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The Ever-Elusive Tetra-*tert*-butylethene (TTBE, 3,4-Di-*tert*-butyl-2,2,5,5-tetramethylhex-3-ene): Further Insight on Its Preparation[‡]

Oliver Klein,[a] Henning Hopf,*[a] and Jörg Grunenberg[b]

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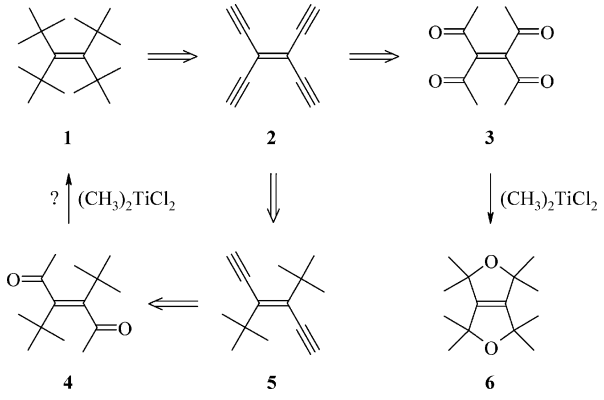
Diketone **4** was prepared by hydrolysis of hexendiyne **5**, the latter being available through McMurry coupling of acetylenic ketone **26**. Upon treatment with dimethyltitanium dichloride, **4** cyclizes into fully alkylated furan derivative **30**; the still unknown tetra-*tert*-butylethene (**1**, TTBE, 3,4-di-*tert*-butyl-2,2,5,5-tetramethylhex-3-ene) was not produced. The structural properties of **4** and the mechanism of its cyclization into **30** are discussed.

Introduction

Looking at the synthetic accomplishments of natural[2] and non-natural products chemistry,[3] it is surprising that a simple and symmetrical hydrocarbon such as tetra-*tert*-butylethene (TTBE, **1**, 3,4-di-*tert*-butyl-2,2,5,5-tetramethylhex-3-ene) so far has escaped all efforts of preparation.[4] According to recent DFT calculations, **1** should be a stable, though strained (calculated strain energy ca. 93 kcal/mol)[5] molecule; however, it is obviously not the energy content of the final molecule that cannot be reached during its (attempted) synthesis, but the steric resistance that so far no synthetic pathway could overcome en route and which forced respective intermediates to break away from the intended synthetic course. Although the attempt described in the present report adds to the still-growing list of failures to synthesize **1**,[6] we believe that our new effort deserves publication, as it increases our knowledge about the preparation of highly hindered organic molecules.

Scheme 1 summarizes some of our strategic thoughts concerning the preparation of **1**. Because of the high strain energy of the hydrocarbon (see above), it makes sense to "smuggle" the strain-producing *tert*-butyl substituents into the target molecule through smaller and hence less strain-producing substituents. Although this "tied-back" approach has been previously unsuccessfully attempted several times,[4] it could well be that in earlier attempts this approach had not been taken far enough. If one "folds" the three methyl groups of a *tert*-butyl substituent completely, in an umbrella-like fashion (and mentally adds a carbon atom), formally one of the sleekest groups in organic chemistry results: the ethynyl function. Performed four times on **1**, tetraethynylethene (**2**, TEE) results. Although available by the efforts of Diederich and coworkers,[7] we, several years ago, tried to use its (formal) hydration product, tetraacetylethene (**3**), an easily available tetraketone,[8] to prepare the title compound. Subjecting it to the well-established method of Reetz for the conversion of methyl ketones into *tert*-butyl moieties[9] disappointingly resulted in the generation of dioxabicyclo[3.3.0]octene derivative **6** only.[10]



Scheme 1. Some strategic considerations to prepare tetra-*tert*-butylethene (TTBE, **1**).

Clearly, to prevent the cyclization, the two vicinal acetyl groups in the *Z* configuration have to be avoided, and rather than employing **3** as a precursor, diethynyl derivative **5** and diketone **4** derived therefrom are better candidates for the generation of **1**. We hence decided to find a preparatively satisfactory route to **4** [(3*E*)-3,4-di-*tert*-butylhex-3-en-2,5-dione].

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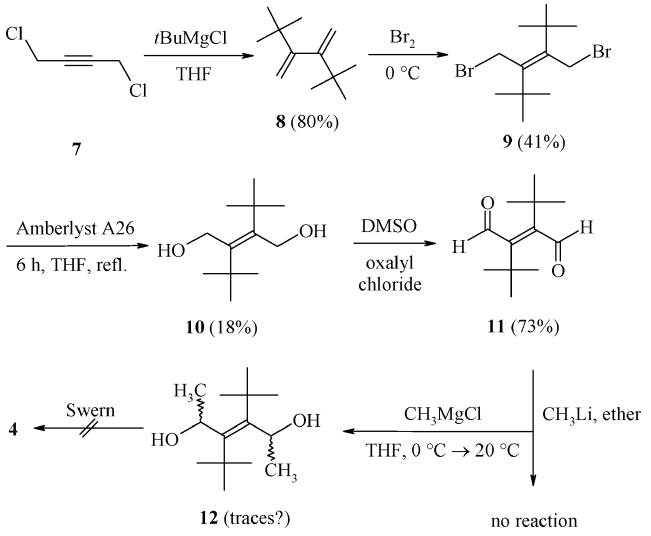
[a] Institut für Organische Chemie, Technische Universität Braunschweig,
Hagenring 30, 38106 Braunschweig, Germany
Fax: +49-531-391-5388
E-mail: H.Hopf@tu-bs.de
[b] Institut für Organische Chemie, Technische Universität Braunschweig, Arbeitsgruppe Computerchemie,
Hagenring 30, 38106 Braunschweig, Germany
Fax: +49-531-391-7744
E-mail: J. Grunenberg@tu-bs.de

Note that in all intermediates the final double bond is always present during the complete synthetic sequence, which avoids the introduction of unsaturation at a late stage of the synthesis where the accessibility of the inner carbon atoms for any (attacking) reagent becomes increasingly difficult.

