finger (refluxing Et_2O) affords pure [^{6}Li]ethyllithium in 20–80% (typically 50–60%) isolated yields. For optimal results, the [^{6}Li]ethyllithium should be freshly sublimed before each use: $^{13}C[^1H]$NMR (17.6 °C, C_6D_6) δ 11.67 and 0.51; ^{1}H NMR (17.6 °C, C_6D_6) δ 1.24 (t, 3 H, J_{H-H} = 7.9 Hz), –0.99 (q, 2 H, J_{H-H} = 7.9 Hz).

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N-(1-Benzotriazol-1-ylalkyl)amides, Versatile α-Amidoalkylation Reagents. 1. α-Amidoalkylation of CH Acids

Alan R. Katritzky,* Juliusz Pernak, Wei-Qiang Fan, and Franciszek Saczewski

Department of Chemistry, University of Florida, Gainesville, Florida 32611-2046

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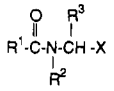
N-(1-Benzotriazol-1-ylalkyl)amides **2**, easily prepared from an amide and an aldehyde with benzotriazole, react smoothly with CH acids under mild conditions to give the α-amidoalkylation products in good yields. Benzotriazole aminals also react with CH acids in the presence of methyl iodide.

Introduction

Amidoalkylations have found versatile applications in organic synthesis as a valuable alternative to the Mannich reaction.[1] In addition to providing ready access to primary and secondary amines, amidoalkylation (for reviews, see refs 2–4) is applicable to a considerably broader spectrum of reactivity than the Mannich reaction and has been used in syntheses of α- and β-amino acids,[5,6] β-amino ketones,[7] β-lactams,[8] and porphyrins.[9] Intramolecular amidoalkylations have received much attention in new approaches to alkaloid synthesis.[10]



1

X = OH, OR, OCOR, Halogen, NHCOR, NR_2

Numerous amidoalkylation reactions have been reported in the last two decades.[2-4] In most cases, the electrophilic amidoalkylation reagents can be represented by the structure **1**,[4] where X is one of the leaving groups indicated and R^2 may be a hydrogen, alkyl, or second acyl group. Compounds sufficiently nucleophilic to undergo reaction with these amidoalkylating agents include carbanions derived from active methylene compounds, activated aromatic and heteroaromatic compounds, olefins, and acetylenes. However, previous methods for amidoalkylation using the presently available reagents **1** with the leaving groups X listed all possess limitations and/or disadvantages:

(a) X = OH. The most frequently used amidoalkylation reagents in recent reports have been *N*-(α-hydroxyalkyl)amides. However, the strongly acidic reaction conditions usually employed, e.g., concentrated sulfuric acid, can produce byproducts or completely divert the course of the reaction.[2] Thus, several attempts to amidomethylate malonic ester with *N*-(hydroxymethyl)benzamide or *N*-(hydroxymethyl)phthalimide in sulfuric acid failed,[11,12] and the amidoalkylation of aliphatic nitro compounds gave low yields (20–33%).[13] In addition, the application of reagents with X = OH appears to be limited to cases where R^3 = CO_2Et, CO_2H, CCl_3, or H.

(b) X = OR or OCOR. These amidoalkylating agents, which are ethers and esters of *N*-(α-hydroxyalkyl)amides, have generally required preparation by electrochemical methods: anodic oxidation of N-alkylated amides in organic acids[14] and alcohols[15] or by other inconvenient routes.[16] Furthermore, the ethers and esters of *N*-(α-hydroxyalkyl)amides employed for the α-amidoalkylation of active CH compounds have mostly been limited to those of cyclic amides.[4]

(c) X = halogen. These reagents are so reactive that it is often difficult to prepare, isolate, purify, and store them.[4,17] They are frequently prepared in situ from *N*-α-hydroxyalkyl precursors and immediately treated with substrate and catalyst, but this often results in low-yield amidoalkylations[17-19] and to side product formation.[4]

(d) X = NHCOR. Although the reagents are easily accessible, the amidoalkylating conditions are usually severe, e.g., concentrated sulfuric acid[20] or hot polyphosphoric acid,[21] under which side reactions are to be expected, especially for active methylene compounds. Only half a molar equivalent of the amide is utilized, and the leaving group is also an amide, which could be inconvenient during purification of amidoalkylated products.

