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Utility of a Polymeric Azide Reagent in the Formation of Di- and Triazidomethane. Their NMR Spectra and the X-ray Structure of Derived Triazoles[1]

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The use of a polymeric azidation reagent for the preparation of explosive azidomethanes at ambient temperature is described. Thus, methyl iodide was converted into methyl azide, methylene bromide and methylene chloride into diazido methane, and bromoform into triazido methane. ^1H and ^{13}C NMR spectra, including $^1J_{CH}$, of the azidomethanes are described. The X-ray diffraction of derived triazole adducts **4** and **5** confirms the structure assignment and indicates in the case of **5** a 1,5-sigmatropic alkyl rearrangement.

Introduction

Organic azides are thermally and photochemically labile compounds but of considerable utility in the generation of other functionalities, e.g. amines via reduction, imines via rearrangement, triazoles and other heterocycles via cycloaddition.[2]

One of the problems in the preparation of low molecular weight azides or of di- or polyazido compounds is their potentially explosive character. Methyl azide can be explosive,[3] and the polyazidomethanes have not yet been reported,[4] presumably because of the limitation provided by the known synthetic procedures, generally requiring heating or product distillation. It is precisely for the synthesis of such sensitive compounds that the use of polymeric reagents[5] is ideally suited. The desirable features of such a reagent are (1) being reactive at ambient temperature or below, (2) being usable as the excess component which can be removed by filtration, and (3) leading to a solution of virtually pure product, thus minimizing purification procedures.

In a preliminary communication we described[4] a very mild method for preparation of alkyl azides, which consists of mixing an alkyl halide or sulfonate with an excess of a polymeric azidation reagent at room temperature in a variety of solvents. We report here the details for the preparation of the reagent and for applying this method to the formation of methyl azide, the rather explosive diazidomethane (**2**), and triazidomethane (azidoform) (**3**), their characterization, and a rearrangement of a tris triazole.

Results and Discussion

The polymeric azidation reagent **1** was prepared from Amberlyte IR-400 quaternary ammonium chloride resin by exchange with azide ions and proper washing. A solution of methyl iodide in acetonitrile-d_3 was mixed with an excess of reagent **1**, at 4 °C for 40 min. NMR indicated complete conversion of the substrate. After removal of the polymer beads by filtration, the resulting solution was examined by ^1H and ^{13}C NMR spectroscopy, which indicated the presence of practically pure methyl azide.

Table I. ^1H and ^{13}C NMR Spectral Data of Azidomethanes[a]

	^1H ppm	^1H: $\upsilon^{1/2}$, Hz	^{13}C ppm[b,c]	$^1J_{CH}$, Hz
n-$C_5H_{11}CH_2N_3$	3.25		51.64[d]	141.5
CH_3N_3	2.98	4.5	37.85	142.5
CH_2N_6 (**2**)	4.48	6.0	66.87	162.5
CHN_9 (**3**)	5.77	3.5	88.64	183.5

[a] Obtained in $CDCl_3$ at 300 MHz with TMS as internal standard on a Bruker AM-300 instrument. [b] Obtained as in *a* but at 75 MHz. [c] Chemical shift of the C attached to N_3, in ppm. [d] C-2 28.95; C-3 26.52; C-4 31.46; C-5 22.61; C-6 13.96.

The preparation of diazidomethane (**2**) was carried out starting either from methylene chloride or from methylene bromide. Though methylene bromide reacts faster than methylene chloride, the latter has the advantage of greater volatility and can be used in large excess (as the solvent). Thus, shaking the azidation polymer in methylene chloride at ambient temperature for 4 weeks, followed by filtration and concentration of the clear liquid, led to a solution of ca. 70% of **2** in methylene chloride. The progress of the reaction was followed by GC. Concentration beyong 70% of **2** was deemed unsafe because attempts to take an infrared spectrum of this solution in an IR cell led to an explosion, as did transfer by pipette and injection of the solution into a GC or mass spectrometer inlet (no problems were encountered on injection of a more dilute solution of **2** into a heated (over 120 °C) GC inlet port).

