Propynal Equivalents and Diazopropyne: Synthesis of All Mono-^{13}C Isotopomers

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Mechanistic and spectroscopic investigations of reactive C_3H_2 hydrocarbons necessitated the preparation of diazopropyne isotopomers bearing mono-^{13}C substitution at each of the three unique positions. The diazo compounds and their tosylhydrazone precursors were prepared from the mono-^{13}C isotopomers of propynal (in the form of either the aldehyde or the diethyl acetal). The introduction of ^{13}C-labeling at either alkyne position in propynal utilized the *Corey–Fuchs* procedure for chain homologation.

Introduction. – Our studies of the family of C_3H_2 hydrocarbons stem from an interest in fundamental issues of structure and bonding, as well as an interest in the harsh chemical environments in which these species are known to exist. C_3H_2 Isomers represent important chemical intermediates in the reaction of atomic carbon with acetylene [1][2], the combustion of fuel-rich hydrocarbon flames [3][4], the chemistry of interstellar space [5–7], and the atmospheric chemistry of Titan [8], the largest moon of Saturn. Substituted propynylidene (propargylene) derivatives also find use as ligands in organometallic chemistry [9][10], where these complexes exhibit interesting reactivity that has been exploited in organic synthesis [11][12]. Our investigations of the photochemistry and spectroscopy of C_3H_2 isomers rely heavily on the study of isotopically-labeled derivatives (^{13}C, ^{2}H) [13–16]. These investigations necessitated the preparation of diazopropyne, a photochemical precursor to the C_3H_2 isomers, bearing a mono-^{13}C label at each of the three unique positions. This requirement, in turn, necessitated the preparation of each of the mono-^{13}C isotopomers of propynal (in the form of either the aldehyde or the diethyl acetal). The synthetic procedures for the preparation of propargyl derivatives with mono-^{13}C labeling at each position may be of some general interest and utility. In the current article, we describe the syntheses of ^{13}C and ^{2}H isotopomers of propynal and diazopropyne.

Results and Discussion. – The basic synthetic strategy for the preparation of diazopropyne involves the preparation of a propargyl derivative at the oxidation state of an aldehyde, followed by conversion to the tosylhydrazone and generation of the diazo compound (*Scheme 1*). This general approach becomes subtly complicated by

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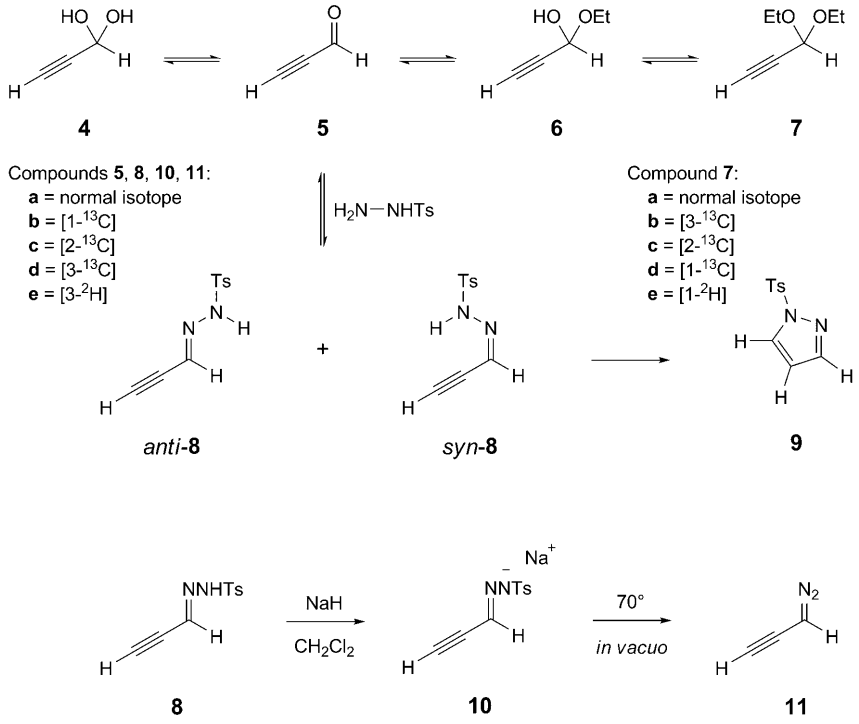
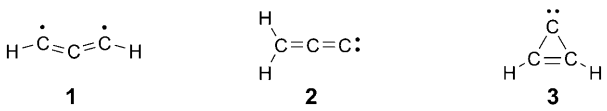
Scheme 1



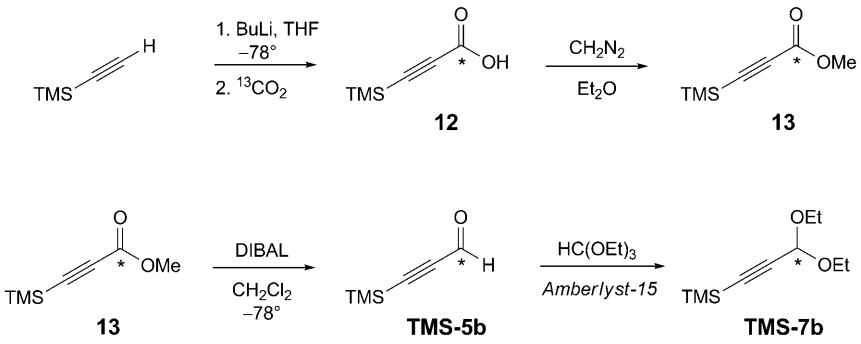
virtue of *i*) equilibration of aldehyde, aldehyde hydrate, hemiacetal, and acetal, *ii*) *syn*/*anti* isomerism in the tosylhydrazone, and *iii*) the propensity of the *syn*-tosylhydrazone to cyclize to the pyrazole.

Our strategy for investigation of the structure of triplet propynylidene (**1**) relied on the introduction of a ^{13}C-label into each of the three different positions in diazopropyne (**11**). Methods for incorporation of ^{13}C are limited by the availability and cost of the ^{13}C source. These two factors necessitated the design of unique syntheses for the propynal tosylhydrazones **8b**–**8d**, the immediate precursors to **11b**–**11d**. The synthesis of unlabeled **8a** is succinct: oxidation of propargyl alcohol to propynal by CrO_3 and reaction of propynal with NH_2NHTs. The first reaction, however, proceeds in poor yield (10–25%), and propynal itself is rather unstable. Therefore, the propynal diethyl acetal (**7**) was chosen as a more desirable target in the synthesis of the ^{13}C-labeled species **8b**–**8d**.



The synthesis of [1-^{13}C]propynal tosylhydrazone (**8b**) is conceptually straightforward. Reaction of lithium (trimethylsilyl)acetylide with $^{13}CO_2$, generated upon treatment of $Ba^{13}CO_3$ with H_2SO_4 [17], incorporated the ^{13}C-label at the appropriate position early in the synthetic sequence, giving the carboxylic acid **12** (*Scheme 2*).

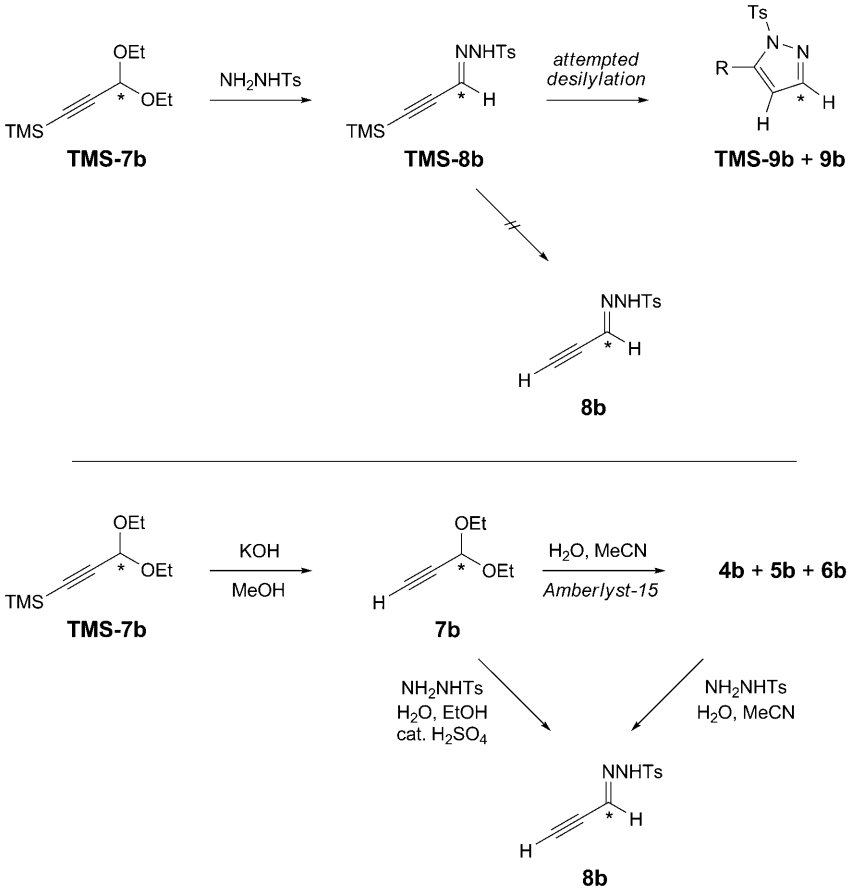
Scheme 2



Transformation of **12** to the methyl ester **13** was effected utilizing CH_2N_2; subsequent diisobutylaluminum hydride (DIBAL) reduction of **13** gave the aldehyde **TMS-5b**. Protection of the aldehyde as its diethyl acetal **TMS-7b** followed. Conversion of **TMS-7b** to 3-(trimethylsilyl)propynal tosylhydrazone (**TMS-8b**) was facile (*Scheme 3*); each attempt at formation of **8b** by desilylation of **TMS-8b**, however, resulted in formation of the cyclized products, 1-tosyl-1*H*-pyrazole (**9b**) and 5-(trimethylsilyl)-1-tosyl-1*H*-pyrazole (**TMS-9b**), in varying ratios. (Unsuccessful attempts included: Bu_4NF [18], $AgNO_3$/KCN [19], KOH in MeOH [20][21], and $Na_2B_4O_7 \cdot 10\ H_2O$ (Borax) in MeOH [22].) Thus, desilylation needed to be executed prior to tosylhydrazone formation. Desilylation of acetal **TMS-7b** with KOH in MeOH afforded acetal **7b**. Condensation of NH_2NHTs with [1-^{13}C]propynal, generated *in situ* from **7b** by acid catalysis, gave the tosylhydrazone *anti*-**8b**, albeit in modest yield (15–35%) and accompanied by formation of pyrazole **9b**. An alternative method for tosylhydrazone formation involves a two-step procedure [23]. Hydrolysis of acetal **7b**, using a heterogeneous acid catalyst, *Amberlyst-15*, in aqueous MeCN, generated an equilibrating mixture of aldehyde hydrate **4b**, aldehyde **5b**, and hemiacetal **6b** (*Scheme 3*). Addition of *p*-toluenesulfonohydrazide afforded tosylhydrazone **8b** in *ca.* 50% yield as a 3 : 1 mixture *anti*/*syn*. Mechanistic details of the hydrolysis are described below.