Results and Discussion

But-2-yn-1,4-diol Derivatives as Starting Materials for (3*E*)-3,4-Di-*tert*-butylhex-3-en-2,5-dione (4)

Our first attempt to prepare diketone **4** is summarized in Scheme 2. Commercially available 1,4-dichlorobut-2-yne (**7**) was converted into 2,3-di-*tert*-butylbuta-1,3-diene (**8**) by treatment with *tert*-butylmagnesium bromide according to a literature procedure in good yield.[11] When bromine was added to hydrocarbon **8** at ice-bath temperature, a product mixture was produced[12] from which 1,4-addition product **9** could be isolated. Although the yield of the process is only fair (ca. 41%) it fulfills two important requirements: the ultimately needed "interior" carbon–carbon double bond is generated and the two bulky substituents are in a *trans* orientation, as demonstrated earlier by X-ray structural analysis[1b] (Scheme 2).



Scheme 2. 2,3-Di-*tert*-butylbuta-1,3-diene (**8**) as a possible intermediate to **1**.

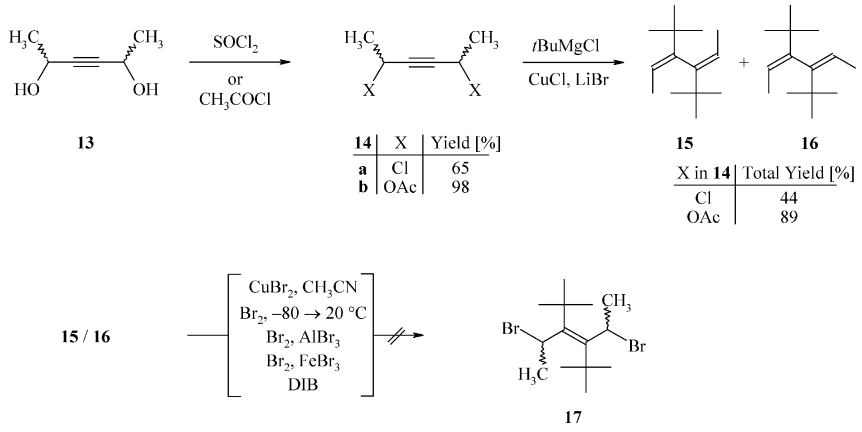
With the **8**→**9** conversion, the end of the dry spell of the synthetic sequence was not yet over. Hydrolysis of dibromide **9** with the ion-exchange resin Amberlyst A 26, a reagent which in its sodium carbonate form has been employed very successfully for the hydrolysis of primary alkyl, allyl, and benzyl halides,[13] furnished **10** in only 18% yield. Fortunately, its Swern oxidation yielded dialdehyde **11** in good yield (73%) so that altogether 1–2 g of this crucial intermediate were available from **9**. The conversion of the latter derivative into **11** by Kornblum reaction[14] gave the dialdehyde directly, but in very disappointing yields of 5% only. The dialdehyde is a slightly yellow, oily liquid at room temperature and could not be subjected to X-ray crystal structure analysis. However, it was shown by AM1 calculation that its two carbonyl groups were rotated out of the C–C double bond plane by ca 84°, causing severe steric hindrance for any further nucleophilic attack (see below). That the conjugation in **11** is reduced is also indicated by the electronic spectrum of the compound, which shows its absorption maximum at 222 nm (see the Experimental section for other spectroscopic data). As these calculations show, the orientation of the oxygen atoms of the dialdehyde is very similar to the position of the two bromine substituents in **9**.[1b]

As **11** was still lacking two carbon atoms for the preparation of **4**, we tried to introduce them by the addition of methyllithium (2 equiv.). Although reaction took place in diethyl ether, we were unable to isolate a component from the complex reaction mixture formed that showed spectroscopic data agreeing with structure **12**. With methyl Grignard, the results were only slightly better. After extensive chromatography we could enrich at least a fraction that gave the correct molecular ion peak for **12** (m/z = 228) and displayed signals for the carbinyl protons in the expected range (δ = 4.9 ppm, ^3J = 6.2 Hz). However, after submitting this mixture to Swern oxidation, neither the ^{1}H nor the ^{13}C NMR spectrum showed any signs that **12** had indeed been produced.

Obviously, we tried to introduce the methyl substituents at too late a stage in the synthesis, when steric hindrance was already significant; therefore, we decided to begin the next route from a C_6 precursor, hex-3-yn-2,5-diol (**13**), commercially available as a mixture of diastereomers (Scheme 3).

By treatment with either thionyl chloride (neat, –30 °C, 65% yield) or acetyl chloride (in *N*,*N*-diethylaniline, quantitative yield) **13** was converted into the known dichlorides[15] and diacetates,[16] respectively. *tert*-Butylation then took place with the reagent prepared from cuprous chloride and lithium bromide[17] to furnish a mixture of conjugated dienes **15** and **16**, as described previously.[18] The two hydrocarbons were produced in a 3:2 ratio, with the *E*,*E* isomer lacking completely.