Evidence for the structure of diazidomethane (**2**) was secured by IR (strong absorption at 2100 cm^{-1}) and ^1H and ^{13}C NMR spectra as well as by formation of a 1:2 cycloadduct **4** with dimethyl acetylenedicarboxylate. The methylene protons of **2** were found at 4.48 ppm, showing an expected downfield shift compared to methyl azide. The corresponding ^{13}C absorption occurred at 66.87 ppm and was correlated through analysis of the residual couplings in several off resonance decoupled spectra as belonging to the same CH_2 group. No other CH_2 absorptions, except for CH_2Cl_2, were present, indicating that the second displacement on an intermediate $ClCH_2N_3$ probably proceeded faster than the first chlorine displacement. The ^{13}C–H coupling constant was also increased compared to methyl azide (see Table I).

The conversion of methylene bromide to **2** was carried out in THF with excess (ca. 2 molar equiv) of azidation polymer. Dilution with the solvent slowed down the dis-

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[1] Synthetic Methods. 33. For part 32, see: Ghera, E.; Maurya, R.; Hassner, A. *Tetrahedron Lett.* **1989**, *30*, 4741.

[2] Biffin, M. E. C.; Miller, J.; Paul, D. B. In *The Chemistry of the Azido Group*; Patai, S., Ed.; Interscience: London, 1971; pp 57. Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297 and references cited.

[3] (a) Grundmann, C. *Angew. Chem.* **1950**, *62*, 410. (b) *Nachr. Chem. Techn.* **1970**, *18*, 26.

[4] Hassner, A.; Stern, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 478.

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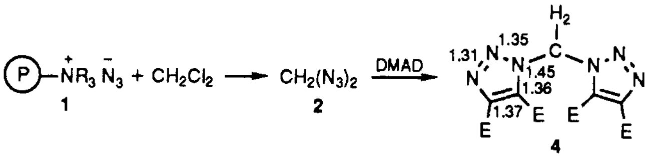
placement process, but the reaction was allowed to proceed to 95% conversion of the substrate (as determined by GC and NMR). Filtration of the reagent and partial evaporation of the solvent led to a solution of **2** in THF, which showed the same spectral characteristics as **2** prepared from methylene chloride.

Treatment of a methylene chloride solution of **2** with dimethyl acetylenedicarboxylate (DMAD) was followed by GC and produced a single adduct **4**. The structure of this 2:1 adduct was evident by IR (absence of azide absorption, presence of two C=O stretching bands at 1750 and 1730 cm^{-1}), NMR (C*H* at 7.38 ppm and the correlated ^{13}C absorption at 59.4 ppm), and X-ray diffraction.



The preparation of triazidomethane lacked the advantage of a volatile starting material that was available in methylene chloride, since chloroform proved rather unreactive. The polymeric reagent was wetted with an equivalent amount of bromoform and allowed to stand for 3 weeks with occasional mixing. After this was washed with ether, both GC and NMR indicated a 50% conversion to triazidomethane **3**. Concentration of the ether left a solution containing ca. 45% of **3**, which already showed explosive properties when handled with a pipette. Alternatively the reaction was carried out using bromoform as the solvent in which the polymeric reagent was suspended. After 7 days 2% conversion of bromoform and 20% conversion of the polymer had taken place. Identification of **3** was by GC retention time and by NMR. Triazidomethane had a C*H* absorption at 5.77 ppm and the correlated ^{13}C at 88.64 ppm. The ^{13}C–H coupling constant had increased to 183.5 Hz. There was again no evidence for intermediates containing bromine and azide functions.

$$CHBr_3 + \mathbf{1} \rightarrow \underset{\mathbf{3}}{CHN_9}$$

Triazide **3** likewise reacted with DMAD, though pure crystals of the 3:1 adduct were more difficult to obtain. ^1H NMR spectra indicated a 3:1 adduct with a notable deshielding of the methine proton at 10.06 ppm, compared to the CH_2 protons in **4** at 7.38 ppm. Surprisingly, NMR showed three sets of methyl and other carbon signals of the same intensity, suggesting that the three triazole rings were not equivalent. The structure of the adduct was revealed by single-crystal X-ray diffraction to be **5** and to consist of a 2-substituted and two 1-substituted triazoles. Apparently, formation of **5** involves a rare case of 1,5-sigmatropic alkyl rearrangement in one of the rings of an initially formed symmetrical tris triazole, possibly to relieve steric crowding, since such a rearrangement had not occurred in the bis adduct **4**. Though acyl and silyl migrations (usually thermal) from N-1 to N-2 in triazoles are well known,[6] previous alkyl migrations are not documented. Alternatively, elimination of a triazole unit from the symmetrical tris triazole, followed by its readdition via N-2 to the resulting amidinium species, could provide **5**.