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Table I. Preparation of Amidoalkylation Reagents *N*-(1-Benzotriazol-1-ylalkyl)amides 2

							calcd			found		
no.	R^1	R^2	yield (%)	mp (°C)	lit. mp[31a] (°C)	solvent	C	H	N	C	H	N
2a	Ph	Ph	60	188–190	188–190	MeOH						
2b	Ph	4-$CH_3OC_6H_4$	63	172–174		MeOH	70.38	5.06	15.63	70.20	5.05	15.58
2c	Ph	$PhCHCH_3$	51	230–232		EtOH	74.14	5.66	15.72	73.83	5.61	15.70
2d	Ph	$PhCH_2$	65	180–182		EtOH	73.67	5.30	16.36	73.69	5.25	16.49
2e	Ph	1-naphthyl	49	212–214		toluene						
2f	Ph	4-$NO_2C_6H_4$	81	219–221		CH_2Cl_2	64.30	4.05	18.76	64.11	3.92	18.81
2g	CH_3	Ph	48	173–176	174–177	benzene						
2h	CH_3	4-$CH_3OC_6H_4$	54	183–185		EtOH	64.84	5.44	18.91	64.94	5.48	18.94

Table II. Products of Amidoalkylation of Diethyl Alkylmalonates

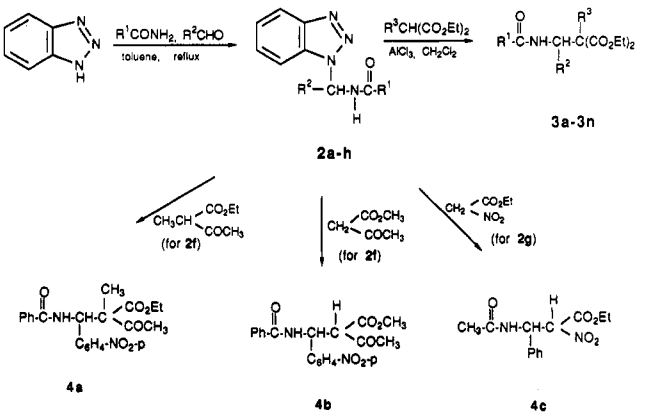
						molecular	calcd[b]			found[b]		
no.	R^1	R^2	R^3	yield (%)	mp[a] (°C)	formula	C	H	N	C	H	N
3a	Ph	Ph	Me	65	77–79	$C_{22}H_{25}NO_5$	68.91	6.57	3.65	68.86	6.50	3.84
3b	Ph	Ph	Et	58	81–83	$C_{23}H_{27}NO_5$	69.50	6.85	3.52	69.60	6.82	3.72
3c	Ph	4-$CH_3OC_6H_4$	Me	69	oil	$C_{23}H_{27}NO_6$	413.1838			413.1843		
3d	Ph	4-$CH_3OC_6H_4$	Et	63	oil	$C_{24}H_{29}NO_6$	428.2073 (M + 1)			428.2068 (M + 1)		
3e	Ph	$PhCH_2$	Me	72	129–131	$C_{23}H_{27}NO_5$	69.50	6.85	3.52	69.62	6.88	3.44
3f	Ph	$PhCH_2$	Et	67	99–100	$C_{24}H_{29}NO_5$	70.05	7.10	3.40	70.07	7.14	3.38
3g	Ph	1-naphthyl	Me	60	111–112	$C_{26}H_{27}NO_5$	72.04	6.28	3.23	71.98	6.26	3.30
3h	Ph	1-naphthyl	Et	55	125–127	$C_{27}H_{29}NO_5$	72.46	6.53	3.13	72.75	6.52	3.22
3i	Ph	4-$NO_2C_6H_4$	Me	67	69–71	$C_{22}H_{24}N_2O_7$	61.68	5.65	6.54	61.32	5.53	6.62
3j	Ph	4-$NO_2C_6H_4$	Et	74	109–110	$C_{23}H_{26}N_2O_7$	62.43	5.92	6.33	62.20	5.92	6.27
3k	Me	Ph	Me	59	oil	$C_{17}H_{23}NO_5$	321.1576			321.1573		
3l	Me	Ph	Et	56	oil	$C_{18}H_{25}NO_5$	336.1811 (M + 1)			336.1813 (M + 1)		
3m	Me	4-$CH_3OC_6H_4$	Me	62	79–81	$C_{18}H_{25}NO_6$	351.1682			351.1694		
3n	Me	4-$CH_3OC_6H_4$	Et	57	oil	$C_{19}H_{27}NO_6$	365.1838			365.1842		

[a] Solvent for recrystallization: ethanol except for **3a** (methanol). [b] HRMS for liquid compounds.

A few other amidoalkylating reagents, e.g., enamides (RCONHCH=CHR) and *N*-acylimines have been reported; however, protonation of enamides by strong acid is generally needed to afford an electrophile capable of amidoalkylation.[22] Moreover, enamides and *N*-acylimines have apparently only been used for the amidoalkylation of aromatic compounds.[23,24]

Recent work in our group has demonstrated the versatility of benzotriazole as a synthetic auxiliary. *N*-(α-Aminoalkyl)benzotriazoles have been utilized advantageously as intermediates in the alkylation of amines[25] and hydrazines[26] and in the preparation of amino esters,[27] amino ketones,[28] and other polyfunctional amino compounds.[29,30] Other benzotriazole derivatives are used in the synthesis of ethers[31] and esters.[32] *N*-(1-Benzotriazolylalkyl)amides and -thioamides (easily prepared by the condensation of benzotriazole, an aldehyde, and an amide or a thioamide) are important synthetic intermediates in the N-alkylation of amides[33] and thioamides.[34]

Scheme I



The benzotriazolate anion is a good leaving group and can be used in place of a halogen or other substituent in many transformations. The benzotriazolyl group has the advantage that many α-benzotriazole derivatives are easily prepared and are more stable than the corresponding α-chloro or α-bromo analogues. In view of our previous results and the value of benzotriazole as a leaving group, we anticipated that the use of *N*-(α-benzotriazol-1-ylalkyl)amide analogues **2** of the frequently used amidoalkylation reagents **1** could provide an attractive alternative method for α-amidoalkylation.

