Novel Products Derived from Unprecedented Transformations of 3,3,3-Trialkynylpropionaldehyde Derivatives

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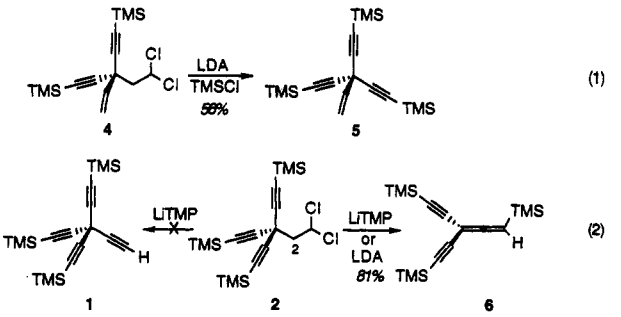
Recent efforts directed toward the synthesis of the trisilylated derivative of tetraethynylmethane (TEM) **1**[1] from trialkynylated precursors bearing either dichloride (e.g., **2**) or α-(phenylthio)hydrazone (e.g., **3**) functionalities were complicated by the failure of precedented alkyne syntheses to deliver the fourth acetylene unit. X-ray structural analysis of **1** (obtained by an alternate route, *vide infra*) revealed that significant geometric distortion accompanied attachment of four alkyne units around a single sp^3 carbon, presumably as a consequence of untoward steric interactions about the molecular core.[1] It is plausible, then, that attempts to convert either dichloride **2** or α-(phenylthio)hydrazone **3** into TEM derivative **1** were compromised by the inherent increase in (steric) strain energy associated with rehybridization of C(2) from sp^3 to sp. Thus, both substrates apparently were diverted down alternate mechanistic pathways which provided polyalkynylated products that are comparably free of steric strain. The unexpected products isolated from dichloride **2** and α-(phenylthio)hydrazone **3** have been characterized, and proposals describing their mechanisms of formation are offered.

The initial attempts to incorporate the final acetylene unit in the polyalkynylmethane targets **1** and **5** focused on base-mediated dehydrohalogenation of the precursor 1,1-dichlorides **2** and **4**, respectively.[3] Thus, treatment of dichloride **4** with LDA furnished the triethynylethenylmethane derivative **5**, presumably via a carbenoid pathway, in 56% yield without event. By analogy, a similar transformation with the trialkynylpropyl dichloride **2** was expected to provide the tetraethynylmethane derivative **1**. However, when dichloride **2** was treated with either LDA or LiTMP at −78 °C, a single product containing two distinct TMS moieties (^1H and ^{13}C NMR) was obtained in 81% yield, ruling out compound **1** as a possible reaction product. The structure of this unexpected species was suggested by its spectral data and later confirmed by X-ray crystallography (Figure 1) to be the remarkable dialkynylated allene **6**.[15] This allene decomposes readily at ambient temperature in $CDCl_3$ solution but can be stored at 0 °C indefinitely.

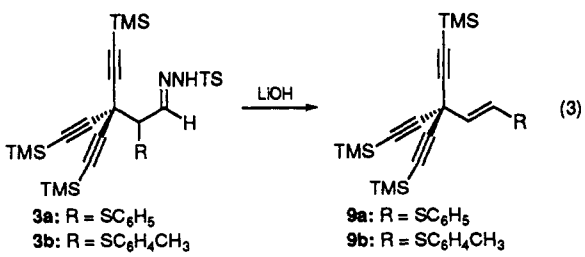
The mechanistic course of this reaction clearly diverges from the precedented pathway operating with dichloride **4**. In general, such dichlorides have been shown to react through initial base-mediated α-elimination of HCl to



generate, via an intermediate carbene, the vinyl chloride, which suffers a subsequent α-elimination of the elements of HCl to furnish a vinylidene carbene[4] and thence the acetylene product through an exceedingly low-energy C–H insertion pathway.[5] However, the formation of allene **6** from dichloride **2** can be rationalized by citing an entirely different course of events, Scheme 1. Thus, formal β-elimination of tris[(trimethylsilyl)alkynyl]methyl anion **8** from the dichloroethane fragment of **2**, followed by protonation at the remote allenic site, may plausibly be responsible for the generation of allene **6**. 1,1-Dichloroethylene (or a 2-carbon fragment derived therefrom) is presumed to account for the remaining carbons of **2**, although we have not detected this volatile species.