Unfortunately, all bromination experiments were unsuccessful and in no case (see Scheme 3 for variation of reaction conditions) could desired **17** be isolated. Under the first two variants,[19] the starting material was reisolated unchanged, even when the temperature was raised to ambient temperature. For bromination in the presence of aluminum tribromide[20] and iron tribromide,[21] as well as with dibromoisocyanuric acid (DIB),[22] more or less complete destruction of the starting material was observed. In these experiments, the color of the reaction mixture turned quickly from deep red to brown and finally to black, and the formation of hydrogen bromide was noted; no defined reaction products could be isolated. It is well known[23] that orthogonal dienes prefer substitution of olefinic hydrogen atoms over the 1,2-addition to the alkene moiety. As far as oligomers from **15/16** are concerned, it could be that **17** is actually formed but – as a highly reactive halide – is converted



Scheme 3. Further conjugated dienes as intermediates in the synthesis of **1**.

into a triene under the reaction conditions by dehydrobromination. This hydrocarbon could easily oligomerize in the presence of hydrogen bromide and a Lewis acid.

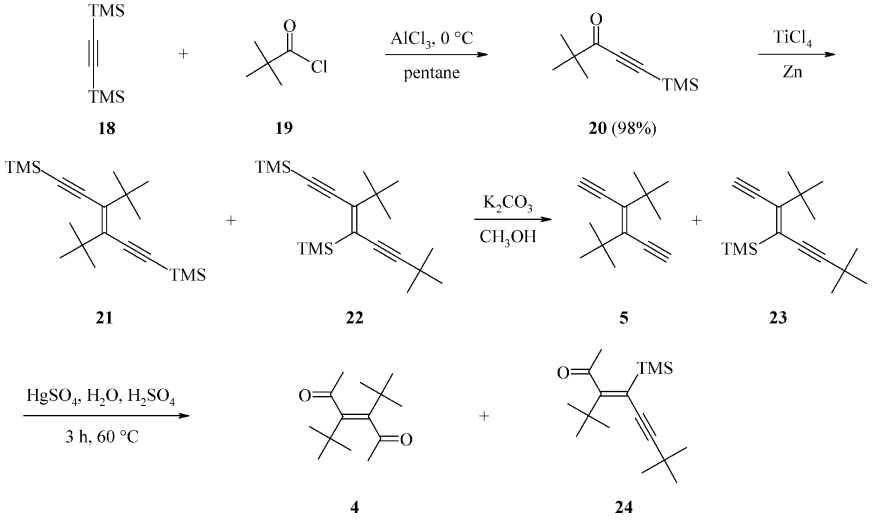
Be it as it may, after these further negative experiments we terminated our experiments to prepare **4** from doubly propargylic substrates and turned our attention to a McMurry-type coupling reaction of suitably substituted acetylenic ketones.

tert-Butyl Ethynyl Ketones as Starting Materials for (3*E*)-3,4-Di-*tert*-butylhex-3-en-2,5-dione (4)

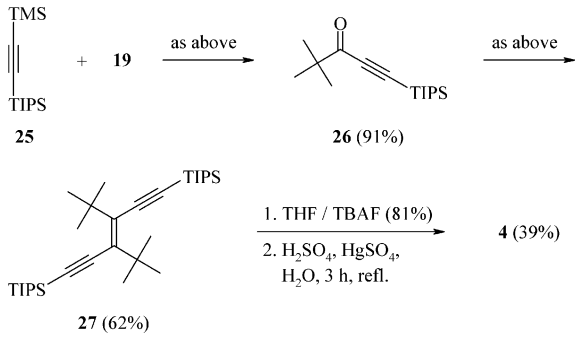
In 1994 we reported on the preparation of various hex-3-en-1,5-diynes by McMurry coupling of appropriate alkynones.[24] Among the hydrocarbons synthesized was diacetylene **5** for which the pathway summarized in Scheme 4 was developed.

This route, optimized in the present study, begins with the Friedel–Crafts acylation of bis(trimethylsilyl)ethyne (**18**) with pivaloyl chloride (**19**) to yield protected acetylenic ketone **20** in quantitative yield.[25] McMurry coupling ($TiCl_4$, Zn) furnished a mixture of dimers **21** and **22** in poor yield (15–20%, ratio 2:1). That rearranged products such as **22** are produced in this process has been noted previously[24] and traced back to the presence of propargylic carbene intermediates that can dimerize along different routes. Desilylation was performed by treatment with potassium carbonate and yielded hexendiynes **5** and **23**. Because the separation of this mixture was difficult, it was subjected directly to hydration to yield **4** (37%) and **24** (36%), two ketones that could be obtained in pure form easily by silica-gel column chromatography with pentane as eluent. Before the physical and chemical properties of **4** are described, a variant of the above coupling will be presented that circumvents the generation of product mixtures; it is presented in Scheme 5.

Applying the acylation with **19** to the TIPS-protected acetylene **25** [TIPS = tris(isopropylsilyl)][26] furnished acetylenic ketone **26**, again in excellent yield. However, when this was reductively dimerized, only desired endiyne **27** was produced. The structure of this important intermediate was de-



Scheme 4. McMurry coupling of acetylenic ketones.



Scheme 5. (3*E*)-3,4-di-*tert*-butylhex-3-en-2,5-dione (**4**) by a specific McMurry coupling.

rived from its spectroscopic data (see Experimental Section). It was confirmed qualitatively by X-ray structure determination, but was beset by disorder problems, which prevented satisfactory refinement.