We now report that *N*-(α-amidoalkyl)benzotriazoles, easily available from condensations of benzotriazole with amides and aldehydes, are indeed excellent reagents for the amidoalkylation of malonic ester and other CH acids. We also describe the reactions of benzotriazole aminals with some CH acids in the presence of methyl iodide, which produce novel products.

Results and Discussion

Preparation of the Amidoalkylation Reagents 2. The amidoalkylation reagents employed, *N*-(1-benzotri-

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Table III. ^{1}H NMR Spectral Data of Amidoalkylation Products 3a–3n[a]

no.	NH (d)	CH	CO_2Et	R^1	R^2	R^3
3a	8.61	5.66 (d)	4.30–4.12 (m), 1.24 (t), 1.20 (t)	7.81 (d, 2 H), 7.50–7.36 (m, 5 H), 7.33–7.25 (m, 3 H)[b]		1.43 (s, CH_3)
3b	8.57	5.72 (d)	4.22 (q), 4.13 (q), 1.21 (t), 1.11 (t)	7.74 (d, 2 H), 7.50–7.30 (m, 8 H)[b]		1.80 (q), 0.84 (t)
3c	8.62	5.91 (d)	4.11 (q, 4 H), 1.12 (t, 6 H)	7.70 (d, 2 H), 7.52 (m, 3 H)	7.31 (d, 2 H), 6.87 (d, 2 H), 3.73 (s, OCH_3)	1.38 (s, CH_3)
3d	8.53	5.69 (d)	4.24 (q), 4.15 (q), 1.23 (t), 1.13 (t)	7.75 (d, 2 H), 7.53 (m, 3 H)	7.35 (d, 2 H), 6.90 (d, 2 H), 3.75 (s, OCH_3)	1.81 (q), 0.85 (t)
3e	8.15	5.03 (t)	4.25 (m), 4.00 (m), 1.23 (t), 1.09 (t)	7.63 (d, 2 H), 7.50–7.40 (m)	7.30–7.13 (m, 5 H)	1.50 (s, CH_3)
3f	8.02	4.89 (t)	4.24 (q), 4.17 (q), 1.25 (t), 1.21 (t)	7.65 (d, 2 H), 7.53–7.44 (m)	7.30–7.14 (m, 5 H)	1.95 (1), 0.92 (t)
3g	8.84	6.88 (d)	4.22 (q), 3.90 (m), 1.19 (t), 0.97 (t)	7.75 (d, 2 H), 7.58–7.45 (m)	8.41 (d, 1 H), 7.94 (d, 1 H), 7.89 (d, 1 H), 7.57 (t, 1 H), 7.52–7.20 (m, 3 H)	1.48 (s, CH_3)
3h	8.76	6.78 (d)	4.28 (m), 4.12 (q), 1.22 (t), 1.08 (t)	7.75 (d, 2 H), 7.30 (m, 3 H)	8.46 (d, 1 H), 7.96 (d, 1 H), 7.80 (d, 1 H), 7.57 (t, 1 H), 7.30–6.98 (m, 3 H)	1.80 (m, 1 H), 1.65 (m), 0.82 (t)
3i	8.88	6.14 (d)	4.15 (q, 4 H), 1.15 (t, 6 H)	7.75 (d, 2 H), 7.60–7.49 (m)	8.22 (d, 2 H), 7.83 (d, 2 H)	1.45 (s, CH_3)
3j	8.73	5.93 (d)	4.23 (q), 4.18 (m), 1.22 (t), 1.13 (t)	7.80 (d, 2 H), 7.55 (m, 3 H)	8.21 (d, 2 H), 7.78 (d, 2 H)	1.91 (m), 0.84 (t)
3k	8.35	5.82 (d)	4.17–4.05 (m, 4 H), 1.16 (t), 1.13 (t)	1.86 (s, CH_3CO)	7.40–7.26 (m, 5 H)	1.32 (s, CH_3)
3l	8.12	5.60 (d)	4.19–4.03 (m, 4 H), 1.20–1.10 (m, 6 H)	1.87 (s, CH_3CO)	7.36–7.24 (m, 5 H)	1.80 (m), 0.77 (t)
3m	8.25	5.76 (d)	4.15–4.02 (m, 4 H), 1.17 (m, 6 H)	1.85 (s, CH_3CO)	7.28 (d, 2 H), 6.85 (d, 2 H), 3.74 (s, OCH_3)	1.31 (s, CH_3)
3n	8.07	5.53 (d)	4.18–4.03 (m, 4 H), 1.17 (t), 1.13 (t)	1.86 (s, CH_3CO)	7.24 (d, 2 H), 6.84 (d, 2 H), 3.72 (s, OCH_3)	1.78 (m), 0.77 (t)

[a] Solvent: DMSO-d_6. [b] R^1 and R^2 signals are overlapped.