That β-elimination of anion **8** competes with α-elimination of Cl^- from intermediate **7** may be attributed to the coincidental convergence of two factors in dichloride **2** that are not present to the same extent in the analogous ethylene species **4**: (1) Some small measure of strain associated with compressing three alkynyl units about a single carbon atom[1] ($C_{sp}{}^3$–$C_{sp}{}^2$ = 1.51 Å, $C_{sp}{}^3$–C_{sp} = 1.45 Å[6]) may elevate the ground state of **2** relative to **4**. Elimination of anion **8** would then contribute to release of this strain. (2) Differential stability of the carbanion **8**, relative to the corresponding (hypothetical) dialkynylethenylmethane anion derived from **4**, may also expedite its ready expulsion. While pK_a's of trialkynylmethanes have not been reported, the pK_a of dialkynylmethanes has been estimated to be ≤ 21.[7]

We next explored the chemistry of α-thioether hydrazones, as described by Shibuya,[8] for installation of the fourth acetylene in this demanding molecular environment. Thus, α-(phenylthio)tosylhydrazone **3a** was treated with LiOH, which surprisingly afforded the vinyl sulfide **9a** in 20% yield. No evidence of alkyne formation was detected. Tetraalkyne **1** was not an intermediate in this transformation, as shown by resubmission experiments. Incor-



poration of the probe nucleophile lithium *p*-thiocresolate in this reaction resulted in the isolation of a 31% yield of a 1:1 mixture of the vinyl sulfides **9a** and **9b**. In control experiments, attempts to add lithium *p*-thiocresolate either to vinyl sulfide **9a** or to phenylthio hydrazone **3a** did not afford the thio exchange products **9b** or **3b**, respectively.

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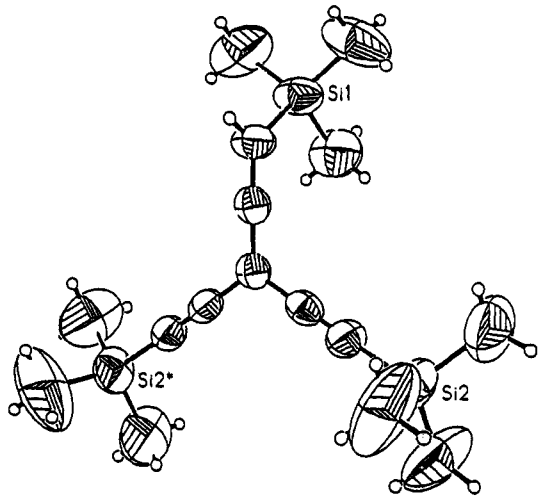
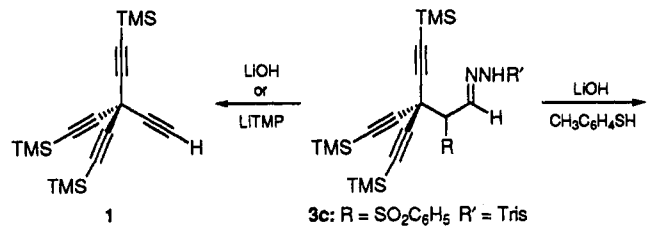
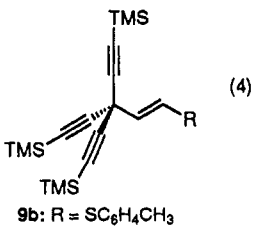


Figure 1. Crystal structure of allene 6.

Incorporation of cyclohexene in the reaction mixture as a carbene trap led to a 23% yield of vinyl sulfide **9a**, but no cyclohexene adducts were detected. Treatment of hydrazone **3a** with LiTMP under reaction conditions which afford silylated TEM 1 from hydrazone **3c**[1] did not provide the TEM derivative 1.

In a reaction similar to the conversion of sulfide **3a** into vinyl sulfide **9a**, treatment of sulfone **3c** with LiOH led to a 66% yield of silylated TEM 1.[9] Addition of cyclohexene to the reaction media did not alter this transformation's course—no cyclohexene–carbene adducts were isolated.[10] The presence of 1 equiv of lithium *p*-thiocresolate in the reaction solution along with hydrazone **3c** and LiTMP led to the isolation of a 7:1 mixture of TEM derivative 1 and vinyl sulfide **9b** in a combined 18% yield, while addition of an excess of lithium *p*-thiocresolate (5 equiv) provided solely the vinyl sulfide **9b** in 38% yield.