The bond lengths clearly reflect the structural features of **5**. For instance, in the 2-substituted triazole ring the C–C bond distance was 1.41 Å and the C=N bond measured 1.33 Å, while the corresponding C=C and C—N distances in the two 1-substituted triazole rings were 1.37 and 1.45 Å, respectively (see Figure 1). These and the other measured bond distances (see supplementary material) are indicative of a fair degree of bond localization in these heterocyclic systems.

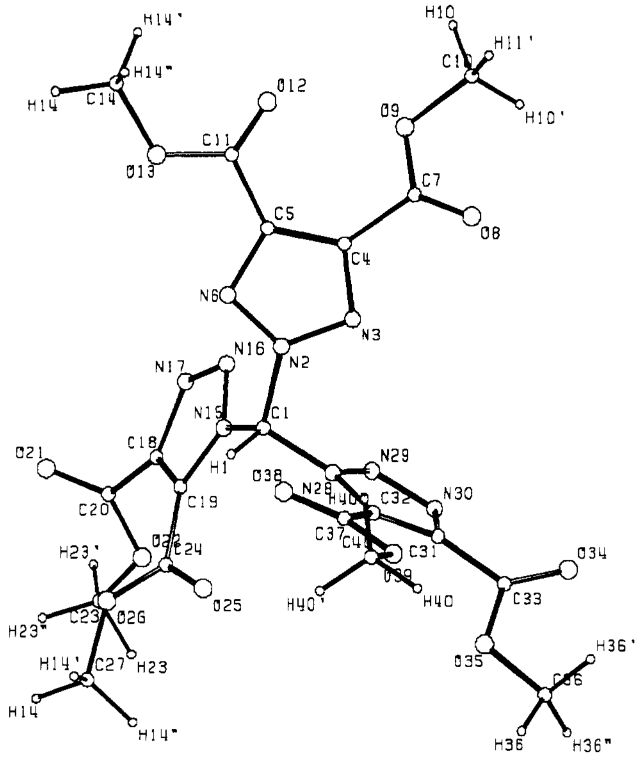
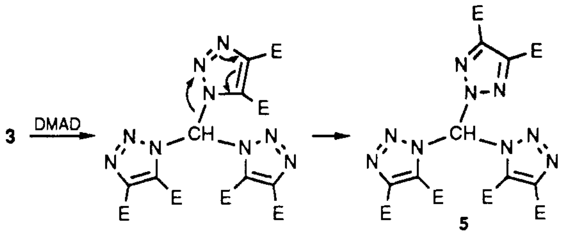


Figure 1. Crystal structure of **5**. Selected bond distances: C(4)–C(5), 1.411 Å; C(4)=N(3), 1.331 Å; C(18)=C(19), 1.371 Å; C(18)–N(17), 1.368 Å.



The NMR data of diazidomethane and triazidomethane permit a useful comparison of geminal effects by the azide function (see Table I). The replacement of a hydrogen by the azido group has a downfield effect on both the proton and carbon resonances, even though the effect is not entirely additive. Though chemically an azide function often shows analogous effects to a bromine substituent, the upfield shift of the carbon resonances[7] caused by multiple substitution with heavy halogens such as Br and I are not observed with N_3.

In the ^1H spectra, the resonances of the azidomethanes are a few hertz wide, probably a result of coupling with ^{14}N, which is not completely averaged out through ^{14}N relaxation. Interestingly, no such broadening is apparent in the ^{13}C NMR spectrum. The one-bond C–H coupling increased with increasing azide substitution; the effects of additional azido groups contribute more than expected by simple additivity (based on methane $^1J_{CH}$ = 125 Hz), as has been seen in other polysubstituted methanes.[8]

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[7] Kalinowski, H. O.; Berger, S.; Braun, S. *^{13}C NMR Spektroskopie*; G. Thieme Verlag: Stuttgart, 1984; p 150.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded on a Brucker AM-300 spectrometer in $CDCl_3$–Me_4Si and are reported in δ values. All solvents were distilled reagent grade. Gas chromatographic analyses were carried out in a Varian 6000 gas chromatograph.