Table IV. ^{13}C NMR Spectral Data of Aminoalkylation Products 3a–3n

no.	CO	CONH	C	CH	OC_2H_5	R^1	R^2	R^3
3a	171.4, 171.3	165.8	62.0	58.0	61.9, 61.5, 13.9, 13.8	134.3, 131.4, 128.3, 126.9	137.5, 128.5, 128.4, 127.9	20.2 (CH_3)
3b	169.6, 169.3	165.2	62.6	55.9	61.5, 61.2, 13.8, 13.7	134.3, 131.6, 128.2, 126.9	137.9, 128.6, 128.1, 127.8	26.2, 9.40
3c	169.9, 169.8	165.9	61.4	55.0	61.3, 13.8	134.6, 131.3, 128.3, 127.3	158.6, 130.2, 129.9, 113.2, 54.8	17.0 (CH_3)
3d	169.8, 169.4	165.1	62.7	55.0	61.5, 61.1, 13.9, 13.8	134.4, 131.5, 128.6, 126.9	158.8, 129.9, 129.4, 113.4, 55.5	26.3, 9.41
3e	170.4, 170.2	166.2	57.0	52.8	61.1, 61.0, 13.8, 13.6	134.7, 131.5, 128.1, 126.8	138.8, 128.9, 128.0, 127.2, 36.1	16.4
3f	169.9, 169.4	166.5	62.3	53.2	61.1, 61.0, 13.9	135.0, 131.1, 128.2, 126.8	139.4, 128.9, 128.0, 126.0, 36.8	25.2, 9.46
3g	170.2, 170.0	165.9	58.5	50.0	61.6, 61.4, 13.7, 13.5	134.3, 131.5, 128.4, 126.2	135.0, 133.1, 131.4, 128.6, 128.2 127.3, 126.0, 125.6, 125.1, 123.5	17.9
3h	169.8, 169.4	165.3	63.4	50.4	61.6, 61.3, 13.8, 13.7	134.1, 131.6, 128.4, 127.0	134.8, 133.1, 131.5, 128.7, 128.6 126.4, 125.7, 125.4, 125.3, 123.3	26.4, 9.67
3i	169.6, 169.2	166.5	58.1	54.8	61.7, 13.7	134.2, 131.1, 128.3, 127.5	146.9, 146.0, 130.2, 123.0	16.5
3j	169.2, 168.9	165.9	62.3	55.2	61.7, 61.4, 13.8, 13.7	134.0, 131.7, 128.5, 127.2	147.0, 145.8, 129.9, 123.1	25.9, 9.33
3k	169.6, 169.4	168.4	58.3	54.5	61.2, 13.7	22.6 (CH_3)	138.7, 128.5, 127.7, 127.3	16.3
3l	169.3, 169.2	168.3	62.5	54.9	61.0, 60.8, 13.7	22.7 (CH_3)	138.7, 128.3, 127.7, 127.4	26.1, 9.36
3m	169.7, 169.5	168.2	58.4	54.9	61.1, 60.8, 13.8	22.6 (CH_3)	158.4, 130.6, 129.7, 113.1, 53.9	16.3
3n	169.4, 169.3	168.2	62.6	55.0	60.8, 61.0, 13.8	22.8 (CH_3)	158.5, 130.6, 129.5, 113.1, 54.5	26.1, 9.41

azol-1-ylalkyl)amides **2a–2h**, were easily prepared by the previously described reaction of benzotriazole, an aldehyde, and an amide in refluxing toluene with azotropic removal of the water.[33] Both aliphatic and aromatic aldehydes gave stable products **2** in good yields (Scheme I), which were fully characterized by their ^{1}H and ^{13}C NMR spectra and by elemental analyses for new compounds (Table I). The ^{1}H and ^{13}C NMR spectra of these *N*-(α-amidoalkyl)-benzotriazoles confirmed that the crystalline products **2a–2k** are all benzotriazol-1-yl isomers and no isomerization to benzotriazol-2-yl derivatives occurred in dimethyl sulfoxide at room temperature, in contrast to the situation usually found for *N*-(α-aminoalkyl)benzotriazoles.[35]

Amidoalkylation of Active Methylene Compounds. The *N*-(α-amidoalkyl)benzotriazoles **2a–2h** reacted smoothly with diethyl methylmalonate or with diethyl ethylmalonate on refluxing in CH_2Cl_2 in the presence of aluminum chloride (Scheme I). The desired products **3a–3n** were obtained in 55–74% yields (Table II), even when steric hindrance was expected, e.g., **3h**, R^1 = Ph, R^2 = 1-naphthyl, R^3 = ethyl (55%). Generally, the amidoalkylations of diethyl methylmalonate gave slightly higher yields than those of diethyl ethylmalonate presumably due to the slightly greater steric effect. Unlike other often used amidoalkylation reagents, which require acid or base catalysis,[36,37] *N*-(α-amidoalkyl)benzotriazoles react in relatively mild conditions with good yields. The byproduct benzotriazole formed during the reaction dissolved in dilute alkali and was easily separated by extraction, making the whole procedure very simple.