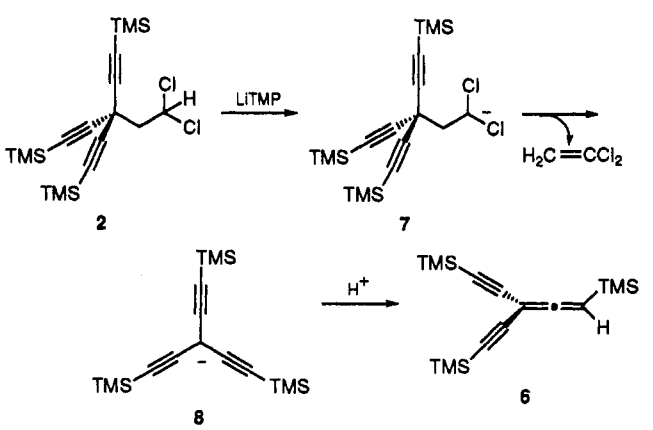




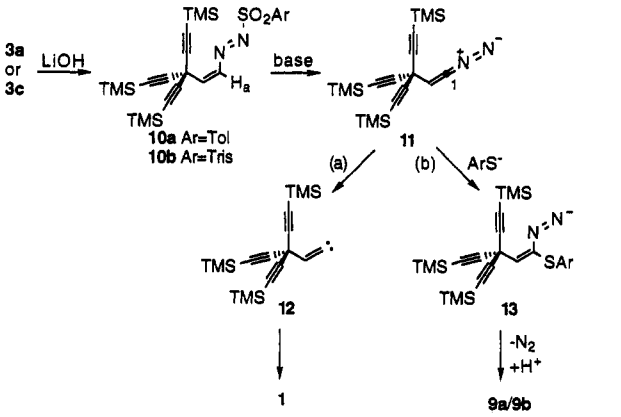
(4)

A hypothesis which accounts for these diverse observations is shown in Scheme 2. The formation of vinyl sulfide **9b** from hydrazone **3a**, coupled with the failure to exchange thiocresol into **3a**, dismisses the possibility of an intramolecular rearrangement. The isolation of vinyl sulfide **9b** along with tetraalkyne 1 from base treatment of **3c** with $LiSC_6H_4CH_3$ present raises the possibility that these reactions proceed through a common intermediate.

Scheme 1



Scheme 2



At present, we speculate that initial elimination of sulfide/sulfinate anion from **3a**/**3c** furnishes vinyl aryl azosulfonates **10a**/**10b**. Subsequent α-hydrogen abstraction (H_a) followed by the elimination of arylsulfinate anion delivers the putative common intermediate 1-diazoethene **11**.[4,11] Two mechanistic pathways are available to intermediate 11: (a) loss of N_2 to provide the transient vinylidene carbene which undergoes facile rearrangement to deliver silylated TEM 1 or (b) addition of a thiolate nucleophile to C(1)[12] followed by the elimination of N_2 and protonation of the intermediate vinyl anion to provide the vinyl sulfide derivatives **9a**/**9b**. The decreased nucleophilicity of sulfinate anion compared with sulfide anion plausibly suppresses the trapping of diazoethene 11 with the former species, and thus, only the product of pathway a, 1, is formed from **3c**.

The incorporation of the fourth acetylene into the sterically hindered environment of 1 proved to be a greater challenge than expected. Two well-documented procedures failed to give the expected alkyne product but rather furnished unusual products through novel mechanisms. In general, the transformations described herein appear to afford products consistent with mechanistic pathways that alleviate steric strain in the molecule.

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(9) LiTMP and LiOH can be used with equal success to convert hydrazone **3c** into TEM derivative 1, as identical 66% yields are observed with either base.
(10) LiTMP was used as the base in this reaction.
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Experimental Section

All reagents were obtained from the Aldrich Chemical Co. (Milwaukee, WI) unless otherwise stated. Et_2O and THF were purified by distillation from sodium/benzophenone ketyl under nitrogen. CH_2Cl_2, cyclohexene, and 2,3-dihydropyran were distilled from CaH_2 under N_2. Solvents for flash chromatography[13] (silica gel adsorbant, Et_2O, and hexane) were distilled from CaH_2 prior to use. Moisture- and oxygen-sensitive reactions were carried out in predried glassware under Ar.

Analytical TLC was performed using precoated silica gel (60 F_{254}) plates (E. Merck). The purity of all title compounds was judged to be ≥90% by ^1H and ^{13}C NMR determinations (see the supplementary material).