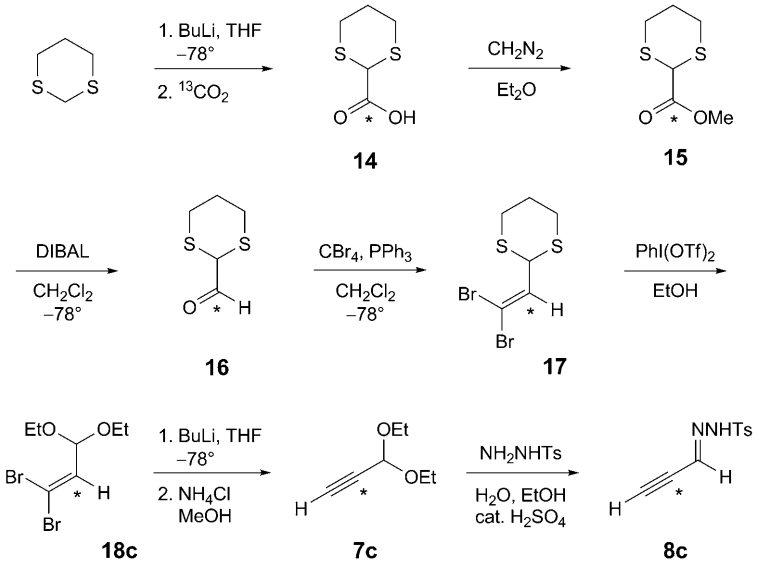
The synthesis of [2-^{13}C]propynal tosylhydrazone (**8c**) presented a greater synthetic challenge; the placement of the label at C(2) necessitated construction of the carbon skeleton one atom at a time (*Scheme 4*). 1,3-Dithiane was a useful starting point, because it serves as a masked carbonyl group and can be utilized for 'umpolung' [24][25]. This reactivity reversal provided the means for incorporation of the ^{13}C label. Nucleophilic reaction of 2-lithio-1,3-dithiane with $^{13}CO_2$ (from reaction of $Ba^{13}CO_3$ with H_2SO_4) gave the acid **14**. Conversion to aldehyde **16** through the ester **15** followed easily. One-carbon homologation of **16** to the olefin **17** was more difficult than

Scheme 3



anticipated, giving 20–30% yields. The literature includes few applications of the *McKelvie–Corey* olefination methodology [26][27] to S-containing molecules, and, to our knowledge, none with dithianes. Under the *McKelvie–Corey* conditions, Ph_3PBr_2 is generated in addition to the desired ylide $Ph_3P{=}CBr_2$ [26]. This contaminant can cause side reactions due to its strong electrophilicity and brominating ability [28]. This does not appear to be the cause of the low yields, however. Generation of the ylide $Ph_3P{=}CBr_2$ by reaction of Ph_3P with CBr_2 (from $CHBr_3$ and ^{t}BuOK) [29], which produces no attendant Ph_3PBr_2 [30], also results in only 25% yield of **17**. The use of Et_3N under otherwise typical *McKelvie–Corey* conditions has been found to suppress side reactions as well [28][30], but this variation was ineffective for us. The relatively high acidity of the α-H-atom in aldehyde **16** due to the neighboring dithiane functionality may perhaps be the cause of the difficulty. Conversion of the dithiane **17** to the diethyl acetal **18c** with $PhI(OTf)_2$ in anhydrous EtOH proceeded well. Treatment of **18c** with BuLi afforded 1,1-diethoxypropyne (**7c**), which was converted to the desired tosylhydrazone **8c**.

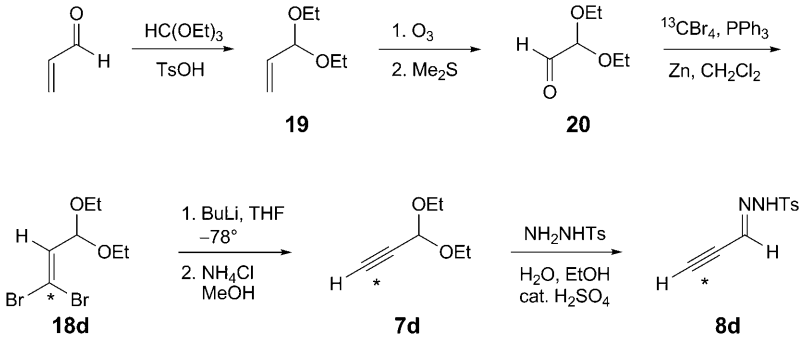
Scheme 4



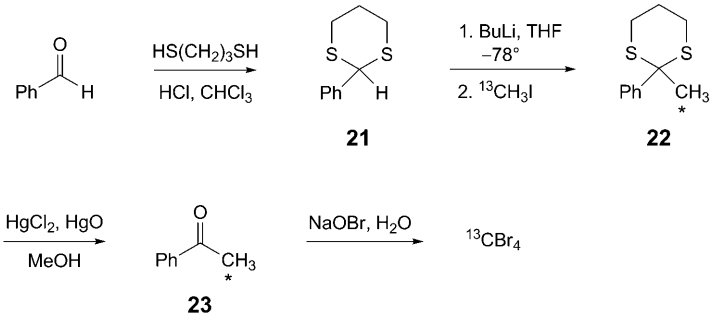
The synthesis of [3-^{13}C]propynal tosylhydrazone (**8d**) is presented in *Scheme 5*. The *Corey – Fuchs* chain-homologation procedure [27] is well-suited for incorporating ^{13}C at the terminal alkyne position [31], given the availability of isotopically labeled $^{13}CBr_4$ (*Scheme 6*) [32]. Thus, reaction of propenal with $HC(OEt)_3$, followed by ozonolysis of olefin **19**, produces 1,1-diethoxyacetaldehyde (**20**). Application of the *Corey – Fuchs* procedure to aldehyde **20** gave the isotopically-labeled dibromoalkene **18d**. Alkene **18d** was converted to tosylhydrazone **8d** in the same manner as described earlier for alkene **18c** (*Scheme 4*).

The synthesis of [3-$^{2}H_1$]propynal tosylhydrazone (**8e**) is shown in *Scheme 7*. Simple deprotonation of unlabeled **8a** with 2 equiv. of base, followed by addition of D_2O, did

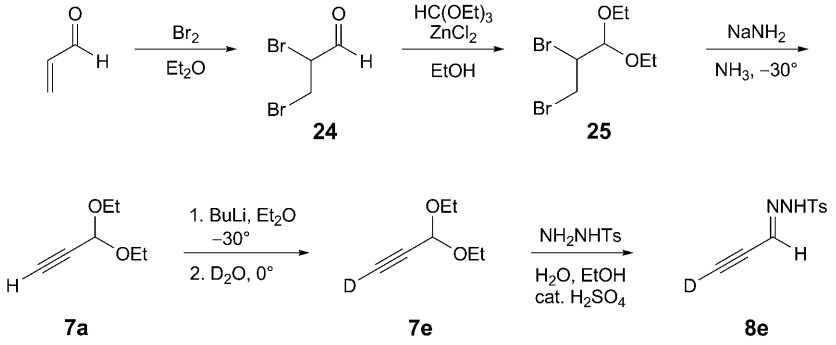
Scheme 5



Scheme 6



Scheme 7



not afford **8e** in a suitable yield. An alternative pathway to tosylhydrazone **8e** proceeds through 3,3-diethoxypropyne (**7a**). Acetal **7a** was obtained from propenal by *i*) bromination to give dibromoaldehyde **24**, *ii*) acetalization to give dibromoacetal **25**, and *iii*) double dehydrohalogenation to give acetal **7a**. (The procedure of *Dehmlow* and *Lissel* may be superior for the preparation of **7a** [33].) Mono-deuteriation of alkyne **7a** to give **7e** was accomplished by treatment with BuLi, followed by D_2O quenching. Acid-catalyzed transformation of **7e** to tosylhydrazone **8e** resulted in a 5% loss of deuterium in the *anti*-isomer of **8e** and a 25% loss in the *syn*-isomer.

Acetal Hydrolysis and Tosylhydrazone Formation. Condensation of propynal (**5a**) and *p*-toluenesulfonohydrazide, under neutral conditions in EtOH at 0°, provides tosylhydrazone **8a** in acceptable yield (>60%). This procedure represents a viable synthesis for unlabeled **8a** only because the preparation of propynal involves *i*) an inexpensive precursor (propargyl alcohol) and *ii*) a procedure that, although cumbersome, can be run on a large scale to compensate for the relatively poor yield. Neither circumstance, however, pertains to the synthesis of isotopically labeled propynal. The acetal derivatives proved to be robust in surviving the strongly basic conditions employed for a variety of steps during the syntheses of isotopically labeled compounds, but the requirement for acid catalysis to hydrolyze the acetal complicated the formation (and isolation) of the tosylhydrazone.

Treatment of propynal diethyl acetal (**7**) with catalytic H_2SO_4 and *p*-toluenesulfonohydrazide in aqueous EtOH provides a rapid preparation of tosylhydrazone **8**. Under the condition of acid catalysis, the crude product mixture typically contains a 1:2 mixture of tosylhydrazone isomers (*anti*-**8**/*syn*-**8**), along with 1-tosyl-1*H*-pyrazole (**9**) and excess unreacted tosylhydrazide. Either tosylhydrazone isomer, or a mixture of both, is suitable for preparing diazopropyne (**11**). The crude product, however, is not sufficiently pure to generate the diazo compound. Chromatographic separation on silica gel affords the *anti*-tosylhydrazone (*anti*-**8**) in *ca.* 20% yield. Unfortunately, the *syn*-tosylhydrazone, *syn*-**8**, cyclizes to pyrazole **9** on the column; these species co-elute and are inseparable.