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Table V. Preparation of Benzotriazole Derivatives 7

no.	R^1	R^2	R^3	yield (%)	mp (°C)	molecular formula	calcd C	calcd H	calcd N	found C	found H	found N
7a	Ph	CH_3CO	CH_3CO	81	91–93	$C_{18}H_{17}N_3O_2$	70.34	5.58	13.76	70.26	5.55	13.75
7b	Ph	CH_3CO	CO_2Et	69	107–109	$C_{19}H_{19}N_3O_3$	67.64	5.68	12.45	67.37	5.64	12.43
7c	Ph	CO_2Et	CO_2Et	76	129–131	$C_{20}H_{21}N_3O_4$	65.38	5.76	11.44	65.41	5.77	11.46
7d	Ph	H	NO_2	60	oil	$C_{14}H_{12}N_4O_2$						
7e	CH_3	CH_3	CH_3CO	19	oil	$C_{12}H_{15}N_3O$	245.1164[a]			245.1155[a]		

[a] HRMS data for oil products.

Table VI. ^1H NMR Spectral Data of Benzotriazole Derivatives 7[a]

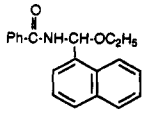
no.	benzotriazole	R^1	CHα	CHβ	R^2	R^3
7a	8.0 (d, 1 H), 7.50–7.25 (m, 3 H)	7.50–7.25 (m, 5 H)	6.45 (d, J = 11.4)	5.75 (d, J = 11.4)	2.10 (s, 3 H)	2.30 (t)
7b	8.0 (d, 1 H), 7.50–7.25 (m, 3 H)	7.50–7.27 (m, 5 H)	6.45 (d, J = 11.4)	5.45 (d, J = 11.4)	2.40 (s, 3 H)	4.05 (q), 1.05 (t)
7c	8.0 (d, 1 H), 7.60–7.26 (m, 3 H)	7.55–7.30 (m, 5 H)	6.40 (d, J = 11.4)	5.20 (d, J = 11.4)	4.03 (q), 1.02 (t)	4.07 (q), 1.06 (t, 3 H)
7d	7.60–7.20 (m, 4 H)	7.50–7.20 (m, 5 H)	6.66 (dd, J = 10, 4.6)	5.93 (dd, J = 14.8, 10)	5.18 (dd, J = 14.8, 4.6)	
7e	7.95 (d, 1 H), 7.60 (d, 1 H), 7.45 (dd, 1 H), 7.30 (dd, 1 H)	1.55 (d, 3 H)	5.60 (m)	5.10 (d)	2.02 (s)	2.40 (s)

[a] Solvent: $CDCl_3$; J values in hertz.

The structures of our α-amidoalkylation products were confirmed by their elemental analyses (Table II) and by spectral methods. The ^1H and ^{13}C NMR chemical shifts and their assignments are listed in Tables III and IV. Because the malonic ester function is attached to a chiral center, in most cases the two ethoxycarbonyl groups are nonidentical in both the ^1H and ^{13}C NMR spectra. Typical downfield doublets were observed for the amide NH group coupled with the adjacent CH. Proton and carbon signals were assigned by the attached proton test and by comparison with other benzotriazole derivatives.

Following these successful results, we examined similar reactions with other active methylene compounds. Ethyl 2-methylacetoacetate, methyl acetoacetate, and ethyl nitroacetate each reacted with (amidoalkyl)benzotriazoles **2f** or **2g** under the same conditions ($AlCl_3/CH_2Cl_2$) to give amidoalkylated derivatives **4a–4c** in 43–55% yields. As expected, two diastereoisomers were formed for **4b** and **4c**, but surprisingly only one form was seen for **4a**. This is clearly indicated in their NMR spectra, in which each proton and each carbon gives two signals (see Experimental Section). The diastereoisomeric ratios were determined from their relative integral values in the ^1H spectra as 2:1 for **4b** and 3:2 for **4c**. No attempt was made to separate the diastereoisomers.

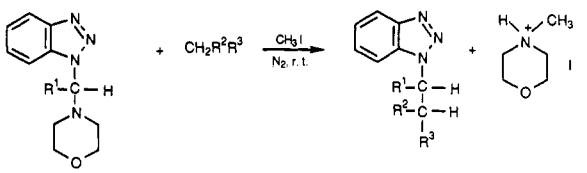
Although the reaction seems to be general, we did encounter one failure: when ethyl 2-methylacetoacetate was treated with *N*-(benzotriazol-1-ylnaphth-1-ylmethyl)-benzamide (**2e**) under similar conditions, *N*-[α-(ethoxy-naphth-1-ylmethyl)benzamide **5** was produced (25%, the only isolated product); the expected amidoalkylation of the acetoacetate was presumably sterically inhibited. Compound **5** was characterized by its ^1H and ^{13}C NMR spectra and by elemental analysis.