1,1-Dichloro-3-ethenyl-5-(trimethylsilyl)-3-[(trimethylsilyl)ethynyl]pent-4-yne (4). PCl_5 (281 mg, 1.35 mmol, 2.0 equiv) was added in one portion to a stirring solution of 3-ethenyl-5-(trimethylsilyl)-3-[(trimethylsilyl)ethynyl]pent-4-ynal[14] (184 mg, 0.67 mmol) in 5 mL of CH_2Cl_2 at −78 °C. After 5 min, TLC analysis indicated that aldehyde was consumed. The reaction solution was poured into 50 mL of Et_2O and 50 mL of ice-cold saturated $NaHCO_3$ solution, the aqueous phase was extracted with 2 × 25 mL of Et_2O, and the combined organic phases were washed with brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography with hexane as eluent to afford 91 mg (41%) of dichloride **4** as a colorless oil: IR (CCl_4) 2140 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.97 (t, 1H, J = 5.6 Hz), 5.80 (dd, J = 16.6, 9.4 Hz, 1H), 5.61 (dd, J = 16.7, 0.6 Hz, 1H), 5.22 (dd, J = 9.4, 0.8 Hz, 1H), 2.69 (d, J = 5.8 Hz, 2H), 0.18 (s, 18 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 137.3, 115.9, 102.4, 89.9, 69.5, 54.9, 38.5, −0.21; MS m/z (relative intensity) 332 (.6), 330 (1), 253 (6); HRMS calcd for $C_{15}H_{24}Cl_2Si_2$ 330.0794, found 330.0781.

3,3-Bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl)pent-1-en-4-yne (5). A solution of dichloride **4** (120 mg, 0.36 mmol) in 2 mL of THF was added dropwise to a stirring solution of LDA (prepared from i-Pr_2NH (251 μL, 1.8 mmol, 5 equiv) and n-BuLi (691 μL of a 2.5M solution in hexane, 1.7 mmol, 4.8 equiv)) in 15 mL of THF at −78 °C, leading to a pink solution. The solution was warmed to −35 °C for 1 h (yellow-brown solution), at which time TMSCl (188 μL, 1.44 mmol, 4 equiv) was added. After 10 min, the now light yellow solution was poured into 25 mL of hexane and 25 mL of ice-cold 1 M H_3PO_4. The aqueous layer was washed with 2 × 25 mL of hexane, and the combined organic phases were washed with brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography with hexane as eluent to furnish 67 mg (56%) of alkene **5** as a white crystalline solid: mp 57–58 °C; IR (CCl_4) 2164 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.93 (dd, J = 16.5, 9.5 Hz, 1H), 5.66 (d, J = 16.5 Hz, 1H), 5.22 (d, J = 9.5 Hz, 1H), 0.19 (s, 27H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 136.1, 114.7, 100.9, 87.2, 33.3, −0.33; MS m/z (relative intensity) 330 (15), 315(21); HRMS calcd for $C_{18}H_{30}Si_3$ 330.1655, found 330.1673.

3,3-Bis[(trimethylsilyl)ethynyl]-1,1-dichloro-5-(trimethylsilyl)pent-4-yne (2). PCl_5 (810 mg, 3.9 mmol, 2.0 equiv) was added in one portion to a stirring solution of 3,3-bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl)pent-4-ynal[1] (674 mg, 1.95 mmol) in 100 mL of CH_2Cl_2 at −78 °C. After 30 min, TLC analysis revealed that the starting aldehyde was gone, and so the reaction solution was poured into 50 mL of Et_2O and 50 mL of ice-cold saturated $NaHCO_3$ solution, and the aqueous phase was extracted with 2 × 20 mL of Et_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, concentrated in vacuo, and the residue was purified by flash chromatography with hexane as eluent to yield 457 mg (63%) of dichloride **2** as a white crystalline solid: mp 57–59 °C; IR (CCl_4) 2123 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.03 (t, J = 5.7 Hz, 1H), 2.89 (d, J = 5.8 Hz, 2H), 0.18 (s, 27H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 100.7, 87.7, 69.0, 55.3, 29.2, −0.42; MS m/z (relative intensity) 404(3), 403 (2), 402 (6), 401 (4), 400 (7), 323 (10); HRMS calcd for $C_{18}H_{30}Cl_2Si_2$ 400.1032, found 400.1043.

3-[(Trimethylsilyl)ethynyl]-5-(trimethylsilyl)penta-1,2-dien-4-yne (6). A solution of dichloride **4** (147 mg, 0.36 mmol) in 2.5 mL of THF was added dropwise to a stirring solution of LDA (prepared from diisopropylamine (0.176 mL, 1.26 mmol, 3.5 equiv) and 2.5 M BuLi in hexane (0.464 mL, 1.16 mmol, 3.3 equiv)) in 5.0 mL of THF at −78 °C. After 2 min, a precipitate had formed, and the reaction was poured into 10 mL of ice-cold 1 M H_3PO_4 and 10 mL of hexane. The aqueous phase was washed with 3 × 10 mL of hexane. The combined organics were washed with 10 mL of brine, dried over Na_2SO_4, filtered, and concentrated in vacuo, and the resulting yellow oil was purified by flash chromatography with pentane as eluent to afford 90 mg (81%) of allene **6** as off-white crystals: mp 136–138 °C; IR (CCl_4) 2961, 2153, 1913, 1602 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 5.16 (s, 1H), 0.65 (s, 18H), −0.05 (s, 9H); ^{13}C NMR (90 MHz, C_6D_6) δ 220.3, 97.6, 96.8, 88.3, 72.2, −0.19, −1.2; MS m/z (relative intensity) 304 (44), 289 (9), 231 (2), 216 (100); HRMS calcd for $C_{16}H_{28}Si_3$ 304.1499, found 304.1476.