Our strategy for optimizing tosylhydrazone formation involved separating the steps of acetal hydrolysis (requiring acid catalysis) and tosylhydrazone formation (best performed under neutral conditions). *Amberlyst-15* serves as a heterogeneous catalyst for acetal hydrolysis; after generating propynal, *in situ*, the catalyst is removed by filtration prior to the addition of *p*-toluenesulfonohydrazide. The hydrolysis of propynal diethyl acetal (**7a**), catalyzed by *Amberlyst-15* in 10% aqueous CD_3CN, was monitored by ^{1}H-NMR spectroscopy (*Fig.*). Although the reaction is slow, a high conversion (*ca.* 85%) of acetal **7a** is achieved. Removal of the heterogeneous catalyst by filtration provides an acid-free solution of propynal (**5a**), hemiacetal **6a**, and aldehyde hydrate **4a**. Addition of *p*-toluenesulfonohydrazide drives this equilibrating mixture to the formation of tosylhydrazone **8a** (3:1 ratio of *anti*-**8a** to *syn*-**8a**; 50% yield). This procedure, which eliminates the use of H_2SO_4, affords a much cleaner product and minimizes the complications that may arise from predominant formation of the *syn*-tosylhydrazone isomer. If the stoichiometry of the reaction is carefully

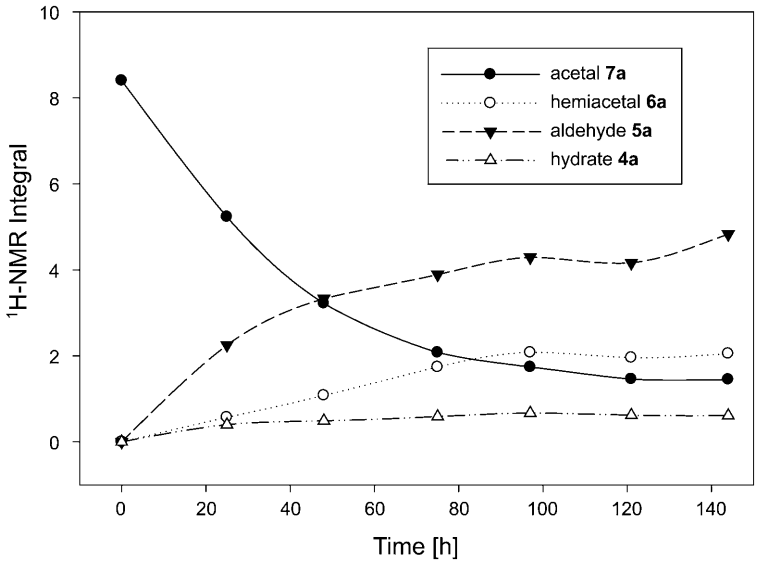


Figure. *Time course for the hydrolysis of prop-1-ynal diethyl acetal* (**7a**), *catalyzed by* Amberlyst-15 *in 10% aq.* CD_3CN *at 25°*

controlled, such that no excess *p*-toluenesulfonohydrazide remains, the mixture of *anti*- and *syn*-**8** obtained by this method may be used in the generation of diazopropyne **11** without further purification.

Conclusions. – Syntheses for each of the mono-^{13}C isotopomers of propynal acetals and tosylhydrazones, along with the corresponding diazo compounds, have been achieved. The availability of these isotopomers enables detailed mechanistic and spectroscopic studies in organic chemistry.

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Experimental Part

Caution! *Propynal* (**5**) *is a lachrymator* [34]. *Due to the possibility of explosive polymerization, propynal* (**5**) *was kept at or below 0° and used within an hour of its isolation. It is not recommended to store propynal* (**5**) *as a neat sample* [35].

Caution! *Diazo compounds, including* CH_2N_2 [36–39] *and diazopropyne* (**11**) [40], *are highly reactive and often explosive. Appropriate safety precautions must be observed.*

General. CH_2Cl_2 was freshly distilled from CaH_2. THF and Et_2O were freshly distilled first from CaH_2 and then from sodium benzophenone ketyl. Column chromatography (CC) was performed using low N_2 pressure with 230–400-mesh silica gel *60* from *EM Science*. All reactions were run under an atmosphere of dry N_2 unless otherwise specified. M.p.: in open capillaries with a *Thomas-Hoover Unimelt* apparatus; uncorrected. UV/VIS Spectra: *Hitachi U-3210* spectrometer; λ in nm (ε in M^{-1} cm^{-1}). IR Spectra: *Nicolet 740* FTIR instrument (liquid N_2 cooled MCT-B detector); in cm^{-1}. ^{1}H-NMR Spectra: *Bruker WP-200* or a *Bruker WP-300* spectrometer, and ^{13}C-NMR spectra: *Bruker WP-270* (^{1}H: 270 MHz ^{13}C: 68 MHz) or a *Bruker WP-300* (^{1}H: 300 MHz, ^{13}C: 76 MHz) spectrometer; chemical shifts (δ) are reported as ppm downfield from internal Me_4Si, *J* in Hz. MS: *Kratos MS-80RFA* spectrometer (DS55/DS90 detector); in *m*/*z* (rel. int.).

Propynal (**5a**). Propargyl alcohol (*Aldrich*) was oxidized using Cr_2O_3 in H_2O with H_2SO_4 under reduced pressure according to the procedure of *Sauer* [34]. Vacuum distillation (130 Torr) of the crude product afforded **5a**. Colorless liquid (11%). B.p. 35° (130 Torr) ([34]: 54–57° (760 Torr)). IR ($CDCl_3$): 3275*s*, 2882*w*, 2099*s*, 1672*s*, 1390*w*, 1041*w*, 953*m*, 691*w*, 622*w*. ^{1}H-NMR ($CDCl_3$): 9.22 (*s*, 1 H); 3.48 (*s*, 1 H).

Propynal Tosylhydrazone (**8a**). Propynal (**5**; 1.48 g, 27.3 mmol) was added dropwise over 5 min to a magnetically stirred slurry of *p*-toluenesulfonohydrazide (5.09 g, 27.3 mmol; *Aldrich*) in 15 ml of abs. EtOH at 0°. After stirring 5 min at 0°, the product precipitated from soln. as a white solid. The mixture was warmed to r.t. and allowed to stir for an additional 45 min. Compound **8a** was collected by suction filtration, washed with cold 70% aq. EtOH, and used without any further purification (3.75 g, 16.9 mmol, 62%). M.p. 118.5–119° (dec) ([41][3]): 130° (dec.)). IR (CH_2Cl_2): 3298*m*, 3266*w*, 3171*w*, 3066*w*, 2100*w*, 1427*w*, 1362*m*, 1170*s*, 1077*m*, 665*m*, 571*s*, 545*m*. ^{1}H-NMR Analysis established the configuration of the product as *anti*-**8a**. ^{1}H-NMR ($CDCl_3$): 8.28 (br. *s*, 1 H); 7.82 (*m*, 2 H); 7.33 (*m*, 2 H); 6.96 (*d*, *J* = 2, 1 H); 3.16 (*d*, *J* = 2, 1 H); 2.44 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 130.1 (2 C); 129.2; 128.2 (2 C); 82.6; 21.7. ^{13}C-NMR ((D_6)DMSO): 143.8; 135.8; 129.8 (2 C); 129.6; 127.1 (2 C); 85.1; 78.6; 21.0. The relatively low solubility of *anti*-**8a** in $CDCl_3$ precluded the detection of the quaternary C-atoms in the ^{13}C-NMR spectrum. These resonances were readily observed in (D_6)DMSO. MS: 222 (M^+, 7), 155 (38), 140 (16), 139 (52), 92 (45), 91 (100), 89 (13), 77 (17), 69 (12). HR-MS: 222.0456 (M^+, $C_{10}H_{10}N_2O_2S^+$; calc. 222.0463).

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[3]) The cited literature does not specify the composition of the sample (*anti*-**8a**, *syn*-**8a**, or a mixture of both) for which the m.p. (dec. point) was reported.

Slight changes in reaction conditions afforded *syn*-**8a**, rather than *anti*-**8a**. Propynal (**5**; 2.0 g, 37 mmol) was added to a magnetically stirred slurry of *p*-toluenesulfonohydrazide (7.0 g, 38 mmol; *Aldrich*) in 60 ml of abs. EtOH at 25°, and the mixture became homogeneous. After stirring several hours, the product precipitated from soln. as a white solid. Compound **8a** was collected by suction filtration and used without further purification (1.73 g, 7.8 mmol, 21%). ^{1}H-NMR Analysis established the configuration of the product as *syn*-**8a**. ^{1}H-NMR ($CDCl_3$): 8.67 (br. *d*, 1 H); 7.83 (*m*, 2 H); 7.33 (*m*, 2 H); 6.61 (*dd*, *J* = 2, 1, 1 H); 3.77 (*dd*, *J* = 2, 1, 1 H); 2.44 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 144.6 (w); 135.2 (w); 129.8 (2 C); 127.9 (2 C); 124.0; 92.2; 72.2 (w); 21.6.

A control experiment established that the geometric isomers of **8** may be interconverted *via* acid catalysis. Heating a soln. of *anti*-**8a** with catalytic H_2SO_4 in aq. EtOH for 30 min at 45° afforded a 1:1 mixture *anti*-**8a**/*syn*-**8a**.

3-(Trimethylsilyl)[1-^{13}C]propynoic Acid (**12**). *Procedure A*. The procedure for the synthesis of acid **12** is an adaptation of that employed for [1-^{13}C]propynoic acid [13][17]. A flame-dried 250-ml flask possessing a sidearm stopcock was charged with 70 ml of dry THF and equipped with an overhead mechanical stirrer. An aliquot of (trimethylsilyl)acetylene (5.71 ml, 3.97 g, 40.4 mmol; *Aldrich*) was added *via* syringe through a septum on the sidearm. After cooling the soln. to −78°, 19.4 ml of 2.08M BuLi (40.4 mmol; *Aldrich*) were added *via* syringe over 20 min, and the soln. was stirred for 40 min. The sidearm was connected to a vacuum line. The soln. was degassed by subjecting it to two freeze–pump–thaw cycles at −196°. To another port of the vacuum line was connected the following apparatus. On a flask containing $Ba^{13}CO_3$ (8.00 g, 40.4 mmol; *Isotec*) was mounted an addition funnel holding 30 ml of conc. H_2SO_4 with a vacuum adaptor. This apparatus was evacuated concurrently with the other flask after the freeze–pump–thaw cycles. With the TMS-acetylide soln. at −78°, H_2SO_4 was added to the $Ba^{13}CO_3$ with vigorous stirring and heating. $^{13}CO_2$ evolved rapidly and was drawn through the gas manifold into the acetylide soln., cooling the latter to −196° to collect as much $^{13}CO_2$ as possible. The reaction flask was then warmed to −78° and stirred for 90 min. The reaction was quenched by dropwise addition of 50 ml of a sat. NH_4Cl/MeOH soln. at −78° followed by 20 ml of 1M HCl. The soln. was allowed to warm to r.t., and then 150 ml of Et_2O and 70 ml of H_2O were added. After separating the layers, the aq. portion was extracted with Et_2O (2 × 50 ml). The combined org. layers were washed with H_2O and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to yield a viscous, light-brown liquid (1.49 g, 10.4 mmol, 26%). B.p. 95–97°/7 Torr ([42]: 62°/0.2 Torr; unlabeled **12**). IR (film): 3400–2400 (br.), 2178*w*, 1651*s*, 1255*s*, 919*s*, 849*s*, 763*m*. ^{1}H-NMR ($CDCl_3$): 8.09 (br. *s*, 1 H); 0.26 (*s*, 9 H). ^{13}C-NMR ($CDCl_3$): 157.44 (CO_2H).