5

Reaction of Benzotriazole Aminals with Some CH Acids in the Presence of Methyl Iodide. As described previously, benzotriazole derivatives with aldehydes and primary or secondary amines are valuable synthetic intermediates, as the benzotriazole moiety is replaceable by a variety of nucleophiles. Quaternization of the non-benzotriazole nitrogen of such Mannich bases should create potentially superior leaving groups.

Scheme II



6 7

The morpholine derivative **6** (R^1 = Ph)[38] was treated with methyl iodide and then allowed to react in situ with a variety of CH acids to give benzotriazole derivatives **7a–7d** in excellent yield. Only reaction between **6** (R^1 = Me) and butanone gave a low yield (19%) of the required product (Scheme II and Table V). The morpholine salt was always a byproduct. Presumably, the quaternized derivative of **6** dissociated and reaction occurred via the resulting Eschenmoser salt. The ^1H and ^{13}C NMR spectra of these novel benzotriazole derivatives **7a–7e** are summarized in Tables VI and VII. The proton NMR spectra are easily assigned; the CH_α and CH_β appear as AB systems with coupling constant 11.4 Hz for **7a–7c** and as an ABX pattern for **7d**. On the basis of their ^{13}C NMR spectra, they are all benzotriazol-1-yl derivatives; no signal for any 2-isomer is observed.

In summary, an alternative approach has been developed for the amidoalkylation of active methylene compounds by using *N*-(benzotriazolylalkyl)amides. When our system is compared with other amidoalkylation reagents, such as *N*-(α-hydroxyalkyl)amide and *N*-(α-chloroalkyl)amide,[3] it is apparent that the method gives similar yields but the conditions are milder, which is particularly important for compounds that are sensitive to acidic or basic media. Moreover, the easily prepared and stable *N*-(benzotriazolylalkyl)amides available from a wide range of aldehydes and the simple workup procedure offer considerable advantages over previous amidoalkylation reagents. Significantly, none of the compounds of Table II have been previously reported.

(38) Katritzky, A. R.; Yannakopoulou, K. *Heterocycles* **1989**, *28*, 1121.

Table VII. ^{13}C NMR Spectral Data of Benzotriazole Derivatives 7

no.	benzotriazole	R^1	Cα	Cβ	R^2	R^3
7a	146.0, 132.7, 127.6, 124.2, 119.8, 109.7	135.8, 129.1, 129.0, 127.6	71.7	61.5	198.8, 30.6	199.6, 31.6
7b	146.0, 132.7, 127.5, 124.2, 119.7, 109.8	135.8, 128.9, 128.8, 127.8	64.0	60.8	199.1, 30.2	165.4, 62.0, 13.7
7c	146.0, 132.9, 127.5, 124.1, 119.8, 109.6	135.3, 129.1, 128.8, 127.9	61.5	57.1	166.1, 61.9, 13.6	166.2, 62.1, 13.7
7d	146.0, 132.5, 127.8, 124.4, 119.9, 109.3	133.8, 129.4, 129.2, 126.7	76.3	59.6		
7e	145.4, 132.3, 127.5, 124.0, 119.5, 109.5	19.5 (CH_3)	72.4	53.2	199.8, 30.7	199.7, 30.5

Further extensions of our novel amidoalkylation reagent to aromatic and heteroaromatic compounds and to olefins and acetylenes are under investigation.

Experimental Section

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. ^1H NMR spectra were obtained on a Varian XL 300 spectrometer with TMS as a standard. ^{13}C NMR spectra were recorded on the same instrument referenced to solvent (δ DMSO-d_6 39.5 or $CDCl_3$ 77.0). The mass spectra were measured on an AEI MS 30 mass spectrometer with an electron beam energy of 70 eV. Elemental analyses were carried out in this department. Compounds 6 were prepared as previously reported.[38]

Preparation of *N*-[(Acylamino)alkyl]benzotriazoles 2. Typical Procedure. A mixture of benzotriazole (11.9 g, 0.1 mol), the aldehyde (0.1 mol), and the appropriate amide (0.1 mol) was refluxed in dry toluene (40 mL) for 24 h. Water formed during the reaction was removed azeotropically by a Dean-Stark apparatus. Toluene was then removed under reduced pressure (60 °C/(30 mmHg)) and the residue poured into diethyl ether (200 mL). The resulting solid was collected and recrystallized from the appropriate solvent (Table I).