2-(Phenylthio)-3,3-bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl)pent-4-ynal, (Toluenesulfonyl)hydrazone (3a). 2-(Phenylthio)-3,3-bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl-)pent-4-ynal[1] (0.5 g, 1.1 mmol) and tosylhydrazide (0.2 g, 1.1 mmol) were dissolved in a minimum amount of CH_3CN. One drop of concd HCl was added and this solution was stirred at ambient temperature for 16 h. The reaction was concentrated in vacuo and the residue was purified by flash chromatography using 10% Et_2O/hexane as eluent to furnish tosylhydrazone **3** (0.42 g, 84%) as a beige solid: mp 64–66 °C; IR (CCl_4) 2170 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.73 (d, J = 8.3 Hz, 1H), 7.21 (m, 9H), 3.92 (d, J = 8.7 Hz, 1H), 2.42 (s, 3H), 0.16 (s, 27H); ^{13}C NMR (50 MHz) δ 146.7, 143.9, 135.6, 133.8, 133.1, 129.7, 128.9, 127.9, 127.8, 99.6, 88.9, 61.8, 34.6, 21.6, −0.49; MS m/z (relative intensity) 622 (0.5), 607 (2), 513 (6), 466 (5).

1-(Phenylthio)-3,3-bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl)pent-1-en-4-yne (9a). A solution of **3a** (48 mg, 0.08 mmol) in 0.25 mL of Et_2O was added dropwise to a suspension of $LiOH·H_2O$ (20 mg, 0.48 mmol, 6 equiv) in 1.0 mL of Et_2O. After being stirred at room temperature for 36 h, the reaction solution was diluted with 10 mL of Et_2O, washed successively with 3 × 5 mL of H_2O and once with 5 mL of brine, dried over Na_2SO_4, filtered, and concentrated. The crude yellow oil was purified by flash chromatography with 2% CH_2Cl_2/hexane as eluent to afford 8 mg (24%) of **9a** as a white solid: mp 94–96 °C; IR (CCl_4) 2173, 1602 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5H), 6.86 (d, J = 14.9 Hz, 1H), 5.81 (d, J = 14.7 Hz, 1H), 0.18 (s, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.7, 129.8, 129.1, 128.0, 127.0, 125.9, 100.5, 87.4, 29.7, −0.36; CIMS m/z (relative intensity) 439 (1), 423 (1), 361 (4), 329 (16); HRMS calcd for $C_{24}H_{34}SSi_3$ 438.1689, found 438.1659.

1-(Tolylthio)-3,3-bis[(trimethylsilyl)ethynyl]-5-(trimethylsilyl)pent-1-en-4-yne (9b). A solution of **3a** (75 mg, 0.12 mmol) in 0.25 mL of Et_2O was added dropwise to a stirring solution of *p*-thiocresol (15 mg, 0.12 mmol, 1 equiv) and $LiOH·H_2O$ (35 mg, 0.8 mmol, 7 equiv) in 1.0 mL of Et_2O. After 36 h at ambient temperature the reaction was diluted with 10 mL of Et_2O, washed with 5 mL of H_2O and then brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting yellow oil was purified by flash chromatography with 25% CH_2Cl_2/hexane as eluent to furnish 14 mg (31%) of a 1:1 mixture of **9a**:**9b**. **9b**: ^1H NMR (360 MHz, $CDCl_3$) δ 7.27 (m, 4H), 6.82 (d, J = 14.7 Hz, 1H), 5.71 (d, J = 14.7 Hz, 1H), 2.34 (s, 3H), 0.17 (s, 27H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 137.3, 130.6, 130.5, 129.9, 127.0, 126.6, 100.7, 87.3, 32.9, 1.1, −.034; CIMS m/z (relative intensity) 453 (2), 361 (0.8), 329 (5).

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra for **2**, **3a**, **4**–**9a**, and **9b** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) Details for the synthesis of the aldehyde will be reported elsewhere.
(15) The authors have deposited atomic coordinates for **6** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.