Procedure B. This procedure incorporates several improvements, relative to *Procedure A*. In *Procedure A*, nucleophilic addition of TMS-acetylide to $^{13}CO_2$ occurred in low yield (26%). Formation of propynoic acid, the desilylated analog of **12**, indicated attack at the TMS group by some species present during the reaction or workup. Removal of NH_4Cl from the quenched soln. dramatically increases the yield (95%) of the reaction. Although subjection to acidic conditions is not a standard method for cleavage of alkyne–Si bonds [43], C–Si bonds have been cleaved at low pH [44]. The acidity of NH_4^+ in the mixture of THF and MeOH found at this stage of the workup is most likely enhanced relative to its acidity in H_2O. This increase in acidity might explain removal of the TMS group by such a weak acid. Another possibility is that Cl^- was responsible for desilylation of the alkyne. Once again, Cl^- is not a standard reagent for cleavage of alkyne–Si bonds, but the poor solvation provided by the mixture of THF and MeOH might have increased the nucleophilicity of Cl^- sufficiently to cause it to attack the silyl group.

It should also be noted that an excess of $Ba^{13}CO_3$, the source of $^{13}CO_2$, was used in the high-yield reactions. This was initially implemented to prevent over-addition of acetylide anion to the initially generated carboxylate. Using excess $Ba^{13}CO_3$ (2 equiv.) in conjunction with NH_4Cl quenching did not, however, increase the yield. The amount of $Ba^{13}CO_3$ in excess was reduced to 1.5 equiv. in later reactions, which used neat MeOH for the quenching, and this caused no reduction in yield. If care is taken to completely trap all of the $^{13}CO_2$ liberated from the $Ba^{13}CO_3$, then a single equivalent of $Ba^{13}CO_3$ should be sufficient and would increase the cost effectiveness of this reaction.

Into a 500-ml flask possessing a stopcock sidearm attached to a N_2/vacuum manifold, $Ba^{13}CO_3$ (8.22 g, 41.5 mmol) was added. To this flask was mounted in order: a 125-ml addition funnel (with

pressure-equalizing sidearm) containing 75 ml of conc. H_2SO_4 and a 100-ml addition funnel filled with *Drierite*® ($CaSO_4$). The top funnel was connected by a rubber hose to a 500-ml three-neck flask containing a stirbar. This flask was also attached to the N_2/vacuum manifold. After evacuating the apparatus, a liquid N_2 bath was placed around the three-neck flask. The H_2SO_4 was then slowly added to the $Ba^{13}CO_3$ resulting in a vigorous reaction releasing $^{13}CO_2$ that solidified in the three-neck flask. As the reaction slowed, the remaining acid was added more rapidly, and the mixture was periodically heated with a heat gun to help drive the reaction to completion. The inlet attached to the three-necked flask was briefly opened to vacuum to pull lingering $^{13}CO_2$ into the cold flask. The apparatus was then vented to dry N_2. Meanwhile, a soln. of TMS-acetylide anion had been prepared by the dropwise addition of 16.4 ml of 2.5M BuLi in hexanes (41 mmol) to a stirred soln. of (trimethylsilyl)acetylene (5.6 ml, 4.0 g, 41 mmol) in 110 ml of dry THF at $-78°$ and under N_2. This soln. was cannula transferred into the liquid N_2 cooled flask where it solidified on top of the $^{13}CO_2$. The liquid N_2 bath was replaced by a dry ice/acetone bath, and after thawing, the mixture was stirred 1 h at $-78°$. The reaction was quenched by the addition of 5 ml of MeOH, followed by 45 ml of 1M HCl. The stirred mixture was allowed to warm to r.t. at which point 90 ml of H_2O and 80 ml of Et_2O were added. The layers were separated, and the aq. layer was extracted with 2×50 ml of Et_2O. The combined org. layers were washed with 50 ml of H_2O and dried ($MgSO_4$). Removal of the solvent by rotary evaporation provided 7.70 g of a colorless oil. Based on ^{1}H-NMR integrations, the oil contained 5.54 g (39 mmol, 95%) of the product **12**, along with THF and BuOH.

Methyl 3-(Trimethylsilyl)[1-^{13}C]propynoate (**13**). Crude **12** (0.7435 g, 5.191 mmol) was dissolved in 30 ml of Et_2O in a CH_2N_2 reactor and cooled to 0°. A soln. of KOH (29.2 g, 521 mmol) in 27 ml of EtOH and 21 ml of H_2O was heated to 60° in the upper chamber of the reactor. To the KOH soln. was added slowly dropwise a soln. of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide ('Diazald'; 1.667 g, 7.78 mmol; *Aldrich*) in Et_2O, over 2.5 h. A yellow soln. of CH_2N_2 in Et_2O distilled into the reaction flask. Additional Et_2O was added to the KOH soln. to flush all CH_2N_2 into the reaction flask, until TLC showed that no **12** remained. The Et_2O soln. containing the ester product was dried (Na_2SO_4). The solvent was removed *in vacuo* at $-23°$. The reaction was repeated with 0.786 g (54.9 mmol) of **12**, and the products were combined. Crude **13** was purified by CC (SiO_2; CH_2Cl_2) to yield 1.286 g (8.20 mmol, 77%). IR (film): 2960*m*, 2902*w*, 2173*w*, 1677*s*, 1433*m*, 1254*m*, 1211*s*, 882*s*, 849*s*. ^{1}H-NMR ($CDCl_3$): 3.78 (*d*, $^3J(^{13}C,H) = 4.2$, 3 H); 0.25 (*s*, 9 H).

3-(Trimethylsilyl)[1-^{13}C]propynal (**TMS-5b**). The conversion of **13** to **TMS-5b** is an adaptation of two diisobutylaluminum hydride (DIBAL) reductions of esters from the literature [45–47]. To a soln. containing 1.29 g (8.18 mmol) of **13** in 60 ml of dry CH_2Cl_2 at $-78°$ was added 9.0 ml of a $-78°$ soln. of 1.0M DIBAL (9.0 mmol; *Aldrich*) in hexanes *via* cannula. The soln. was stirred for 2.3 h, and the reaction was quenched by dropwise addition of 20 ml of sat. NH_4Cl/MeOH over 35 min. After stirring at $-78°$ for another 30 min, 20 ml of 1M HCl were added, and the flask was warmed to 20°. The mixture was extracted with CH_2Cl_2 (2×20 ml). The combined org. layers were washed with aq. $NaHCO_3$, aq. NaCl, and H_2O, and dried (Na_2SO_4). Removal of solvent by rotary evaporation afforded 0.613 g (5.89 mmol, 72%) of **TMS-5b**. Clear, colorless oil. IR (film): 2962*m*, 2903*w*, 2727*w*, 2154*w*, 1632*s*, 1253*m*, 1090*m*, 985*m*, 847*s*, 763*m*. ^{1}H-NMR ($CDCl_3$): 9.16 (*d*, $^1J(^{13}C,H) = 193$, 1 H); 0.26 (*s*, 9 H).

3,3-Diethoxy-1-(trimethylsilyl)[3-^{13}C]propyne (**TMS-7b**). A mixture of aldehyde **TMS-5b** (0.613 g, 5.89 mmol), $HC(OEt)_3$ (4.70 ml, 4.19 g, 28.3 mmol), and *Amberlyst-15* [48] (0.0793 g) was stirred at 0° for 2.3 h, until TLC indicated the absence of any unreacted **TMS-5b**. The mixture was filtered, and $HC(OEt)_3$ was removed by rotary evaporation, yielding crude **TMS-7b**. Purification was accomplished by flash CC (SiO_2; CH_2Cl_2 or 5% AcOEt/hexanes), affording **TMS-7b** (0.782 g, 3.88 mmol, 66%). Clear, colorless liquid. IR (film): 2977*m*, 2932*w*, 2885*w*, 2183*w*, 1321*m*, 1251*m*, 1089*s*, 1053*s*, 1028*m*, 997*m*, 855*s*, 846*s*, 761*m*. ^{1}H-NMR ($CDCl_3$): 5.25 (*d*, $^1J(^{13}C,H) = 168$, 1 H); 3.76 (*dqd*, *AB* of ABX_3, $J = 9.5, 7.2, 3, 2$ H); 3.60 (*dqd*, *AB* of ABX_3, $J = 9.5, 7.2, 3, 2$ H); 1.24 (*t*, X_3 of ABX_3, $J = 7.2$, 6 H); 0.19 (*s*, 9 H). ^{13}C-NMR ($CDCl_3$): 92.0 ($HC(OEt)_2$).

3,3-Diethoxy[3-^{13}C]propyne (**7b**). A soln. of **TMS-7b** (0.782 g, 3.88 mmol) in 0.1M KOH in 95% MeOH (10 ml) was stirred for 20 min at 20°. The soln. was diluted with 10 ml of H_2O and 10 ml of CH_2Cl_2, and the layers were separated. The aq. layer was extracted with CH_2Cl_2 (3×6 ml), and the combined org. layers were washed with H_2O (2×10 ml) and dried (Na_2SO_4). Rotary evaporation of

solvent yielded **7b** (0.406 g, 3.17 mmol, 82%). Clear, colorless liquid. IR (film): 3280*m*, 2979*m*, 2934*m*, 2888*m*, 2124*w*, 1323*m*, 1113*s*, 1091*s*, 1052*s*, 999*s*, 953*w*. ^{1}H-NMR ($CDCl_3$): 5.27 (*dd*, $^1J(^{13}C,H) = 168$, $^4J(H,H) = 1.9$, 1 H); 3.75 (*dqd*, *AB* of ABX_3, $J = 9.5, 7.2, 3, 2$ H); 3.59 (*dqd*, *AB* of ABX_3, $J = 9.5, 7.2, 3, 2$ H); 2.55 (*dd*, $^3J(^{13}C,H) = 3.9$, $^4J(H,H) = 1.9$, 1 H); 1.25 (*t*, X_3 of ABX_3, $J = 7.0$, 6 H). ^{13}C-NMR ($CDCl_3$): 92.0 ($H^{13}C(OEt)_2$).

[1-^{13}C]Propynal Tosylhydrazone (**8b**). *Procedure A*. Acid-catalyzed conversion of acetal **7b** to **8b** employs a method similar to that set forth by *Kirmse* and *Engelmann* [49]. To a slurry of *p*-toluenesulfonohydrazide (0.589 g, 3.17 mmol; *Aldrich*) in H_2O (2.8 ml), H_2SO_4 (0.2 ml), and EtOH (0.7 ml) was added quickly **7b**. The slurry became a homogeneous soln. in 5 min. The temp. was raised to 45°, and stirring was effected for 1.4 h. A tan precipitate formed as the temp. was lowered to 0°. The mixture was treated with 6 ml of CH_2Cl_2, and the layers were separated. The aq. layer was extracted with CH_2Cl_2 (3×4 ml). The combined org. layers were washed with 5% aq. $NaHCO_3$ (3×10 ml), aq. NaCl (2×9 ml), and H_2O (2×7 ml). The aq. layers were back-extracted with CH_2Cl_2. The org. layers were dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The aq. layer was neutralized to pH 7 and re-extracted with CH_2Cl_2, yielding additional product. NMR Spectra indicated the presence of two isomers of **8b** and a cyclized isomer, *1-tosyl-1*H-*[3-^{13}C]pyrazole* (**9b**). Flash CC (SiO_2; (AcOEt/CH_2Cl_2 14 : 86) led to isolation of one isomer (**8b**, assigned as the *anti* isomer; 0.286 g, 1.13 mmol, 36%); however, separation of the second isomer (**8b**, assigned as the *syn* isomer) from the pyrazole side-product was unsuccessful.