Deprotection under harsher conditions than those above yielded hydrocarbon **5** in good yield (81%), and when desilylation and hydration were carried out in a one-pot reaction diketone **4** was produced in 39% yield. Using this improved route, **4**, a slightly yellow solid (m.p. 98 °C), was obtained in 50 to 100 mg lots, enough for further experimentation.

The Structure of (3*E*)-3,4-Di-*tert*-butylhex-3-en-2,5-dione (4)

Structure in Solution

The structure (conformation) of **4** in deuteriochloroform is revealed by its NMR spectra. In both the proton and the carbon spectra all signals are doubled, giving a first hint that **4** exists in two conformations. From the integration of the proton signals a conformer ratio of 2.8:1 is derived. That, in fact, we are dealing with rotamers, and not with constitutional isomers, is shown by the same connectivity in the C,H-correlation as well as the COLOC spectra. The protons of the *tert*-butyl groups (conformer I: δ = 1.15 ppm; conformer II: δ = 1.17 ppm) display couplings with the carbon atoms to which they are directly bound (conformer I: δ = 30.9 ppm; conformer II: δ = 34.1 ppm). Furthermore, the COLOC spectrum shows cross peaks of these hydrogen atoms through two bonds to the quaternary carbon atoms of the $(CH_3)_3C$ substituents (conformer I: δ = 34.6 ppm; conformer II: δ = 34.1 ppm, respectively) and through three bonds to the carbon atoms of the C–C double bond (conformer I: δ = 144.7 ppm; conformer II: δ = 145.5 ppm). The hydrogen atoms of the acetyl groups (conformer I: δ = 2.397 ppm; conformer: δ = 2.404 ppm) show direct couplings to the corresponding carbon atoms (C,H correlation, COLOC; conformer I: δ = 35.0 ppm; conformer II: δ = 34.8 ppm) and in addition cross peaks through two bonds with the signals of the carbonyl group (conformer I: δ = 208.0 ppm; conformer: δ = 208.4 ppm).

Because unique assignment of individual conformers on the exclusive basis of the above NMR experiment is not trivial, we resorted to theoretical methods. A combination of force-field simulations (conformational analysis) and quantum chemical calculations at the DFT level of theory was performed to assess the stability of the two conformers (see the Experimental Section for details). The result is shown in pictorial form in Figure 1.

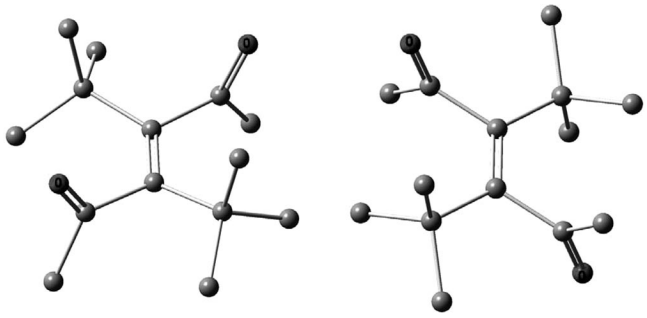
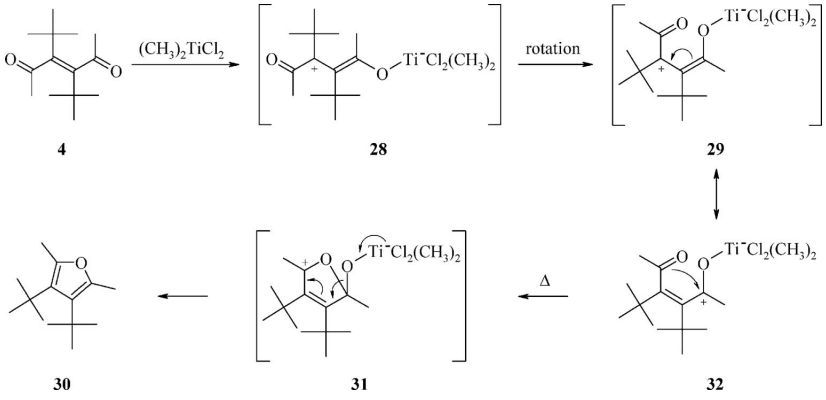


Figure 1. Optimized gas-phase structures for both rotamers of **4** at the M05–2X/tz level of theory (see text). Both conformers, the C_2 symmetric (left) and the C_i symmetric (right), exhibit approximately the same energy. The acetyl functions are rotated ca. 85° out of the plane defined by the central, slightly elongated double bond [1.338 Å C_2 rotamer; 1.340 Å C_i rotamer; experimental data[28] of the C_i rotamer: central double bond: 1.344 (3) Å, rotation of acetyl function: 78.71(6)°].

The M05–2X functional in combination with a polarized triple zeta basis set [6-311+G(d,p)][27] was used, because we are dealing with many noncovalent intramolecular interactions. It turned out that in the gas phase both isomers have nearly the same energy with a very tiny preference (0.05 kcal/mol) in favor of the C_i symmetric (*transoid*; Figure 1, right) conformer. Whereas this should lead to a 1:1 mixture in the gas phase (assumed that the barrier of interconversion is not too high), any slightly polar medium should favor the C_2 symmetric conformer, which has quite a substantial dipole moment of 4.3 debye computed at the same level of theory as mentioned above (Figure 1, left). A tiny difference in the energies of solvation for both rotamers of ca. 0.5 kcal/mol would be enough to explain the measured 2.8:1 equilibrium. Furthermore, we must include entropic contributions. As the C_2 symmetric conformer is chiral, both enantiomers contribute to the total free energy. The entropy of racemization again favors the C_2 symmetric conformer by ca. 0.41 kcal/mol at room temperature ($\Delta G = -RT\ln 2$). We hence propose that the major conformer in $CDCl_3$ is the *syn* conformer (*syn*-**4**).

