.11, 60.62, 41.70, 41.62, 35.09, 34.64, 26.74, 14.35, 14.04, 13.99, 13.18. Consideration of relative peak intensities suggests that the peaks at δ 14.35 and 14.04 each correspond to two unresolved resonances. IR (neat) 2982, 2941, 2459 (w), 1731 (s), 1555 (s), 1460, 1381, 1261, 1226, 1189, 1164, 1126, 1097, 1079, 1032, cm^{-1}. MS (FAB) m/z (rel intensity) 190 (M + H, 21), 123 (34), 103 (37), 75 (39), 73 (100), 69 (43), 57 (71), 55 (31), 43 (30). HRMS (FAB) calcd for $C_8H_{15}NO_4$ + H 190.1079, found 190.1076. Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.52; H, 8.07; N, 7.04.

Butyl 4-nitro-3-(4-chlorophenyl)butyrate (14). R_f 0.20 (3:2 dichloromethane/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, J = 6.5 Hz, 2 H), 7.17 (d, J = 6.5 Hz, 2 H), 4.71 (dd, J = 6.8, 12.6 Hz, 1 H), 4.60 (dd, J = 8.1, 12.6 Hz, 1 H), 4.03 (t, J = 7.3 Hz, 2 H), 3.97 (ddt, J = 6.8, 8.1, 7 Hz, 1 H), 2.82−2.63 (AB, 2 H), 1.60−1.45 (m, 2 H), 1.35−1.17 (m, 2 H), 0.89 (t, J = 7.3 Hz, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 170.35, 136.75, 133.88, 129.19, 128.72, 79.15, 64.86, 39.62, 37.57, 30.44, 18.95, 13.55. IR (neat) 2962, 2935, 1902 (w), 1732 (s), 1556 (s), 1495, 1379, 1269, 1249, 1226, 1190, 1175, 1096, 1016, 830, cm^{-1}. MS (FAB) m/z (rel intensity) 300 (M + H, 45), 226 (25), 197 (52), 75 (25), 73 (46), 57 (100), 55 (43), 43 (35), 41 (49), 29 (46). Anal. Calcd for $C_{14}H_{18}ClNO_4$: C, 56.10; H, 6.05; N, 4.67. Found: C, 56.25; H, 5.94; N, 4.56.

1-(Nitromethyl)-1-[(butoxycarbonyl)methyl]cyclohexane (16). R_f 0.22 (38% dichloromethane in hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 2 H), 4.07 (t, J = 6.6 Hz, 2 H), 2.51 (s, 2 H), 1.55−1.27 (m, 14 H), 0.93 (t, J = 6.6 Hz, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 171.21, 81.25, 64.26, 39.04, 36.89, 33.51, 30.56, 25.41, 21.10, 19.10, 13.55. IR (neat) 2959 (s), 2935 (s,b), 2868 (s), 2453 (w), 2338 (w), 1732 (s), 1549 (s), 1458 (s), 1434, 1380 (s), 1364, 1243, 1202 (s), 1178 (s), 1135, cm^{-1}. MS (FAB) m/z (rel intensity) 258 (M + H, 95), 256 (22), 184 (100), 95 (50), 93 (20), 67 (20), 57 (25), 55 (25), 41 (41), 29 (24). Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 61.08; H, 8.97; N, 5.26.

1-(Nitromethyl)-1-[(1-butoxycarbonyl)ethyl]cyclohexane (17). R_f 0.29 (1:1 dichloromethane/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.72 (d, J = 11.0 Hz, 1 H), 4.49 (d, J = 11.0 Hz, 1 H), 4.20−4.05 (m, 2 H), 2.89 (q, J = 7.2 Hz, 1 H), 1.73−1.37 (m, 10 H), 1.26 (t, J = 7.1 Hz, 3 H), 1.14 (d, J = 7.2 Hz, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.53, 79.65, 60.27, 42.47, 39.39, 30.43, 30.17, 25.08, 20.93, 13.99, 11.39. Consideration of relative peak intensities suggests that the peak at δ 20.93 corresponds to two unresolved resonances. MS (FAB) m/z (rel intensity) 244 (M + H, 100), 198 (34), 123 (25), 109 (12), 95 (16), 81 (21), 55 (13). Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.10; H, 8.96; N, 5.61.