Data of anti-**8b**. ^{1}H-NMR ($CDCl_3$): 8.14 (br. *d*, $^3J(^{13}C,H) = 5$, NH); 7.83 (*m*, 2 tosyl H); 7.34 (*m*, 2 tosyl H); 6.95 (*ddd*, $^1J(^{13}C,H) = 172$, $^4J(H,H) = 1.9, 0.5$, N=^{13}CH); 3.18 (*dd*, $^3J(^{13}C,H) = 5.0$, $^4J(H,H) = 1.9$, C≡CH); 2.44 (*s*, Me). MS: 223 (M^+, 3), 160 (7), 159 (51), 158 (5), 155 (11), 140 (5), 139 (14), 92 (26), 91 (100). HR-MS: 223.0494 (M^+, $C_9{}^{13}CH_{10}N_2O_2S^+$; calc. 223.0497).

Data of syn-**8b**: ^{1}H-NMR ($CDCl_3$): 8.67 (br. *d*, $^3J(^{13}C,H) = 5$, NH); 7.83 (*m*, 2 tosyl H); 7.34 (*m*, 2 tosyl H); 6.61 (*ddd*, $^1J(^{13}C,H) = 200$, $^4J(H,H) = 1.8, 0.5$, N=^{13}CH); 3.78 (*dd*, $^3J(^{13}C,H) = 4.5$, $^4J(H,H) = 1.8$, C≡CH); 2.44 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 123.6 (N=^{13}C).

Data of **9b**: ^{1}H-NMR ($CDCl_3$): 8.12 (*ddd*, $^3J(^{13}C,H) = 9.0$, $J = 0.5, 2.8$, N−CH); 7.90 (*m*, 2 H); 7.72 (*ddd*, $^1J(^{13}C,H) = 178$, $J = 0.5, 1.8$, N=^{13}CH); 7.34 (*m*, 2 H); 6.39 (*ddd*, $^2J(^{13}C,H) = 6.0$, $J = 1.8, 2.8$, C−CH); 2.42 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 145.2.

[1-^{13}C]Propynal Tosylhydrazone (**8b**). *Procedure B.* In a 5-ml round-bottom flask, a mixture of **7b** (0.080 g, 0.62 mmol) and 0.17 g of *Amberlyst-15* in 2 ml of 15% aq. CD_3CN was stirred in air for 72 h. The mixture was filtered by passing through a glass wool plug in a *Pasteur* pipette to remove the *Amberlyst-15*. The catalyst beads were then rinsed with 1 ml of CD_3CN. The filtrate was cooled in a 10-ml *Erlenmeyer* flask to 0°. *p*-Toluenesulfonohydrazide (0.046 g, 0.24 mmol) was added to the filtrate, and the mixture was stirred in air for 20 min. According to ^{1}H-NMR, the hydrazide had been completely consumed, but unreacted **5b** remained. An additional 0.028 g (0.15 mmol) of *p*-toluenesulfonohydrazide was added, and the mixture was stirred for 30 min. The cloudy soln. was transferred to a separatory funnel, and 5 ml of CH_2Cl_2 and 10 ml of H_2O were added. Following separation, the aq. layer was extracted with 2×5 ml of CH_2Cl_2. The combined org. layers were then washed with 10 ml of H_2O and dried (Na_2SO_4). Removal of the solvent by rotary evaporation provided colorless, slightly oily needles of **8b** (0.07 g, 0.3 mmol; 50% yield relative to acetal **7b**; 75% conversion of *p*-toluenesulfonohydrazide). The crystals were a 3 : 1 mixture of *anti*-**8b** and *syn*-**8b**, and contained no hydrazide, as determined by ^{1}H-NMR. ^{1}H-NMR ($CDCl_3$; *anti*-**8b**): 8.29 (br. *d*, 1 H); 7.84 (*m*, 2 H); 7.34 (*m*, 2 H); 6.96 (*dd*, $^1J(^{13}C,H) = 172$, $J = 2$, 1 H); 3.17 (*dd*, $J = 5, 2$, 1 H); 2.44 (*s*, 3 H); *syn*-**8b**: 8.67 (br. *d*, 1 H); 7.83 (*m*, 2 H); 7.33 (*m*, 2 H); 6.61 (*ddd*, $^1J(^{13}C,H) = 200$, $J = 2, 1, 1$ H); 3.77 (*dd*, J = 5, 2, 1 H); 2.44 (*s*, 3 H).

1,3-Dithiane-2-[^{13}C]carboxylic Acid (**14**). The procedure for the synthesis of **14** is an adaptation of that employed for [1-^{13}C]propynoic acid [13][17]. A flame-dried, three-neck, 500-ml flask was charged with 1,3-dithiane (7.10 g, 59.1 mmol; *Eastman*, *Aldrich*), dry THF (152 ml), and a stir bar. After cooling the soln. to −20°, 24.8 ml of 2.5M BuLi in hexanes (62.0 mmol; *Aldrich*) were added dropwise over 40 min *via* syringe through a septum on the sidearm. The soln. was stirred for 90 min. In the meantime, a separate apparatus was assembled for generation of $^{13}CO_2$. In a 250-ml round-bottom flask equipped with a sidearm stopcock was placed 23.5 g (118 mmol) of $Ba^{13}CO_3$ (*Cambridge Isotope Laboratories*). A pressure-equalizing addition funnel containing 145 ml of conc. H_2SO_4 was placed on this flask. A

condenser filled with *Drierite*® was mounted on the addition funnel. The condenser was connected to a 500-ml, three-neck, round-bottom collection flask (equipped with stir bar and two septa) by a rubber vacuum hose. This entire apparatus was flushed with Ar for 2 h. After flushing, the system was closed. The collection flask was placed in liquid N_2. The H_2SO_4 was added to the $Ba^{13}CO_3$ slowly at first, then quickly. A heat gun was used to warm the flask, ensuring complete reaction. Solid $^{13}CO_2$ condensed in the collection flask for 30 min. The lithio-1,3-dithiane soln. was cooled to $-78°$, and then it was transferred *via* cannula onto the solid $^{13}CO_2$ in the collection flask. After *ca.* 20 min, the frozen soln. in this flask was warmed to $-78°$, whereupon the soln. thawed and stirring was effected for 30 min. The temp. then was raised to $-41°$, and stirring was continued for 3 h. The reaction was quenched by dropwise addition of sat. NH_4Cl in MeOH (26 ml) at $-41°$. After slowly warming the mixture to 20°, 110 ml of H_2O and 150 ml of Et_2O were added. After separating the layers, the aq. layer was extracted with Et_2O (3×40 ml) to remove any unreacted 1,3-dithiane. The remaining aq. layer was carefully acidified with 3.3M HCl until a white precipitate persisted, which was extracted with Et_2O (4×50 ml). A second addition of 3.3M HCl resulted in formation of more white precipitate, also extracted with Et_2O. After washing with 60 ml of NaCl soln., the org. layers were dried (Na_2SO_4 and $MgSO_4$), and the solvent was removed, affording crude **14**. The entire procedure was repeated with 6.83 g of 1,3-dithiane and 22.4 g of $Ba^{13}CO_3$. Recrystallization of both crude products from hexane/benzene 85:15 gave pure **14** (9.03 g, 0.0546 mmol, 47% rel. to 1,3-dithiane). M.p. 112–113° ([50]: m.p. 112–113.5°). IR (KBr): 3310–2460 (br., O–H), 1655*s* ($^{13}C{=}O$). ^{1}H-NMR ($CDCl_3$): 4.18 (*d*, $^2J(^{13}C,H) = 6.5$, 1 H); 3.42 (*ddd*, $J = 14, 12, 3, 2$ H); 2.60 (*ddd*, $J = 14, 5, 3, 2$ H); 1.95–2.22 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 173.9 (CO_2H). MS: 165 (M^+, 16), 131 (29), 119 (100), 100 (10), 91 (9), 85 (10), 75 (12), 73 (11).

Methyl 1,3-Dithiane-2-[^{13}C]carboxylate (**15**) [50]. Because of the large amount of starting material **14** and the explosive nature of CH_2N_2, the conversion of **14** to **15** was run six times on 1.5-g samples. The acid **14** was dissolved in 37 ml of Et_2O in a CH_2N_2 reactor and cooled to 0°. A soln. of 30 g of KOH in 30 ml of EtOH and 24 ml of H_2O was heated to 70° in the upper chamber of the reactor. To the KOH soln. was added slowly dropwise a soln. of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide ('Diazald'; *Aldrich*) in Et_2O until the reaction soln. maintained a slight yellow color, indicating the presence of unreacted CH_2N_2. The Et_2O soln. containing the ester product was dried (Na_2SO_4 and $MgSO_4$). Evaporation of solvent from all six runs afforded 8.23 g (45.9 mmol, 85%) of **15**. M.p. 29–30°. IR ($CDCl_3$): 1689*s* ($^{13}C{=}O$). ^{1}H-NMR ($CDCl_3$): 4.19 (*d*, $^2J(^{13}C,H) = 6.5$, 1 H); 3.79 (*d*, $^3J(^{13}C,H) = 3.8$, 3 H); 3.42 (*ddd*, $J = 14, 11, 3, 2$ H); 2.61 (*ddd*, $J = 14, 5, 3, 2$ H); 1.95–2.22 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 170.3 (CO_2Me).

1,3-Dithiane-2-[^{13}C]carboxaldehyde (**16**). To a soln. of **15** (4.00 g, 22.3 mmol) in 200 ml of CH_2Cl_2 at $-78°$ were added 24.5 ml of 1.0M DIBAL (*Aldrich*) in hexanes, over 45 min. After 2 h of stirring at $-78°$, the reaction was quenched by dropwise addition of 30 ml of NH_4Cl in MeOH, and by addition of 20 ml of 1M HCl 30 min later. After the mixture slowly warmed to r.t., 60 ml of H_2O were added. The layers were separated, and the aq. layer was extracted with CH_2Cl_2 (2×100 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. (2×110 ml), aq. NaCl soln. (110 ml), and H_2O (110 ml). The solvent was removed after drying (Na_2SO_4 and $MgSO_4$). The above procedure was repeated with another 4.31 g of **15**. The crude product was a *ca.* 1:1 mixture of **16** and its methyl hemiacetal. By running the mixture through a SiO_2 column (CH_2Cl_2 elution), the hemiacetal was easily converted to **16** (5.38 g, 36.1 mmol, 78%). IR (film): 2926*m*, 2698*w*, 1678*s* ($^{13}C{=}O$), 1424*m*. ^{1}H-NMR ($CDCl_3$): 9.52 (*d*, $^1J(^{13}C,H) = 183$, 1 H); 4.11 (*d*, $^2J(^{13}C,H) = 6$, 1 H); 3.04 (*ddd*, $J = 15, 12, 3, 2$ H); 2.57 (*m*, 2 H); 1.95–2.15 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 188.2 (CHO).