Polymeric Azidation Reagent 1. Amberlyte IR-400 quaternary ammonium resin was washed with 1.5 times its volume of warm dimethylformamide, twice with methanol, and then water. It was washed with twice its volume of 20% NaN_3 solution, then three times each with deionized water, until the eluents gave no precipitate with $AgNO_3$. Polymer 1 was obtained after washing three times each with 30% MeOH, 60% MeOH, MeOH, 50% MeOH–ether, and ether. After being dried at room temperature in vacuum it contained 2.55 mmol of azide per gram of polymer. For subsequent reactions 1 can be used either before or after drying. The reagent is stable to the hammer test and can be kept on the shelf for months (preferably wet with the last washing solvent) without deterioration.

Diazidomethane 2. (A) From Methylene Chloride. Polymer beads 1 (70 mL or ca. 45 g) were washed in a column three to four times with twice their volume of chloroform and again with methylene chloride and were then allowed to stand at 20 °C with 1.5 times their volume of methylene chloride for 3 weeks. After filtration, the polymer was washed with 1 volume of methylene chloride and the combined solutions were concentrated on a rotovap at room temperature. The clear solution (73% of **2**) was examined by GC, IR, and NMR. It exploded when transferred by pipette. GC (1.8 m OV225/Chromosorb column, injection temperature 120 °C, column 50 °C, detector 120 °C, filament 150 °C, t_R 4.2 min): 19.4% CH_2Cl_2; 5.8% $CHCl_3$; 73.5% **2**; 1.3% unidentified material of t_R 2.6 min. IR (exploded on NaCl plate) in dilute solution: 2100 cm^{-1}. ^{1}H NMR ($CDCl_3$, 60 MHz): δ 4.5 ($\upsilon^{1/2}$ = 6 Hz). ^{13}C NMR ($CDCl_3$): 66.87 ppm (t, $^1J_{CH}$ = 162.5 Hz). Ratio of CH_2Cl_2: 1:8 (due to partial evaporation of CH_2Cl_2 before dilution with $CDCl_3$).

(B) From Methylene Bromide. Polymer 1 (40 mL, wet with CH_2Cl_2) was washed twice with an equal volume of THF, and then 25 mL of THF and 1.4 mL (20 mmol) of CH_2Br_2 were added. The wet beads were left to stand for 45 days with occasional shaking, and the progress of the reaction was followed by GC (decrease of CH_2Br_2 t_R of 2.65 min and increase in CH_2N_6 t_R of 4.2 min) until CH_2Br_2 had virtually disappeared (95% conversion). After filtration the THF was partially evaporated and $CDCl_3$ was added. GC and NMR showed identical characteristics as **2** from method A.

1,1′-Methanobis(4,5-dicarbomethoxy-1,2,3-triazole) (4). A solution of **2** in CH_2Cl_2 (0.5 mL) as obtained by method A was diluted with methylene chloride, and dimethyl acetylenedicarboxylate (DMAD) (0.7 mL, 5.7 mmol) was added. After 4 days at room temperature, the solvent was removed in vacuum and the oily residue was dissolved in warm ether and let stand to give white crystals of **4**, mp 120–122 °C. IR: 3050, 2960, 1750, 1730 cm^{-1}. ^{1}H NMR ($CDCl_3$, 60 MHz): δ 7.38 (s, 2 H), 4.01 and 3.94 (12 H). ^{13}C NMR: 159.7 and 158.3 (C=O), 140.3 and 130.5 (C=C), 59.4 (CH_2, t, $^1J_{CH}$ = 132 Hz), 53.9 and 52.9 (Me). Anal. Calcd for $C_{13}H_{14}N_6O_8$: C, 40.84; H, 3.69; N, 21.98. Found: C, 40.84; H, 3.95; N, 22.25. Crystal data (see 4 and supplementary material): monoclinic, space group $P21/c$, a = 13.090 (1) Å, b = 15.808 (1) Å, β = 97.62 (1)°, c = 8.260 (1) Å, V = 1705.7 (8) Å^3, M_r = 380.36, Z = 4, D_o = 1.481 g cm^{-3}.