Methyl 1-(2-Nitro-1-phenylethyl)cyclohexanecarboxylate (27). Mp 89−91 °C. R_f 0.20 (7% MTBE in dichlo-

(12) (a) Nitroethylene **19** and 1-nitropropene **7**: Buckley, G. D.; Scaife, C. W. *J. Chem. Soc.* **1947**, 1471. Grob, C. A.; von Sprecher, H. *Helv. Chim. Acta* **1952**, *35*, 902. Hurd, C. D.; Nilson, M. E. *J. Org. Chem.* **1955**, *20*, 927. (b) (Nitromethylidene)cyclohexane (**15**): Cunico, R. F. *J. Org. Chem.* **1990**, *55*, 4474. Dauben, H. J., Jr.; Ringold, H. J.; Wade, R. H.; Pearson, D. L.; Anderson, A. G., Jr.; Cope, A. G.; Baxter, W. N.; Cotter, R. J. *Organic Syntheses*; Wiley: New York, 1963; Coll. Vol. IV, p 221. 1-(Nitromethyl)cyclohexanone was converted to its acetate by refluxing it with excess actetyl chloride in chloroform for 20 h. (c) Huitric, A. C.; Kumler, W. D. *J. Am. Chem. Soc.* **1956**, *78*, 614.

(13) Ireland, E. E.; Wipf, P.; Armstrong, J. D., III. *J. Org. Chem.* **1991**, *56*, 650.

romethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25- 7.12 (m, 3 H), 7.02−6.93 (m, 2 H), 4.87−4.70 (m, 2 H), 3.59 (s, 3 H), 3.49 (dd, J = 5.4, 10.1 Hz, 1 H), 2.20−2.07 (m, 1 H), 1.83−1.73 (m, 1 H), 1.62−1.39 (m, 4 H), 1.23−0.97 (m, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.75, 135.68, 128.76, 128.26, 128.06, 76.57, 52.33, 51.69, 50.27, 33.63, 31.86, 25.56, 23.34, 22.93. IR (Nujol mull) 2463 (w), 2313 (w), 2043 (w), 1995 (w), 1982 (w), 1714 (s), 1557 (s), 1429, 1226 (s), 1214 (s), 1150, 1137, 998, 758, 707 (s), cm^{-1}. MS (FAB) *m/z* (rel intensity) 292 (M + H, 99), 260 (29), 245 (73), 185 (52), 105 (33), 91 (72), 81 (45), 79 (22), 77 (23). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.26; N, 4.81. Found: C, 66.04; H, 7.29; N, 4.75.

General Procedure for Alkylation of Ketene Silyl Acetals with Nitroethylene. Procedure B. This procedure differs from procedure A primarily because nitroethylene/ketene silyl acetal mixtures and nitroethylene/MABu mixtures have very limited stability even at −78 °C. An oven dried 50 mL three-neck round bottom flask was equipped with a 10 mL addition funnel having an external cooling jacket capable of maintaining the addition funnel contents at −78 °C. The flask was loaded with a solution of 1.57 g (6.00 mol) of 2,4,6-tri-*tert*-butylphenol in 16 mL of anhydrous methylene chloride. The solution was degassed in a stream of nitrogen and then cooled to 0 °C. Neat trimethylaluminum (0.288 mL, 3.00 mmol, *extremely pyrophoric!*) was added to the solution dropwise over 2−3 min via syringe. When the gas evolution became slow (5 min), the solution was warmed to 25 °C and stirred 1 h. The solution was then cooled to −78 °C (some precipitate may form), and a −78 °C solution of the ketene silyl acetal (2.73 mmol) in 5 mL of methylene chloride was added all at once via the addition funnel. The −78 °C addition funnel was immediately loaded with a solution of nitroethylene (2.73 mmol) in 5 mL of methylene chloride. After 2 min, the cold nitroolefin solution was added to the reaction mixture dropwise over 1 min. The mixture was stirred an additional 20 min at −78 °C and then it was allowed to warm to 25 °C. Anhydrous sodium sulfate (0.50 g) was added, followed by 0.50 g of sodium sulfate decahydrate. The desired product was then isolated as described in procedure A. In reactions involving nitroethylene as the nitroolefin component, small quantities of a tri-*tert*-butylphenol−nitroethylene adduct are typically observed at R_f values intermediate between those of tri-*tert*-butylphenol and the desired product. Yields are given in Table 2.

Butyl 4-Nitro-2-methylbutyrate (20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52−4.40 (AB of ABX_2 system, $J_{AX} \approx J_{BX}$ = *ca.* 7 Hz, 2 H), 4.11 (t, J = 6.6 Hz, 2 H), 2.57 (tq, J = *ca.* 7, 7.1 Hz, 1 H), 2.37−2.25 (six line m, 1 H), 2.22−2.09 (six line m, 1 H), 1.64 (tt, J = 6.6, 7.0 Hz, 2 H), 1.39 (tq, J = 7.0, 7.3 Hz, 2 H), 1.25 (d, J = 7.1 Hz, 3 H), 0.95 (t, J = 7.3 Hz, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 174.90, 73.39, 64.75, 36.53, 30.56, 30.51, 19.07, 17.22, 13.65. MS (FAB) *m/z* (rel intensity) 204 (M + H, 42), 358 (29), 204 (42), 130 (40), 75 (33), 73 (38), 57 (99), 55 (64), 43 (33), 41 (70), 29 (42). Anal. Calcd for $C_9H_{17}NO_4$: C, 53.19; H, 8.43; N, 6.89. Found: C, 53.25; H, 8.68; N, 6.55.