Data of 1,3-Dithiane-2-[^{13}C]carboxaldehyde, Methyl Hemiacetal. ^{1}H-NMR ($CDCl_3$): 4.78 (*ddd*, $^1J(^{13}C,H) = 144$, $J = 12, 3, 1$ H); 3.66 (br. *t*, $J = 3$, 1 H); 3.49 (*d*, $^3J(^{13}C,H) = 5$, 3 H); 3.31 (*dd*, $^2J(^{13}C,H) = 5$, $J = 12$, 1 H); 3.20 (*m*, 2 H); 2.50–2.60 (*m*, 2 H); 1.95–2.15 (*m*, 2 H).

2-(2,2-Dibromo[1-^{13}C]ethenyl)-1,3-dithiane (**17**). The transformation of **16** to **17** utilized a modified literature procedure [26][27][51][52]. A soln. of freshly sublimed CBr_4 (15.8 g, 47.7 mmol; *Aldrich*) in 20 ml of CH_2Cl_2 was added dropwise to a soln. of PPh_3 (24.4 g, 93.0 mmol, recrystallized from hexane; *Aldrich*) in 85 ml of CH_2Cl_2 at 0° and stirred for 90 min. The resulting yellow-orange ylide soln. was cooled to $-78°$, whereupon a soln. of **16** (3.21 g, 21.5 mmol) in 20 ml of CH_2Cl_2 was added dropwise to it. After the soln. was stirred at $-78°$ for 85 min, 400 ml of hexane was added slowly to it. The resulting mixture was allowed to warm to 20°. The hexane/CH_2Cl_2 mixture containing precipitated $O{=}PPh_3$ was

decanted from a very sticky red-brown residue through a glass frit. To ensure complete removal of **17**, the residue was redissolved in 20 ml of CH_2Cl_2; 125 ml of hexane was added, causing further precipitation of $O{=}PPh_3$. This mixture was decanted through a glass frit. This procedure was repeated twice. The filtrate was concentrated by rotary evaporation to a white-yellow solid, which was washed repeatedly with hexane and filtered to extract **17**, which was obtained as a yellow liquid upon rotary evaporation. A yield was not calculated, for **17** was used crude in the next reaction due to its presumed instability. ^{1}H-NMR ($CDCl_3$): 6.54 (*dd*, $^1J(^{13}C,H) = 168$, $J = 10$, 1 H); 4.76 (*dd*, $^2J(^{13}C,H) = 5.7$, $J = 10$, 1 H); 2.90 (*m*, 4 H); 2.05–2.16 (*m*, 1 H); 1.88–2.02 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 134.2 ($Br_2C{=}CH$).

1,1-Dibromo-3,3-diethoxy[2-^{13}C]prop-1-ene (**18c**). Conversion of **17** to **18c** employed the dethioacetalization procedure of *Stork* and *Zhao* [53]. To a soln. of crude **17** (from 3.21 g (21.5 mmol) of **16**) in 40 ml of dry EtOH was added all at once [bis(trifluoroacetoxy)iodo]benzene (14.0 g, 32.6 mmol; *Aldrich*). The soln. was stirred 40 min at 20°, then it was poured into 70 ml of sat. aq. $NaHCO_3$ soln. This mixture was extracted with Et_2O (4 × 60 ml). The combined org. layers were washed with 50 ml of H_2O and dried ($MgSO_4$). Rotary evaporation, followed by flash CC through SiO_2, yielded **18c** as a clear, slightly yellow liquid. The overall yield for transformation of **16** to **18c** was 1.24 g (4.30 mmol, 20%). IR (film): 3026*w*, 2978*m*, 2930*w*, 2880*w*, 1685*w*, 1594*w*, 1475*w*, 1444*w*, 1370*m*, 1333*m*, 1117*s*, 1058*s*, 763*m*. ^{1}H-NMR ($CDCl_3$): 6.57 (*dd*, $^1J(^{13}C,H) = 166$, $J = 6.5$, 1 H); 5.07 (*d*, $J = 6.5$, 1 H); 3.52–3.75 (*m*, 4 H); 1.24 (*t*, $J = 7$, 6 H). ^{13}C-NMR ($CDCl_3$): 136.0 ($Br_2C{=}CH$).

3,3-Diethoxy[2-^{13}C]propyne (**7c**). The conversion of **18c** to **7c** employed the same procedure as that described for the conversion of **18d** to **7d** (*vide infra*). The yield of **7c** was 44% (0.417 g, 3.23 mmol). IR (film): 3279*m* ($HC{\equiv}C$), 2978*m*, 2932*m*, 2883*m*, 2076*w* ($C{\equiv}C$), 1445*w*, 1329*m*, 1118*s*, 1056*s*, 1012*m*. ^{1}H-NMR ($CDCl_3$): 5.27 (*dd*, $^2J(^{13}C,H) = 3.1$, $J = 1.9$, 1 H); 3.75 (*dq*, *AB* of ABX_3, $J = 9.5, 7, 2$ H); 3.59 (*dq*, *AB* of ABX_3, $J = 9.5, 7, 2$ H); 2.55 (*dd*, $^2J(^{13}C,H) = 49$, $J = 1.9$, 1 H); 1.25 (*t*, X_3 of ABX_3, $J = 7$, 6 H). ^{13}C-NMR ($CDCl_3$): 79.0 ($HC{\equiv}C$).

[2-^{13}C]Propynal Tosylhydrazone (**8c**). The procedure for preparation of **8c** is identical to that for **8b** (*Procedure A*, *vide supra*). As before, we were able to isolate the *anti*-isomer, *anti*-**8c**, whereas the *syn*-isomer, *syn*-**8c**, was contaminated with the corresponding tosylpyrazole.

Data of anti-**8c** (0.133 g, 0.596 mmol, 18%). ^{1}H-NMR ($CDCl_3$): 8.03 (br. *s*, NH); 7.83 (*m*, 2 tosyl H); 7.34 (*m*, 2 tosyl H); 6.94 (*dd*, $^2J(^{13}C,H) = 8$, $J = 2.0$, 1 H); 3.17 (*dd*, $^2J(^{13}C,H) = 50$, $J = 2.0$, 1 H); 2.44 (*s*, 3 H). MS: 223 (M^+, 46), 160 (11), 159 (91), 158 (11), 157 (12), 156 (17), 155 (100), 140 (35), 139 (25), 129 (14). HR-MS: 223.0498 (M^+, $C_9{}^{13}CH_{10}N_2O_2S^+$; calc. 223.0497).

Data of syn-**8c** (0.162 g, 0.726 mmol, 22%). ^{1}H-NMR ($CDCl_3$): 8.66 (br. *s*, NH); 7.72 (*m*, 2 tosyl H); 7.34 (*m*, 2 tosyl H); 6.62 (*dd*, $^2J(^{13}C,H) = 10$, $J = 1.0$, 1 H); 3.77 (*dd*, $^2J(^{13}C,H) = 50$, $J = 1.0$, 1 H); 2.44 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 72.2.

*Data for 1-Tosyl-1*H*-[4-^{13}C]pyrazole* (0.081 g, 0.363 mmol, 11%). ^{1}H-NMR ($CDCl_3$): 8.11 (*dd*, $^2J(^{13}C,H) = 9$, $J = 2.7$, 1 H); 7.90 (*m*, 2 tosyl H); 7.73 (*dd*, $^2J(^{13}C,H) = 11$, $J = 1.5$, 1 H); 6.39 (*dd*, $^1J(^{13}C,H) = 178$, $J = 1.5$, 1 H); 2.42 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 108.7.

3,3-Diethoxyprop-1-ene (**19**). Compound **19** was prepared from freshly distilled propenal (4.80 ml, 4.03 g, 1.8 mmol; *Aldrich*) and $HC(OEt)_3$ (12.2 ml, 10.9 g, 73.3 mmol; *Aldrich*) catalyzed by TsOH (0.0079 g, 0.042 mmol; *Aldrich*) according to the procedure of *Dedieu et al.* [54][55]. The acetal **19** was isolated by reduced-pressure distillation (47°/22 Torr) ([54][55]: b.p. 123–125°/760 Torr) in 74% yield ($d = 0.837$ g/ml). IR (film): 3085*w* (C=C*H*), 1649*w* (C=C). ^{1}H-NMR ($CDCl_3$): 5.86 (*ddd*, $J = 17.5, 10.5, 5.0$, 1 H); 5.39 (*ddd*, $J = 1.0, 1.7, 17.5$, 1 H); 5.28 (*ddd*, $J = 1.0, 1.7, 10.5$, 1 H); 4.87 (*td*, $J = 1.0, 5.0$, 1 H); 3.43–3.74 (*m*, 4 H); 1.15 (*t*, $J = 7.0$, 6 H).

2,2-Diethoxyacetaldehyde (**20**). Compound **20** was prepared according to the procedure of *Stetter* and *Mohrmann* [56–58]. A soln. of **19** (9.6 ml, 8.04 g, 61.7 mmol) in 60 ml of EtOH was cooled to −78°. A stream of O_3 in O_2 was bubbled through the soln., until, it retained a light blue color, indicating excess of O_3, *ca.* 2 h. N_2 was bubbled through the soln. for 10 min, and Me_2S (5.12 ml, 4.31 g, 69.4 mmol) was added dropwise. The soln. was warmed to 20° and stirred for 14 h. The product at this point is 1,1,2-triethoxyethan-2-ol, the hemiacetal of **20**. After removal of most of the EtOH *via* rotary evaporation, the product was subjected to reduced-pressure distillation using a 30-cm *Vigreux* column. The first fraction is EtOH, which is eliminated from the hemiacetal, leaving **20** in the pot. The second fraction comes over at a head temp. of 45–50°/0.5 Torr, containing a 7:1 mixture of **20** and its ethyl hemiacetal, and a trace of

Me_2SO. Care must be taken to discontinue the distillation before substantial amounts of Me_2SO begin to collect. Hydrated and polymerized forms of **20** [57] and protected hemiacetals of **20** [58] generally react as the free aldehyde, so further purification was not attempted. The yield of **20** was 43%. ^{1}H-NMR ($CDCl_3$): 9.46 (*d*, *J* = 2.0, 1 H); 4.59 (*d*, *J* = 2.0, 1 H); 3.55–3.83 (*m*, 4 H); 1.27 (*t*, *J* = 7.0, 6 H).

Data of 1,1,2-Triethoxyethan-2-ol. ^{1}H-NMR ($CDCl_3$): 4.59 (*dd*, *J* = 2.0, 10.5, 1 H); 4.38 (*d*, *J* = 2.0, 1 H); 3.48–3.95 (*m*, 6 H); 3.05 (*d*, *J* = 10.5, 1 H); 1.18–1.29 (*m*, 9 H).