In the solid state **4** prefers the *anti* conformation as reported by us in an earlier publication.[28] The acetyl functions are rotated ca. 80° out of the plane defined by the central, slightly elongated double bond [1.344(3) Å]. To avoid steric repulsion, the C–C(*tert*-butyl) single bonds are markedly longer [1.555(2) Å] than in noncrowded ethylenes.



Scheme 6. Dimethylation of (3*E*)-3,4-di-*tert*-butylhex-3-en-2,5-dione (**4**).

Cyclization of (3*E*)-3,4-Di-*tert*-butylhex-3-en-2,5-dione (4)

Application of the quaternization method of Reetz[9] to **4** produced a complex mixture from which we could isolate by silica-gel column chromatography only one defined product: fully alkylated furan derivative **30**, formed in 34% yield as a colorless, not very stable oil (Scheme 6).

The structure of **30** follows from its spectroscopic data (see Experimental Section) and in particular from its NMR spectral data {^{1}H NMR: δ = 1.43 (s, 18 H, *tert*-butyl), 2.34 ppm (s, 6 H, CH_3). ^{13}C NMR: δ = 143.8 (s, C-2), 129.1 (s, C-3), 33.7 [q, C(CH_3)$_3$], 31.8 [s, C(CH$_3$)$_3$], 17.6 ppm (q, CH_3)} and the mass spectrum with a molecular ion peak at m/z = 208 (42%). These signals were found to change with time when **30** was kept at room temperature for extended periods of time, accompanied by a color change from colorless via red to finally black.

We propose that **30** is generated from **4** by the steps illustrated in Scheme 6. The cyclization begins, as discussed in the literature,[9] with the formation of adduct **28** of dimethyl dichlorotitanium and **4**. In this complex the central double bonds between the olefinic carbon atoms is replaced by an allylic system, thus allowing rotation between C-3 and C-4. Whether a coplanar arrangement as indicated in **29** ↔ **32** is really achieved is doubtful, as it puts the two bulky substituents into the least favorable orientation. However, even if only partial rotation, that is, into an orthogonal arrangement of the two *tert*-butyl moieties, is reached, it brings the uncomplexed oxygen atom close to the developed positive charge, allowing cyclization as illustrated by the closure of **32** to **31**. In the final step, **31**→**30**, one oxygen atom of the substrate is transferred to the titanium atom.

Column chromatography also yielded a minute amount of an (impure) fraction that displayed a singlet at δ = 1.25 ppm in its proton spectrum, and a quartet in the ^{13}C spectrum at δ = 29.6 ppm; ^{13}C signals in the olefinic region could not be detected. Although in the mass spectrum a signal was registered with the correct mass for **1** [m/z = 252 (4.3%)], we consider our evidence as too weak to claim generation of the title compound. A peak of this mass was also observed in the GC–MS of the product mixture produced when dibromodi-*tert*-butylmethane was treated with sodium or potassium.[4,29]

Conclusions

Although the conditions for preparing **1** from **4** were, in our opinion, ideal (i.e., *trans* orientation of the two acetyl functions and an excellent, general method for producing *tert*-butyl groups from acetyl ketones[9]), our substrate preferred to cyclize to furan derivative **30**, evidently a consequence of the reduction of the double bond barrier in intermediate **28/29**. Because this abolishment is unavoidable in this approach to **1** we are terminating our efforts to reach this synthetic goal by alkylation of **3** or **4** or related compounds.

Experimental Section

General: Chromatography: TLC: Polygram Sil G/UV 254 (Macherey–Nagel); CC: Kieselgel 60 (70–230 mesh, Merck) and aluminum oxide (neutral, activity III–IV, Woelm). M.p. Kofler hot stage (uncorr.). ^{1}H and ^{13}C NMR: in deuteriochlorform (int. TMS), Bruker AC 200 (200.1 and 50.3 MHz, resp.), Bruker AM 400 (400.1 and 100.6 MHz). IR: KBr pellets or film (neat), Nicolet 320 FT-IR. UV/Vis: if not noted otherwise in acetonitrile, Beckman UV 5230. MS: EI at 70 eV, Finnigan MAT 8430. GC–MS: fused silica capillary column, Carlo–Erba HRGC 5160/Finnigan MAT 4515 (EI, 40 eV).

Computational Details: The Merck Molecular Force Field (MMFF) implemented in the MacroModel software package (MacroModel 9.0; Maestro 8.0 interface) was used in a first step in order to scan the conformational space by a Monte Carlo torsional sampling procedure. The resulting two stable conformers were further optimized by quantum chemical methods. We employed the M05–2X meta hybrid functional and a 6-311+G(d,p) basis set implemented in the Gaussian03 program, characterizing the two stationary points as minima by frequency calculations.