Methyl 4-Nitro-2-phenylbutyrate (22). Mp 30−32 °C. R_f 0.23 (3:1 dichloromethane/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.13 (m, 5 H), 4.37−4.15 (m, 2 H), 3.65 (t, J = 8 Hz, 1 H), 3.62 (s, 3 H), 2.75−2.59 (six line m, 1 H), 2.47−2.30 (six line m, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 172.93, 136.88, 129.12, 128.03, 127.79, 72.99, 52.38, 47.91, 30.46. IR (Nujol mull) 2417 (w), 2364 (w), 2100 (w), 1979 (w), 1960 (w), 1731 (s), 1548 (s), 1436 (s), 1316, 1272 (s), 1233 (s), 1196, 1170 (s), 1160 (s), 734, cm^{-1}. MS (FAB) *m/z* (rel intensity) 224 (M + H, 100), 221 (51), 177 (35), 121 (42), 117 (82), 91(43), 77 (37), 75 (34), 73 (59), 57 (78). Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.42; H, 5.87; N, 6.03.

Methyl 1-(2-Nitroethyl)cyclohexanecarboxylate (28). R_f 0.32 (1:1 dichloromethane/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.40−4.28 (m, 2 H), 3.69 (s, 3 H), 2.28−2.16 (m, 2 H), 2.12−1.99 (m, 2 H), 1.65−1.47 (m, 2 H), 1.42−1.17 (m, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 175.57, 71.64, 51.86, 45.41, 36.18, 33.70, 25.40, 22.72. IR (neat) 2938 (s), 2859, 1728 (s), 1556 (s), 1454, 1434, 1385, 1365, 1331, 1276, 1231, 1213, 1155, 1137, 1103, cm^{-1}. MS (FAB) *m/z* (rel intensity) 216 (M + H, 99), 184 (39), 169 (76), 109 (73), 81 (38), 73 (39), 67 (32), 57 (23), 55 (23), 41 (30). Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.80; H, 7.92; N, 6.29.

***cis*- and *trans*-3-Methyl-4-phenyl-2-pyrolidinone (30 and 31).** To a mixture of 429 mg (1.71 mmol) of ethyl 2-methyl-4-nitro-3-phenylbutyrate diastereomers **9** (6.3:1 ratio) dissolved in 2.5 mL of methanol were added 539 mg of ammonium formate and 117 mg of 10% Pd/C. A mild exotherm was observed. After stirring overnight, the solution was filtered and the solvent was removed from the filtrate by evaporation at reduced pressure. The residue was partitioned between 75 mL of dichloromethane and 20 mL of distilled water. The aqueous phase was washed with two successive 15 mL portions of distilled water, and the combined organic extracts were dried ($MgSO_4$). The solvent was removed by evaporation at reduced pressure. ^{1}H-NMR analysis revealed a 6.3:1 ratio of diastereomers. An analytical sample obtained by repeated crystallization from cyclohexane contained a 19:1 ratio of diastereomers and had mp 102−103.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): The major isomer gave (in full): δ 7.35−6.99 (m, 5 H), 6.37 (bs, 1 H), 3.57 (dd, J = 9.6, *ca.* 9 Hz, 1 H), 3.32 (dd, J = 9.6, 9.6 Hz, 1 H), 3.10 (ddd, J = 10.7, 9.6, *ca.* 9 Hz, 1 H), 2.49 (dq, J = 10.7, 7.0 Hz, 1 H), 1.13 (d, J = 7.0 Hz, 3 H). The minor isomer gave (in part): δ 3.73−3.62 (m, 2 H), 2.78−2.65 (dq, J = 7.4, 7.0 Hz, 1 H), 0.75 (d, J = 7.4 Hz, 3 H). ^{13}C-NMR (MHz, $CDCl_3$): The major isomer gave δ 179.89, 140.38, 128.85, 49.96, 47.71, 43.49, 13.98. The minor isomer gave: δ 180.83, 139.81, 128.31, 127.86, 127.01, 46.35, 44.45, 40.61, 11.37. IR (Nujol mull) 3202 (b), 3152 (b), 3102, 3040, 3028, 2313 (w), 1957 (w), 1695 (s), 1497, 1484, 1359, 1249 (s), 756 (s), 701 (s), 605, cm^{-1}. MS (EI) *m/z* (rel intensity) 175 (M^+, 40), 175 (40), 119 (10), 118 (99), 117 (43), 115 (10), 91 (21), 77 (10), 65 (10), 63 (7), 51 (17). Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.02; H, 7.51; N, 7.90.

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