1,1-Dibromo-3,3-diethoxy[1-^{13}C]prop-1-ene (**18d**). The transformation of aldehyde **20** to **18d** utilized a modified literature procedure [27][51][52]. To a mixture of Zn powder (2.40 g, 36.6 mmol; *Fisher*) and Ph_3P (9.55 g, 36.4 mmol; *Aldrich*) in 90 ml of CH_2Cl_2 at 0° was added dropwise a soln. of $^{13}CBr_4$ (11.7 g, 35.7 mmol) in 85 ml of CH_2Cl_2. The mixture was warmed to 20° and became a fine lavender slurry as it stirred for 44 h. After recooling the mixture to 0°, a soln. of **20** in 20 ml of CH_2Cl_2 was added to it over 30 min. The temp. was returned to 20°, and stirring was continued for 4 h. Hexane (160 ml) was added, and the mixture was filtered. The solvent was removed from the filtrate, yielding an off-white solid and an oil. The two were washed repeatedly with hexane (4 × 15 ml), and the solid ($Ph_3P{=}O$) was filtered from the soln. The crude product obtained upon rotary evaporation was purified by flash chromatography (FC; SiO_2; CH_2Cl_2) to afford **18d** (2.01 g, 6.76 mmol, 38%). Clear, yellow liquid. IR (film): 1686*w* (C=C). ^{1}H-NMR ($CDCl_3$): 6.58 (*d*, *J* = 6.5, 1 H); 5.07 (*dd*, *J* = 6.5, $^2J(^{13}C,H)$ = 4.5, 1 H); 3.48–3.76 (*m*, 4 H); 1.24 (*t*, *J* = 7.0, 6 H). ^{13}C-NMR ($CDCl_3$): 93.4.

3,3-Diethoxy[1-^{13}C]propyne (**7d**). The procedure for the conversion of **18b** to **7d** was similar to those described in [51][52]. To a soln. of **18d** (1.95 g, 6.76 mmol) in 25.0 ml of dry THF at −78° was added 2.5M BuLi in hexanes (5.41 ml, 13.5 mmol; *Aldrich*) *via* syringe. The soln. was stirred for 90 min at −78° and warmed to 20° for 10 min. The soln. was poured into 24 ml of sat. aq. NH_4Cl soln. and 12 ml of CH_2Cl_2. After separation of the layers, the aq. layer was extracted with CH_2Cl_2 (4 × 15 ml). The combined org. layers were washed with aq. NaCl soln. (2 × 50 ml) and H_2O (50 ml), and dried ($MgSO_4$). The solvent was removed by rotary evaporation. Reduced-pressure distillation afforded clear, colorless **7d** (0.450 g, 3.48 mmol, 52%). IR (neat): 3266*m*, 2979*m*, 2932*m*, 2890*m*, 2101*w* ($^{13}C{\equiv}C$), 1118*m*, 1056*m*, 1011*w*. ^{1}H-NMR ($CDCl_3$): 5.27 (*dd*, $^3J(^{13}C,H)$ = 3.4, *J* = 1.8, 1 H); 3.75 (*dq*, *AB* of ABX_3, *J* = 9.5, 7.2, 2 H); 3.59 (*dq*, *AB* of ABX_3, *J* = 9.5, 7.2, 2 H); 2.55 (*dd*, $^1J(^{13}C,H)$ = 252, *J* = 1.8, 1 H); 1.25 (*t*, X_3 of ABX_3, *J* = 7.2, 6 H).

[3-^{13}C]Propynal Tosylhydrazone (**8d**). The procedure for preparation of **8d** was identical to that for **8b** (*Procedure A*, *vide supra*). As before, we were able to isolate one isomer, *anti*-**8d**, whereas the other isomer, *syn*-**8d**, was contaminated with the corresponding tosylpyrazole.

Data of anti-**8d** (0.109 g, 0.489 mmol, 14%). ^{1}H-NMR ($CDCl_3$): 8.06 (br. *s*, NH); 7.83 (*m*, 2 tosyl H); 7.34 (*m*, 2 tosyl H); 6.94 (*ddd*, $^3J(^{13}C,H)$ = 4.2, *J* = 0.8, 2.0, N=CH); 3.18 (*dd*, $^1J(^{13}C,H)$ = 256, *J* = 2.0, $H^{13}C{\equiv}C$), 2.44 (*s*, 3 H). MS: 223 (M^+, 2), 160 (9), 159 (70), 158 (10), 155 (13), 92 (13), 91 (100). HR-MS: 223.0489 (M^+, $C_9{}^{13}CH_{10}N_2O_2S^+$; calc. 223.0497).

Data of syn-**8d**. ^{1}H-NMR ($CDCl_3$): 8.66 (br. *s*, NH); 7.83 (*m*, 2 tosyl H); 7.33 (*m*, 2 tosyl H); 6.62 (*dd*, $^3J(^{13}C,H)$ = 5.5, *J* = 1.5, N=CH); 3.78 (*dd*, $^1J(^{13}C,H)$ = 257, *J* = 1.5, 1 H, $H^{13}C{\equiv}C$), 2.44 (*s*, 3 H).

*Data for 1-Tosyl-1*H*-[5-^{13}C]pyrazole.* ^{1}H-NMR ($CDCl_3$): 8.11 (*dd*, $J(^{13}C,H)$ = 195, *J* = 3.0, N−^{13}CH); 7.90 (*m*, 2 tosyl H); 7.73 (*dd*, $J(^{13}C,H)$ = 4.5, *J* = 1.8, N=CH); 7.34 (*m*, 2 tosyl H); 6.39 (*ddd*, $J(^{13}C,H)$ = 9.5, *J* = 1.8, 3.0, C−CH); 2.42 (*s*, 3 H).

2-Phenyl-1,3-dithiane (**21**) [59]. Dry HCl gas was bubbled through a soln. of 20.0 ml of propane-1,3-dithiol (21.6 g, 199 mmol; *Aldrich*) and 20.0 ml of PhCHO (20.9 g, 197 mmol; *Mallinckrodt*) in 150 ml of $CHCl_3$ for 5 min at 0°. The reaction was brought to 20° as it stirred for 45 min. The soln. was washed with H_2O (2 × 50 ml), 10% KOH soln. (3 × 50 ml), and H_2O (2 × 50 ml). The org. layer was treated with charcoal, dried (Na_2SO_4), and filtered. After evaporation of the solvent, the crude product was recrystallized from MeOH, affording **21** as colorless needles (34.4 g, 175 mmol, 89%). M.p. 71–72° ([59]: m.p. 69.0–69.8°). ^{1}H-NMR ($CDCl_3$): 7.27–7.51 (*m*, 5 H); 5.17 (*s*, 1 H); 2.86–3.15 (*m*, 4 H); 1.90–2.22 (*m*, 2 H). MS: 198 ($[M+2]^+$, 10), 197 ($[M+1]^+$, 11), 196 (M^+, 100), 153 (11), 135 (11), 131 (39), 123 (19), 122 (94), 121 (76), 105 (28), 91 (24).

2-([^{13}C]Methyl)-2-phenyl-1,3-dithiane (**22**) [32]. To a soln. of **21** (13.9 g, 70.8 mmol) in 120 ml of THF at −78° were added dropwise 28.3 ml of 2.5M BuLi in hexanes (70.8 mmol; *Aldrich*) *via* syringe. Upon stirring for 2.7 h, a yellow suspension developed, to which was added $^{13}CH_3I$ (2.28 ml, 10.0 g,

70.0 mmol; *Isotec*). After stirring for an additional 40 min, the suspension was placed in a freezer for 20 h (−17°). The mixture was diluted with 50 ml of 1M HCl and 200 ml of H_2O, and was extracted with pentane/CH_2Cl_2 1:1 (3 × 100 ml). The combined org. layers were washed with H_2O (2 × 75 ml) and dried ($MgSO_4$). The solvent was removed *via* rotary evaporation, affording crude **22** in quant. yield (14.8 g). ^{1}H-NMR ($CDCl_3$): 7.93–7.97 (*m*, 2 H); 7.22–7.43 (*m*, 3 H); 2.65–2.77 (*m*, 4 H); 1.86–2.01 (*m*, 2 H); 1.79 (*d*, $^1J(^{13}C,H) = 130$, 3 H).

1-Phenyl[2-^{13}C]ethanone (**23**) [59]. To a soln. of crude **22** (14.8 g, 70.0 mmol) and $HgCl_2$ (28.0 g, 103 mmol; *Mallinckrodt*) in 450 ml of 95% MeOH was added red HgO (11.0 g, 51.0 mmol; *Baker*). The resulting suspension was refluxed for 3.6 h. After cooling to 20°, the suspension was suction filtered, and the filter cake was washed with CH_2Cl_2 (4 × 80 ml). The volume of filtrate was reduced to 200 ml by rotary evaporation and shaken with 400 ml of 25% $AcONH_4$ soln. The aq. phase was extracted with pentane/CH_2Cl_2 1:1 (4 × 100 ml). All the org. layers were combined, washed with NaCl soln., and dried (Na_2SO_4). After removal of solvent, the crude product was purified by FC (SiO_2; $CHCl_3$) to yield **23** (7.26 g, 60.0 mmol, 86%). ^{1}H-NMR ($CDCl_3$): 7.95–8.00 (*m*, 2 H); 7.44–7.58 (*m*, 3 H); 2.62 (*d*, $^1J(^{13}C,H) = 128$, 3 H).

Tetrabromo[^{13}C]methane [59]. A soln. of NaOBr was prepared by dissolving NaOH (28.9 g, 723 mmol) in 210 ml of H_2O and slowly adding Br_2 (14.8 ml, 45.9 g, 287 mmol; *Mallinckrodt*) to it at 0°. The ketone **23** was added slowly, and the soln. was stirred at 20° for 4 h, during which $^{13}CBr_4$ was formed as a precipitate. After filtering from the soln. and washing with H_2O, the crude $^{13}CBr_4$ was dissolved in Et_2O. This soln. was washed twice with an aq. soln. of $NaHSO_3$, once with aq. NaCl soln., and was dried ($MgSO_4$). Removal of solvent by rotary evaporation yielded an off-white solid, $^{13}CBr_4$ (12.1 g, 364 mmol, 61%). M.p. 89.5–91.0° ([59]: m.p. 91–92°).

2,3-Dibromo-1,1-diethoxypropane (**25**) [60]. Br_2 (4.6 ml, 89.3 mmol; *Mallinckrodt*) was added dropwise to a soln. of freshly distilled propenal (5.90 ml, 88.3 mmol; *Aldrich*) in 10 ml of Et_2O at −35°. After the addition was complete, the soln. was warmed to 0° and stirred for 20 min. To the resulting soln. of 1,2-dibromopropenal (**24**) was added $HC(OEt)_3$ (16.2 ml, 97.4 mmol; *Aldrich*), 1 ml of 95% EtOH, and $ZnCl_2$ (0.53 g, 3.9 mmol; *Mallinckrodt*). After stirring at 15° for 1 h, the soln. was poured onto 30 ml of cold H_2O, and the layers were separated after shaking. The org. layer was dried (K_2CO_3). Rotary evaporation afforded **25** as a clear, colorless liquid, used without further purification (19.0 g, 65.7 mmol, 74%): ^{1}H-NMR ($CDCl_3$): 4.69 (*d*, *J* = 4.5, 1 H); 4.19 (*dt*, *J* = 4.5, 6.0, 1 H); 3.59–3.90 (*m*, diastereotopic C*H*$_2$Me and C*H*$_2$Br, 6 H); 1.27 (*t*, *J* = 7.0, 3 H); 1.26 (*t*, *J* = 7.0, 3 H).