Bromine Addition to 8: To a solution of **8** (75.0 g, 0.45 mol) in carbon tetrachloride (250 mL) at 0 °C was added bromine (72.3 g,

23.3 mL, 0.452 mol) in carbon tetrachloride (100 mL) keeping the temperature at 0 °C. After stirring for 1 h at this temperature, the solvent was removed in vacuo; compound **9** precipitated and was removed by vacuum filtration. After washing with cold petroleum ether, adduct **9** (60.4 g, 41%) was obtained as slightly yellow needles. M.p. 92–93 °C. ^{1}H NMR (200.1 MHz): δ = 1.42 [s, 18 H, $(CH_3)_3$-C], 4.1–4.9 (m, 4 H, CH_2) ppm. ^{13}C NMR (50.3 MHz): δ = 31.3 (s, C_q), 32.0 (q, CH_3), 34.8 (t, CH_2), 110.8 (s, olefinic C) ppm. IR (KBr): $\tilde{\nu}$ = 2965 (s), 1210 (s), 634 (s) cm^{-1}. MS: *m*/*z* (%) = 326 (1.4) [M$^+$], 247 (1.1), 165 (4.5), 83 (100), 57 (46).

Preparation of 10

Preparation of Amberlyst A-26 in the Na(CO$_3$)$^-$ Form: Amberlyst A-26 (chloride form, 34 g) was placed in a chromatography column and sodium carbonate solution (1 M, 2 L) was slowly passed through. Subsequently the ion exchange resin was washed with methanol, acetone, and diethyl ether and dried for 2 h under high vacuum. Yield: 17 g A-26 in the sodium carbonate form.

Hydrolysis: To a suspension of A 26 (ca. 100 g) in THF (250 mL) was added **9** (12.3 g, 38 mmol), and the mixture was stirred vigorously for 6 h at room temperature. The resin was removed by filtration and washed carefully with dichloromethane and methanol. The combined organic washings were concentrated to ca. 50 mL, and the solution was placed into an ice box for crystallization to yield **10** (2.2 g, 18%) as colorless plates. M.p. 152 °C. ^{1}H NMR (400.1 MHz): δ = 1.33 [s, 18 H, $(CH_3)_3C$], 4.39 (m, 4 H, CH_2) ppm. ^{13}C NMR (100.6 MHz): δ = 32.77 (q, CH_3), 36.56 (s, C_q), 60.85 (t, CH_2), 147.49 (s, –C=) ppm. IR (KBr): $\tilde{\nu}$ = 3286 (br. s), 2873 (s) 1624 (m), 1399 (s), 1367 (s) cm^{-1}. MS (70 eV, CI, NH_3+): *m*/*z* (%) = 200 (64) [M$^+$], 183 (100), 144 (26), 58 (8).

Swern Oxidation of 10: A solution of oxalyl chloride (2.45 g, 1.68 mL, 19.3 mmol) in anhydrous THF (40 mL) was cooled to –60 °C and a solution of DMSO (3.2 g, 2.98 mL, 42 mmol) in anhydrous dichloromethane (40 mL) was added within 15 min. After stirring for 10 min, a solution of **10** (1.40 g, 7 mmol) in dry dichloromethane (100 mL) was added over 40 min. When the addition was complete the mixture was stirred for additional 10 min, followed by the addition of triethylamine (19.9 g, 24.7 mL, 0.177 mol). After stirring for 15 min, the mixture was warmed to room temperature, water was added, and the organic phase carefully washed with water. The dried (sodium sulfate) organic phase was concentrated to a few mL and the remainder was purified/separated by column chromatography on alumina (petroleum ether/diethyl ether, 9:1) to yield **11** (1.0 g, 73%) as a yellow oil. ^{1}H NMR (400.1 MHz): δ = 1.17 [s, 18 H, $(CH_3)_3C$], 10.28 (s, 2 H, CHO) ppm. ^{13}C NMR (100.6 MHz): δ = 31.24 (q, CH_3), 36.71 (s, C_q), 146.77 (s, –C=), 200.21 (d, *C*HO) ppm. IR (KBr): $\tilde{\nu}$ = 2968 (s), 2927 (s), 1752 (s), 1592 (m) cm^{-1}. UV: λ (log ε) = 222 nm (3.81). MS: *m*/*z* (%) = 196 (10) [M$^+$], 195 (64), 167 (26), 139 (54), 57 (100). For the attempted methylation of **11**, see Results and Discussion.

***tert*-Butylation of 2,5-Dichloro-hex-3-yne (14a, Mixture of Isomers):** To a suspension of magnesium (16.4 g, 0.68 mmol) in anhydrous THF (40 mL) was added a few drops of *tert*-butyl chloride, followed by a few drops of 1,2-dibromoethane for activation. After the reaction was started by slight warming, the main fraction of *tert*-butyl chloride (73 mL, 62.5 g, 0.68 mmol) in THF (180 mL) was added at such as rate as to keep the mixture under gentle reflux. To complete the Grignard formation, the solution was stirred for 12 h at room temperature, and the now-clear, black solution was transferred into a dropping funnel. At –35 °C, the Grignard reagent was added to a mixture of cuprous bromide (0.385 g, 2.68 mmol) and 2,5-dichloro-hex-3-yne.[15] After stirring for an additional 3 h at 0 °C, the mixture was hydrolyzed under ice cooling. After careful extraction with ether the organic phases were combined, dried (sodium sulfate), and the solvents were removed in vacuo. The remaining oil was purified by column chromatography (silica gel) to yield a mixture of **15** and **16** (9.3 g, 44%). Further purification by silica gel chromatography provided two main fractions: fraction 1, 3.2 g, consisting largely of **16**, and fraction 2, 5.9 g of a mixture of **15** (39%) and **16** (61%). Data for **15**: ^{1}H NMR (200.1 MHz): δ = 1.09 [s, 18 H, $(CH_3)_3C$], 1.47 (d, ^3J = 6.74 Hz, 6 H, CH_3), 5.58 (q, ^3J = 6.74 Hz, 2 H, =CH–) ppm. Data for **16**: ^{1}H NMR (200.1 MHz): δ = 1.02 [s, 9 H, $(CH_3)_3C$], 1.12 [s, 9 H, $(CH_3)_3$-C] 1.62 (d, ^3J = 6.80 Hz, 3 H, CH_3), 1.82 (d, ^3J = 6.60 Hz, 3 H, CH_3) 4.98 (q, ^3J = 6.80 Hz, 1 H, =CH–), 5.40 (q, ^3J = 6.60 Hz, 1 H, =CH–) ppm. All other spectroscopic data as well as the preparation of **15** and **16** from diacetates **14b**[16] are given in ref.[18] For the attempted bromine addition to **15** and **16**, see the Results and Discussion.