1-Benzotriazol-1-yl-*N*-benzoyl-1-(4-methoxyphenyl)-methylamine (2b): ^1H NMR (DMSO-d_6) δ 10.22 (d, 1 H, J = 7 Hz, NH), 8.20 (d, 1 H), 8.12 (d, 1 H), 8.05–7.96 (m, 3 H), 7.60–6.90 (m, 7 H), 7.00 (d, 2 H), 3.77 (s, 3 H, OCH_3); ^{13}C NMR δ 167.3 (CO), 160.0, 145.8, 133.5, 132.4, 129.1, 128.9, 128.7, 128.6, 128.4, 127.9, 124.6, 119.7, 114.4, 111.7, 75.6 (CH), 66.4 (OCH_3).

1-Benzotriazol-1-yl-*N*-benzoyl-2-phenylpropylamine (2c): ^1H NMR (DMSO-d_6) δ 10.03 (d, 1 H, NH), 8.05–6.92 (m, 15 H), 4.22–4.12 (m, 1 H, C2-H), 1.60 (d, 3 H, CH_3); ^{13}C NMR δ 167.5 (CO), 144.8, 141.8, 133.5, 132.8, 132.4, 128.9, 128.5, 128.1, 127.7, 127.4, 127.0, 124.0, 119.1, 111.4, 68.7 (C1), 43.3 (C2), 19.7 (CH_3).

1-Benzotriazol-1-yl-*N*-benzoyl-2-phenylethylamine (2d): ^1H NMR (DMSO-d_6) δ 9.97 (d, 1 H, NH), 8.10 (d, 1 H), 8.05 (d, 1 H), 7.90 (d, 2 H), 7.60–7.33 (m, 7 H), 7.23 (t, 2 H), 7.16 (t, 2 H), 3.90–3.78 (m, 2 H, CH_2); ^{13}C NMR δ 166.6 (CO), 145.0, 136.1, 132.9, 132.2, 131.9, 129.3, 128.4, 128.3, 127.6, 127.3, 126.8, 124.0, 119.0, 111.1, 64.8 (CH), 38.7 (CH_2).

***N*-[Benzotriazol-1-yl(4-nitrophenyl)methyl]benzamide (2f)**: ^1H NMR (DMSO-d_6) δ 10.42 (d, 1 H, J = 8 Hz, NH), 8.46 (d, 1 H, J = 8 Hz, CH), 8.34 (d, 2 H), 8.16 (d, 1 H), 8.02 (m, 3 H), 7.75 (d, 2 H), 7.65–7.45 (m, 5 H); ^{13}C NMR δ 167.0 (CO), 147.7, 145.3, 143.3, 132.7, 132.2, 128.8, 128.4, 128.0, 127.9, 124.5, 123.7, 119.5, 111.2, 65.2 (CH).

***N*-[Benzotriazol-1-yl(4-methoxyphenyl)methyl]acetamide (2h)**: ^1H NMR (DMSO-d_6) δ 9.75 (d, 1 H, NH), 8.08 (d, 1 H), 7.90 (d, 1 H), 7.86 (d, 1 H), 7.55 (t, 1 H), 7.42 (t, 1 H), 7.35 (d, 2 H), 6.97 (d, 2 H), 3.74 (s, 3 H, OCH_3), 1.98 (s, 3 H, CH_3); ^{13}C NMR δ 170.2, 160.0, 145.7, 132.1, 128.8, 128.6, 127.9, 124.6, 120.7, 114.5, 111.5, 65.5, 55.6, 22.7.

Amidoalkylation of Active Methylene Compounds, Typical Procedure. A mixture of the *N*-(1-benzotriazol-1-ylalkyl)amide (0.01 mol), diethyl alkylmalonate (0.012 mol), and aluminum chloride (2.66 g, 0.02 mol) in dry CH_2Cl_2 (40 mL) was refluxed for 4 h and poured into ice–water (40 mL). The organic layer was washed with 2 M NaOH solution (30 mL) and water (30 mL) and dried over $MgSO_4$ (10 g). The solvent was evaporated and the residue recrystallized from alcohol or purified by column chromatography on silica gel using $CHCl_3$ as the eluant. The data for products of general formula 3 are summarized in Tables II–IV.

Ethyl 2-methyl-2-[(benzoylamino)(4-nitrophenyl)-methyl]-3-oxobutyrate (4a): prisms (EtOH); 55%; mp 151–153 °C; ^1H NMR (DMSO-d_6) δ 8.82 (d, J = 9.6 Hz, 1 H, NH), 8.22 (d, J = 8.7 Hz, 2 H), 7.83 (d, J = 8.7 Hz, 2 H), 7.75 (d, 2 H), 7.62–7.50 (m, 3 H), 6.14 (d, J = 9.6 Hz, 1 H, CH), 4.18 (q, 2 H, OCH_2), 2.21 (s, 3 H, $COCH_3$), 1.43 (s, 3 H, CH_3), 1.16 (t, 3 H, CH_2CH_3); ^{13}C NMR δ 204.0 (CO), 171.1 (CO_2), 166.2 (CONH), 146.8, 146.2, 134.1, 131.7, 130.2, 128.5, 127.4, 123.0, 64.1 (C), 61.8 (OCH_2), 54.4 (CH), 26.1, 16.6, 13.8. Anal. Calcd for $C_{21}H_{22}N_2O_6$: C, 63.31; H, 5.57; N, 7.03. Found: C, 63.29; H, 5.55; N, 7.01.