3,3-Diethoxypropyne (**7a**). Double dehydrohalogenation of **25** followed a literature procedure [60]. Compound **25** (9.18 g, 31.6 mmol) was added dropwise to a suspension of $NaNH_2$ (4.38 g, 112 mmol; *Aldrich*) in *ca.* 70 ml of NH_3 at −34° as the flask was swirled. Residual **25** was washed into the suspension with 20 ml of Et_2O, and swirling was continued for 15 min. The flask was then placed on a 40° oil bath and flushed with N_2 to drive off the NH_3. Ice (38 g) and Et_2O (20 ml) were added to the residue. The layers were separated, and the aq. layer was extracted with Et_2O/pentane 1:1 (6 × 30 ml). The combined org. layers were dried (K_2CO_3), and the solvent was removed by rotary evaporation. Reduced-pressure distillation (3–4 Torr) yielded pure **7a** (3.05 g, 23.8 mmol, 75%). ^{1}H-NMR ($CDCl_3$): 5.27 (*d*, *J* = 1.8, 1 H); 3.75 (*dq*, *AB* of *ABX*$_3$, *J* = 9.5, 7.2, 2 H); 3.59 (*dq*, *AB* of *ABX*$_3$, *J* = 9.5, 7.2, 2 H); 2.55 (*d*, *J* = 1.8, 1 H); 1.25 (*t*, *X*$_3$ of *ABX*$_3$, *J* = 7.2, 6 H). ^{13}C-NMR ($CDCl_3$): 91.1; 79.1 (w); 73.6; 61.0 (2 C); 15.1 (2 C).

3,3-Diethoxy[1-$^2H_1$]propyne (**7e**). Preparation of the lithium acetylide of **7a** was accomplished according to the procedure of *Barbot* and *Miginiac* [61]. A soln. of 2.5M BuLi in hexane (8.80 ml, 22.0 mmol; *Aldrich*) was added dropwise over 20 min to a soln. of **7a** (2.30 ml, 19.6 mmol) in 15 ml of Et_2O, maintained at −30°. After the soln. was stirred for an additional 40 min, the reaction was quenched by dropwise addition of 15 ml of D_2O. After warming to 20°, the layers were separated, and the aq. layer was extracted with Et_2O/pentane 1:1 (7 × 10 ml). The org. layer was dried (Na_2SO_4). After evaporation of the solvent, **7e** was purified by reduced-pressure distillation (1.75 g, 13.5 mmol, 69%). IR (film): 2581*s* (≡C–D), 2219*m* (C≡C). ^{1}H-NMR ($CDCl_3$) (reveals no detectable acetylenic protons, indicating complete deuteration): 5.27 (*s*, 1 H); 3.75 (*dq*, *AB* of *ABX*$_3$, *J* = 9.5, 7.2, 2 H); 3.59 (*dq*, *AB* of *ABX*$_3$, *J* = 9.5, 7.2, 2 H); 1.25 (*t*, *X*$_3$ of *ABX*$_3$, *J* = 7.2, 6 H). ^{13}C-NMR ($CDCl_3$): 90.9; 60.9; 15.0.

[3-$^2H_1$]Propynal Tosylhydrazone (**8e**). The procedure for preparation of this tosylhydrazone was identical to that for **8b** (*Procedure A*, *vide supra*).

Data for anti-**8e**. ^{1}H-NMR ($CDCl_3$): 8.23 (br. *s*, 1 H); 7.82 (*m*, 2 H); 7.34 (*m*, 2 H); 6.96 (*s*, 1 H); 2.45 (*s*, 3 H). The absence of an alkyne resonance at 3.17 ppm established that *anti*-**8e** retained a high level of isotopic incorporation.

Data of syn-**8e**. ^{1}H-NMR ($CDCl_3$): 8.66 (br. *s*, 1 H); 7.84 (*m*, 2 H); 7.34 (*m*, 2 H); 6.62 (*s*, 1 H); 2.44 (*s*, 3 H). 3.77 (*d*, $J = 1.5$, 1 H). The presence of an alkyne resonance at 3.77 ppm (*d*) established that the isotopic purity of *syn*-**8e** was *ca.* 70%.

*Data of 1-Tosyl-1*H-*[5-$^2H_1$]pyrazole.* ^{1}H-NMR ($CDCl_3$): 7.90 (*m*, 2 tosyl H); 7.73 (*d*, $J = 1.8$, 1 H); 7.34 (*m*, 2 tosyl H); 6.39 (*m*, 1 H); 2.42 (*s*, 3 H). The presence of an alkene resonance at 8.11 ppm (*d*) established that the isotopic purity of 1-tosyl-1*H*-[5-$^2H_1$]pyrazole was *ca*. 65%.

Propynal Tosylhydrazones, Sodium Salts **10a**–**10e**. A dispersion of 60% NaH/mineral oil (1 equiv.; *Aldrich*) was added to a stirred soln. of **8** (*ca.* 70–100 mg) in 10–15 ml of CH_2Cl_2. After 1 h, 25 ml of pentane were added, causing the salt **10** to precipitate as an off-white solid. The salt was collected by suction filtration, washed with cold pentane, and dried *in vacuo*. The product was crushed to a fine powder and used without further purification.

Diazopropyne (**11a**), *Diazo[1-^{13}C]propyne* (**11b**), *Diazo[2-^{13}C]propyne* (**11c**), *Diazo[3-^{13}C]propyne* (**11d**), *and Diazo[3-$^2H_1$]propyne* (**11e**). Synthesis and manipulation of these compounds requires extreme caution. We encountered one explosion of **11**, and others have as well [40]. We worked with small quantities (< 50 mg) of diazopropyne, keeping the sample cold (– 94°) and under vacuum or dry N_2 to minimize the risk of explosion.

The freshly prepared salt **10** was placed in a 10-ml round-bottom flask. A glass adapter arm (essentially a short-path distillation column) connected the flask to a collection tube. The system was evacuated (> 1 Torr), and the salt was heated to 40° for 15 min. Pyrolysis was then effected by raising the temp. to 70° for 60 min. The yellow diazopropyne condensed in the collection tube, which had been cooled with liquid N_2. The liquid N_2 bath was replaced with a hexane slush bath (– 94°), and the system was vented with dry N_2. After the collection tube was transferred to a matrix-isolation apparatus, the sample was subjected to two freeze–pump–thaw cycles at – 94°. After the pressure in the matrix-isolation system had fallen below 5×10^{-6} Torr, diazopropyne was sublimed from the – 94° slush bath and co-deposited with Ar on a CsI window maintained at 30 K (for IR experiments).

Data for **11a**. IR (Ar, 10 K): 3333*s*, 3320*w*, 3098*w*, 2123*m*, 2117*w*, 2072v*s*, 1362*w*, 1353*w*, 1054*m*, 827*w*, 700*w*, 683*m*, 616*w*, 528*m*, 475*m*, 360*w*, 355*w*, 350*m*.

Data for **11b**. IR (Ar, 10 K): 3338*w*, 3332*s*, 3091*w*, 2120*m*, 2104*w*, 2091*w*, 2064v*s*, 1364*w*, 1328*m*, 1052*m*, 821*w*, 700*w*, 683*m*, 615*w*, 527*m*, 470*m*.

Data for **11c**. IR (Ar, 10 K): 3317*s*, 3305*w*, 3097*w*, 2115*w*, 2108*m*, 2065v*s*, 1353*w*, 1049*m*, 824*w*, 678*w*, 614v*w*, 525*m*, 474*m*.

Data for **11d**. IR (Ar, 10 K): 3332*m*, 3098*w*, 2110*s*, 2096*s*, 2052v*s*, 1361*w*, 1354*w*, 1054*m*, 685*w*, 610*w*, 528*m*, 471*m*, 353*w*, 344*m*.

Data of **11e**. IR (Ar, 10 K): 2610*m*, 2597*m*, 2124*m*, 2118*m*, 2087v*s*, 1351*w*, 1068*w*, 1053*w*, 977v*w*, 957v*w*, 819*w*, 814*w*, 682*w*, 534*w*, 528*w*, 476*m*.

Solution NMR and UV/VIS Spectroscopy of **11a**. Compound **11a** was prepared, as described above, using 0.042 g (0.17 mmol) of the tosylhydrazone sodium salt. Freshly prepared **11a** was dissolved in CD_3CN (*ca.* 2 ml). Using a volumetric pipette, 1.00 ml of this soln. was removed, and a benzene standard (0.019 g, 0.24 mmol) was weighed into this aliquot on an anal. balance. ^{1}H-NMR ($CDCl_3$, 298 K): 4.50 (*d*, $J = 2$, 1 H); 3.82 (*d*, $J = 2$, 1 H). Comparison of ^{1}H-NMR integrations revealed a concentration ratio [benzene]/[diazopropyne] 10.3 : 1, so the concentration of **11a** in the NMR sample was 0.024M. Another aliquot (1.00 ml) of the original soln. of **11a** (without added benzene) was removed by volumetric pipette and diluted with MeCN to the mark in a 100-ml volumetric flask, and 3.00 ml of this soln. was further diluted to the mark in a 10-ml volumetric flask. This soln. of **11a**, with a concentration of 7.1×10^{-5} M, exhibited an electronic absorption at 250 nm with an absorbance value of $A = 1.19$ in a 1-cm quartz cuvette. UV/VIS (MeCN, 298 K): 250 (16000). Although **11a** undergoes slow decomposition in soln. at r.t., this procedure is likely to be adequate in providing an order-of-magnitude estimate for the extinction coefficient of this exceedingly fragile species.

Solution NMR Spectroscopy of Acetal Hydrolysis. Compound **7a** (0.093 g, 0.73 mmol) and benzene (0.12 g, 1.5 mmol; internal NMR integration standard) were dissolved in 2 ml of 10% aq. CD_3CN and

stirred magnetically. *Amberlyst-15* (0.21 g) was added. Aliquots were periodically removed by pipette for ^{1}H-NMR analysis and subsequently returned to the reaction mixture after analysis. Stirring was ceased during removal of the aliquot, in order to allow the *Amberlyst-15* catalyst to settle to the bottom of the flask and not be taken up in the pipette. The relative concentrations of acetal **7a** (5.18 ppm), hemiacetal **6a** (5.31 ppm), aldehyde **5a** (9.09 ppm), and aldehyde hydrate **4a** (5.45 ppm) in soln. were determined by ^{1}H-NMR integration relative to internal benzene (7.37 ppm). Similar studies showed that increasing the percentage of H_2O increases the rate of conversion. The benefit of increased hydrolysis rate, however, is offset by the physical degradation of catalyst beads at higher H_2O concentration. The beads degrade to form a fine powder that is difficult to remove by filtration.

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