Hydration of the Mixture of 5 and 23: To the reagent mixture prepared from water (10 mL), mercuric sulfate (90 mg, 0.3 mmol), and concentrated sulfuric acid (0.2 mL) was added at 60 °C a solution of hexendiynes **5** (91 mg, 0.48 mmol) and **23** (58 mg, 0.23 mmol) in THF (5 mL), prepared from **20** as described in the literature.[24] After stirring at 60 °C for 3 h, the mixture was cooled to room temperature, water (20 mL) was added, and the product mixture isolated by careful extraction with diethyl ether. The organic phases were combined, dried (sodium sulfate), and the solvent was removed in vacuo. The remaining yellow solid was separated by column chromatography (silica gel, pentane/diethyl ether, 10:1) and two fractions were isolated. Several recrystallizations (pentane/methanol/dichloromethane) of fraction 1 afforded **4** (40.0 mg, 37%) as pale-yellow needles. Fraction 2 afforded **24** (20.0 mg, 36%) as a colorless oil. Data for **4**: M.p. 98 °C. ^{1}H and ^{13}C NMR: see Results and Discussion. IR (KBr): $\tilde{\nu}$ = 2967 (s), 1686 (s), 1656 (m), 1470 (m), 1372 (s), 1365 (s) cm^{-1}. UV: λ (log ε) = 218 nm (3.21, sh.). MS: *m*/*z* (%) = 224 (12) [M$^+$], 209 (4), 181 (100), 167 (24), 125 (32), 57 (18), 43 (71). $C_{14}H_{24}O_2$ (224.34): calcd. C 72.74, H 10.77; found C 72.54, H 10.60. HRMS: calcd. for $C_{14}H_{24}O_2$ 224.1776; found 224.1770. Data for **24**: ^{1}H NMR (400.1 MHz): δ = 0.14 [s, 9 H, $(CH_3)_3Si$], 1.26 [s, 9 H, $(CH_3)_3C$], 1.33 [s, 9 H, $(CH_3)_3$-C], 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR (100.6 MHz): δ = 207.7 (s, C-2), 168.0 (s, C-3), 119.4 (s, C-4), 113.3 (s, C-6), 79.4 (s, C-5), 35.9 (s, C_q), 33.7 (q, CH_3), 30.6 (q, CH_3), 29.0 (q, CH_3), 28.6 (s, C_q), –0.4 ppm. [(CH_3)$_3$Si]. IR (film): $\tilde{\nu}$ = 2968 (s), 1699 (s), 1656 (m), 1471 (s), 1377 (s), 1363 (s) cm^{-1}. UV: λ (log ε) = 244 nm (3.89). MS: *m*/*z* (%) = 281 (12) [M$^+$], 221 (74), 73 (100), 57 (22). HRMS: calcd. for $C_{17}H_{33}OSi$ 281.2301; found 281.2318.

1-Triisopropylsilyl-4,4-dimethyl-pent-1-yn-3-one (26): To a suspension of aluminum trichloride (1.35 g, 10.1 mmol) in pentane (15 mL) was added at 0 °C under an atmosphere of nitrogen a solution of **25** (2.14 g, 8.4 mmol)[26] and **19** (1.07 g, 1.09 mL, 8.8 mmol) in pentane (10 mL). After stirring for 45 min at 0 °C and 1 h at room temperature, the reaction mixture was poured onto ice (6 g). The organic phase was separated, and the aqueous phase was extracted several times with pentane. The combined organic phases were washed with saturated. hydrogen carbonate solution and dried (sodium sulfate). After solvent removal, the remaining brown oil (2.96 g) was purified by silica gel column chromatography (pentane/diethyl ether, 30:1) to afford **26** (2.05 g, 91%) as a slightly yellow oil. ^{1}H NMR (400.1 MHz): δ = 1.05–1.18 [m, 21 H, $(C_3H_7)_3$-Si], 1.22 [s, 9 H, $(CH_3)_3Si$] ppm. ^{13}C NMR (100.6 MHz): δ = 193.7 (s, C-3), 102.3 (s, C-2), 96.6 (s, C-1), 44.5 (s, C_q), 26.0 [q, (CH_3)$_3$-Si], 18.4 (q) and 11.0 [d, $(C_3H_7)_3Si$] ppm. IR (film): $\tilde{\nu}$ = 2963 (s), 2144 (m), 1672 (s), 1477 (s), 1392 (s), 1367 (s) cm^{-1}. UV: λ (log ε) = 234 nm (3.79). MS: *m*/*z* (%) = 265 (8) [M$^+$], 251 (100), 223 (58),

209 (40), 181 (18), 85 (26), 57 (12), 43 (24). $C_{16}H_{30}OSi$ (266.50): calcd. C 72.11, H 11.35; found C 72.11, H 11.41.