Methyl 2-[(benzoylamino)(4-nitrophenyl)methyl]-3-oxobutyrate (4b): microcrystals (EtOH); 43%; mp 142–144 °C; ^1H NMR (DMSO-d_6) δ (major diastereoisomer) 9.08 (d, J = 8.4 Hz, NH), 8.24 (d, 2 H), 7.82–7.73 (m, 4 H), 7.58–7.45 (m, 3 H), 5.83 (dd, J = 8.4 Hz, 11.5, CHNH), 4.56 (d, J = 11.5 Hz, CH), 3.51 (s, CO_2CH_3), 2.36 (s, $COCH_3$) (minor diastereoisomer) 9.06 (d, J = 8.7 Hz, NH), 8.22 (d, 2 H), other aromatic signals overlapped with major diastereoisomer 5.85 (dd, J = 8.7, 10.5 Hz, CHNH), 4.67 (9d, J = 10.5 Hz, CH), 3.70 (s, CO_2CH_3), 2.15 (s, $COCH_3$); ^{13}C NMR δ 200.6 and 200.1 (CO), 167.3 and 166.6 (CO_2), 165.9 (CONH), 147.8, 147.6, 146.9, 146.8, 133.9, 133.7, 131.7, 131.6, 129.1, 128.9, 128.4, 127.3, 123.6, 123.5, 62.9, 52.7, 52.6, 51.9, 51.5, 30.0, 39.7. Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.40; H, 4.90; N, 7.47.

Ethyl 3-(acetylamino)-2-nitro-3-phenylpropionate (4c): prisms (EtOH); 50%; mp 143–146 °C; ^1H NMR (DMSO-d_6) δ (major diastereoisomer) 8.76 (d, J = 9.3 Hz, NH), 7.49–7.28 (m), 6.14 (d, J = 8.4 Hz, CHCO), 5.84 (dd, J = 9.3, 8.4 Hz, CHNH), 4.06 (q, 2 H, OCH_2), 1.90 (s, CH_3), 0.99 (t, CH_3) (minor diastereoisomer) 8.56 (d, NH), 7.49–7.28 (m), 6.01 (d, CHCO), 5.80 (dd, 1 H, CHNH), 4.22 (m, 2 H, OCH_2), 1.86 (s, CH_3), 1.19 (t, CH_3); ^{13}C NMR δ (major diastereoisomer) 169.1 (CO_2), 162.6 (CONH), 136.6, 128.6, 128.2, 127.3, 90.4 ($CHNO_2$), 62.8 (OCH_2), 52.2 (CHNH), 22.5 (CH_3), 13.4 (CH_3) (minor diastereoisomer) 168.9, 162.8, 136.9, 128.7, 128.4, 127.7, 89.1, 63.0, 52.2, 22.5, 13.6. Anal. Calcd for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.75; N, 9.99. Found: 55.85; H, 5.70; N, 9.87.

***N*-(α-Ethoxynaphth-1-ylmethyl)benzamide (5)**: prisms; 25%; mp 166–168 °C; ^1H NMR (DMSO-d_6) δ 9.34 (d, J = 8.0 Hz, NH), 8.10–7.88 (m, 6 H), 7.60–7.44 (m, 6 H), 7.04 (d, J = 8.0 Hz, 1 H, CH), 3.88–3.67 (m, 2 H, OCH_2), 1.28 (t, 3 H, CH_3); ^{13}C NMR δ 167.0 (CONH), 135.6, 134.0, 133.7, 132.1, 130.8, 129.0, 128.9, 128.7, 128.2, 126.8, 126.1, 125.6, 124.2, 123.5, 78.0 (CH), 63.5 (CH_2), 15.6 (CH_3). Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 7.27; N, 4.59. Found: C, 78.23; H, 6.31; N, 4.56.

Preparation of 3-(Benzotriazol-1-ylphenylmethyl)pentane-2,4-dione (7a). To a solution of 1-(morpholinophenylmethyl)benzotriazole 6 (2.94 g, 0.01 mol) and 2,4-pentanedione (5 g, 0.05 mol) in THF (30 mL) was added dropwise under nitrogen methyl iodide (1.56 g, 0.011 mol) in THF (5 mL). The reaction mixture was stirred at room temperature for 12 h and then diluted with 30 mL of diethyl ether. The *N*-methylmorpholinium iodide that precipitated was separated by filtration, and the filtrate was evaporated to dryness under reduced pressure. The oily residue was chromatographed on silica gel using $CHCl_3$ as the eluant and recrystallized from benzene–petroleum ether to give 7a (2.4 g, 81%).

Compound 7b to 7e were prepared similarly except for 7d where the solvent THF was replaced by nitromethane.