Triazidomethane 3. Polymer 1 (30 mL, wet with ether) was dried in vacuum, 2 mL (22.9 mmol) bromoform was added, and the wet polymer was left for 22 days with occasional mixing. The polymer was washed twice with 20 mL of ether. GC (1 m, $^3/_8$ in. OV225 column, injection 160 °C, column 70 °C, detector 120 °C) indicated 50% conversion to **3**, t_R 7.7 min ($CHBr_3$ retention time 5.9 min). Partial evaporation of the ether left a solution which by GC and NMR contained ether–$CHBr_3$–CHN_9 in a ratio of 10:34:35. Transfer of this solution into an NMR tube led to an explosion. ^{1}H NMR ($CDCl_3$) of **3**: δ 5.77 ($\upsilon^{1/2}$ = 3.5 Hz). $CHBr_3$: δ 6.86. ^{13}C NMR 88.64 ppm (d), $^1J_{C-H}$ = 183.5 Hz.

2-(Bis(4′,5′-dicarbomethoxy-1′,2′,3′-triazol-1′-yl)methyl)-4,5-dicarbomethoxy-1,2,3-triazole (5). To the above solution of **3** in $CDCl_3$ was added 3.5 equiv of dimethyl acetylenedicarboxylate, and the reaction was followed by GC until **3** had almost vanished. After evaporation and trituration of the oil with ether the solid was dissolved in hot ethanol and let crystallize, which led to two sets of hand-separated crystals, **5** (major), mp 109 °C, and A (minor, unidentified), mp 126 °C. After recrystallization, **5** melted at 110–112 °C. ^{1}H NMR: δ 10.06 (s, CH), 4.00, 3.97, and 3.96 (three, Me). ^{13}C NMR: 53.21, 53.21, and 54.14 (three OMe), 80.73 (d), 129.10 and 141.26 (C-5 and C-4 of 1-alkyltriazoles)[9] and 142.03 (C-4, C-5 of 2-alkyltriazole),[9] 157.75, 159.14, and 159.43 (three C=O). MS: m/e 537 ($M^+ - N_2$, 5), 381 (M − triazole, 100), 353 (381 − N_2, 95). Anal. Calcd for $C_{19}H_{19}N_9O_{12}$: C, 40.35; H, 3.36. Found: C, 40.93; H, 3.40. Crystal data (see also Figure 1 and supplementary material): triclinic, space group $P1$, a = 8.839 (1) Å, α = 110.37 (2)°, b = 13.463 (2) Å, β = 101.63 (2)°, c = 13.944 (2) Å, τ = 106.31 (2)°, V = 1407.9 (2) Å^3, $C_{19}H_{18}N_9O_{12}\cdot C_3H_8O$ M_r = 662, Z = 2, D_c = 1.374 g cm^{-3}.

Methyl Azide. Because of the high volatility of methyl azide the reaction was carried out in CD_3CN (suitable for NMR spectral analysis) in a polypropylene solid–liquid separator with a Teflon 15-μm synter. To this vial, kept at 0–5 °C, were added 0.8 mL of CD_3CN, 0.61 g of polymer 1 (1.5 mg of azide), and 25 μL of MeI. The vial was shaken intermittently for 40 min. The liquid was separated from the polymer beads by pulling the plunger, and the solution was examined immediately by IR and NMR. IR: 2087 (N_3), 2245 (CN), 3530, 3360 cm^{-1} (OH). ^{1}H NMR indicated the absence of MeI and the presence of MeN_3 (2.98 ppm) together with an impurity of MeOH (presumably due to residual OH or H_2O on the polymer). ^{13}C NMR showed MeN_3 at 37.85 ppm. Bubbling Ar through the solution removed the volatile MeN_3.[3]

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Registry No. **2**, 107585-03-5; **3**, 107585-04-6; **4**, 125475-81-2; **5**, 125475-82-3; DMAD, 762-42-5; Amberlyte IR-400, 69431-33-0; methyl azide, 624-90-8; azide, 14343-69-2.

Supplementary Material Available: Crystal data for 4 and 5 (14 pages). Ordering information is given on any current masthead page.

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