McMurry Coupling of 26: To a mixture of titanium tetrachloride (1.13 g, 0.65 mL, 6.0 mmol) and anhydrous tetrahydrofuran (15 mL) was added under an atmosphere of nitrogen and ice cooling zinc dust (714 mg, 10.9 mmol) and anhydrous pyridine (370 mg, 0.38 mL, 4.7 mmol). A solution of ketone **26** (1.25 g, 4.7 mmol) in anhydrous THF (8 mL) was added, and the reaction mixture was stirred for 30 min at 0 °C followed by further stirring at room temperature for 2 h. For workup, the reaction mixture was hydrolyzed (10% aq. potassium carbonate solution, 25 mL), the black precipitate was removed by filtration through a Büchner funnel and washed with pentane (100 mL). The precipitate was dissolved with dilute hydrochloric acid, and the resulting aqueous phase was thoroughly extracted with diethyl ether. After neutralization with hydrogen carbonate solution, the organic phases were united and dried (sodium sulfate). The solvent was removed in vacuo and the resulting yellow oil (1.13 g) was purified by silica gel column chromatography to afford **27** (0.73 g, 62%) as colorless needles. M.p. 48 °C. ^{1}H NMR (400.1 MHz): δ = 1.10 [m, 42 H, $(C_3H_7)_3Si$], 1.39 [s, 18 H, $(CH_3)_3C$] ppm. ^{13}C NMR (100.6 MHz): δ = 138.7 (s, C-3), 108.8 (s, C-2), 106.8 (s, C-1), 35.7 (s, C_q), 30.0 [q, $(CH_3)_3C$], 18.6 (q) and 11.5 [d, $(C_3H_7)_3Si$] ppm. IR (KBr): $\tilde{\nu}$ = 2957 (s), 2127 (m), 1463 (s), 1392 (s), 1362 (s) cm^{-1}. UV: λ (log ε) = 312 (4.38), 300 (4.42), 296 (4.42), 288 nm (4.34, sh.). MS: *m*/*z* (%) = 500 (40) [M$^+$], 457 (100), 157 (20). HRMS: calcd. for $C_{32}H_{60}Si_2$ 500.4234; found 500.4218. $C_{32}H_{60}Si_2$ (500.92): calcd. C 76.72, H 12.07; found C 76.78, H 12.01.

Desilylation of 27: To a solution of tetrabutylammonium fluoride (TBAF) in THF (8 mL, 8.0 mmol) was added water (0.2 mL, 200 mg, 11.1 mmol) and diacetylene **27** (0.951 g, 1.90 mmol). The mixture was stirred for 44 h at room temperature, diethyl ether was added, and the organic phase was washed carefully with water. After drying (sodium sulfate), the solvent was removed in vacuo, and the residue obtained was purified by column chromatography (silica gel, pentane) to afford **5** (0.290 g, 81%) identified by spectral comparison with the authentic material.[24]

Desilylation/Hydration of 27: As described above, **27** (0.150 g, 0.30 mmol) was desilylated; however, to the reaction mixture were added a few crystals of mercuric sulfate and concentrated sulfuric acid (0.2 mL). After additional water (10 mL) was added, the mixture was heated to reflux for 3.5 h. Extractive workup resulted in a yellow solution (0.171 g), which by column chromatography on silica gel yielded **4** (26 mg, 39%), identical in its spectroscopic properties with the data discussed above and in the main section.

Methylation of 4 with Dimethyltitanium Dichloride: A solution of dimethylzinc in toluene (2 M, 3.93 mL, 7.87 mmol) was injected into anhydrous dichloromethane (10 mL) at –12 °C under an atmosphere of nitrogen. To this solution was added titanium tetrachloride (0.87 mL, 1.49 g, 7.87 mmol) at such a rate as to hold the temperature at –12 °C. After stirring for 30 min the reaction mixture was cooled to –50 °C and a solution of **4** (55 mg, 0.25 mmol) in anhydrous dichloromethane (10 mL) was added. The mixture was stirred overnight while its temperature increased to ambient temperature. For workup, the product mixture was poured into ice water (250 mL), the aqueous phase was thoroughly extracted with diethyl ether, and the combined organic fractions were dried with sodium sulfate. After solvent removal by rotary evaporation the yellow residue was purified by column chromatography (silica gel, pentane) to provide two fractions: the first fraction afforded **30** (17 mg, 34%) as a colorless oil and a second fraction afforded a minute amount (<5 mg) of sample as a mixture of components. Some spectroscopic data not contradicting **1** as being part of this mixture are discussed in the Results and Discussion section. Data for **30**: ^{1}H NMR (400.1 MHz): δ = 1.43 [s, 18 H, $(CH_3)_3C$], 2.34 (s, 6 H, CH_3) ppm. ^{13}C NMR (100.6 MHz): δ = 143.8 (s, C-2), 129.1 (s, C-3), 33.7 [q, $(CH_3)_3C$], 31.8 [s, $(CH_3)_3C$], 17.6 (q, CH_3) ppm. IR (film): $\tilde{\nu}$ = 2957 (s), 1649 (w), 1470 (s), 1379 (s), 1364 (s), 1051 (s) cm^{-1}. UV: λ (log ε) = 266 (2.52), 216 nm (3.38, sh.). MS: *m*/*z* (%) = 208 (42) [M$^+$], 193 (100), 151 (20), 57 (25).

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