Sterically Congested Molecules, 17[◇]

Novel Syntheses of α,α,β-Tri-*tert*-butyl Compounds

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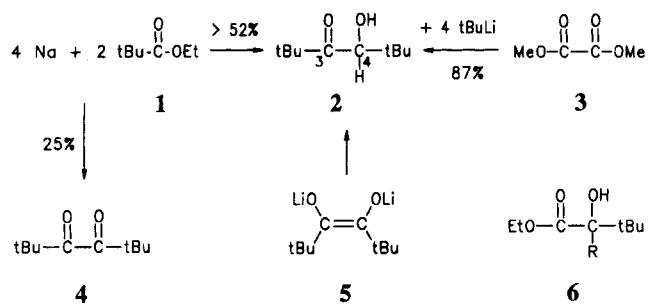
Pivaloin (**2**), prepared from ethyl pivalate (**1**) or from dimethyl oxalate (**3**), reacts with *tert*-butyllithium by reduction (45% of **10**) and addition (45% of **9**), whereas the corresponding Barbier variant takes a different course. Productive transformations of the α,α,β-tri-*tert*-butyl glycol **9** lead to α,β,β-tri-*tert*-butylethanone (**17**, overall 4 steps), or α,α,β-tri-*tert*-butylethene (**20**, 3 or 4 steps), or α,β,β-tri-*tert*-butyl-β-hydroxyethanone (**19**, 3 steps, also by Grignard addition to bipivaloyl **4**). Steric congestion is assessed by searches for restricted internal rotation.. The alkene **20** and its epoxide **27** are studied with respect to NMR assignments and chemical degradation.

We describe short routes to several α,α,β-tri-*tert*-butyl compounds which are either new or have been previously prepared only by long or inefficient procedures. Some of their properties are reported to show how intramolecular mobility and chemical reactivity may depend on the overcrowding caused by three *tert*-butyl ("tBu") groups.

A. Preparation and *tert*-Butylation of Pivaloin

Pivaloin (**2**) is the common source of all material described in this work but is commercially no longer available[2]. For its preparation from ethyl pivalate (**1**) and sodium metal, the leading references[3] are rather laconic and do not mention the considerable amount (ca. 25%) of yellow bipivaloyl (**4**) generated in the process. We preferred to run this acyloin condensation on large scales in ether[3a] to provide for an easier separation of **4**[4] and purification of **2** that yielded at least 52% of colourless pivaloin, with the ^{1}H NMR doublet splitting typical[5] of the very clean material. Diketone **4** was certainly formed by a protolytic disproportionation of its radical anion that would have either been present as one of the primary products or perhaps resulted from rapid oxidation[6] of the expected[7] enediolate **5**. Trapping of **5** with chlorotrimethylsilane did not appear to be helpful in view of a much lower reported[7] yield.



For a quicker but more expensive alternative small-scale preparation of pivaloin (**2**), we recommend the strongly exothermic addition of dimethyl oxalate (**3**) as a dilute ether solution to four equivalents of (pentane-diluted) *tert*-butyllithium. This method is more productive than the original procedure[8] using diethyl oxalate and does not give bipivaloyl (**4**). It appears inevitable to conclude that the enediolate **5** had been formed here by reduction by part of the *tert*-butyllithium. We have also confirmed the interesting observation[9] that the corresponding Barbier reaction with diethyl oxalate in ether affords very little pivaloin but mainly monoesters like **6** (R = H or tBu).

Access to the family of α,α,β-tri-*tert*-butyl compounds was achieved by the hitherto unexplored interaction of **2** in ether with *tert*-butyllithium. Equimolar amounts produced only the expected alkoxide **7** at 0°C, proven by trapping as the known[10] silyl ether **8**. Therefore, **7** was also the first intermediate when we added 2.85 equivalents of *tert*-butyllithium to pivaloin (**2**) in ether at −70°C. The conversion became fast at 0°C and was terminated at room temperature. Separation of **2** (8%, presumably from unreactive **5**) from the two diols **9** and **10** (45% each) showed that addition and reduction had occurred with equal rates and were faster than the enolization of **2**. If the reaction was carried out with **2** in pentane solution, reduction became dominant (56% of **10** isolated) over addition (ca. 30% of **9**). Trying to save one equivalent of *tert*-butyllithium, we failed in the following two attempts: Use of the silylated pivaloin (**8**) in ether gave also mainly **10**, along with other substances, but no adduct **9**, whereas the potassium analog of alkoxide **7** (from KH) reacted exothermically even at −28°C, with evolution of gases on warm-up, and furnished **2**, **9** and **10** in the usual mixture but together with unidentified products. With two equivalents of potassium hydride in ether, the less soluble analog of **5** was generated, which was found to be inert toward *tert*-butyllithium for hours at room temperature, returning **2** quantitatively upon work-up.

[◇] Part 16: Ref.[1].

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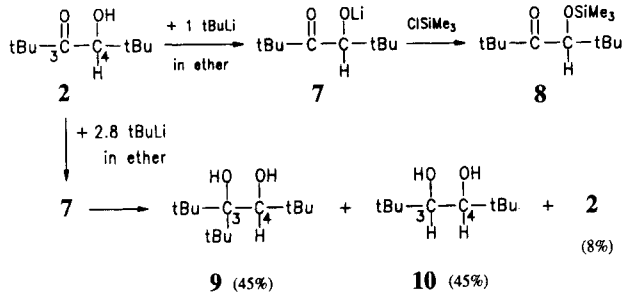
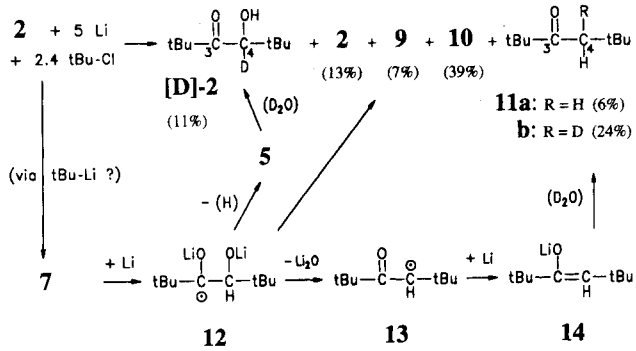


The depicted interaction of **2** with *tert*-butyllithium exhibited no signs of a single-electron-transfer (SET) mechanism, as indicated by the following, quite dissimilar product pattern: Searching for a cheaper route from **2** to glycol **9** under Barbier-type conditions (Li metal and *tert*-butyl chloride) in THF and working-up with deuterium oxide, we recovered a well-defined mixture of 24% of **2** (45% 4-deuterated) and only 7% of **9**, but 39% of **10** and 30% of the dehydroxylated product[11–16] **11a/b** (80% 4-monodeuterated, $^2J_{HD}$ = 2.7 Hz).

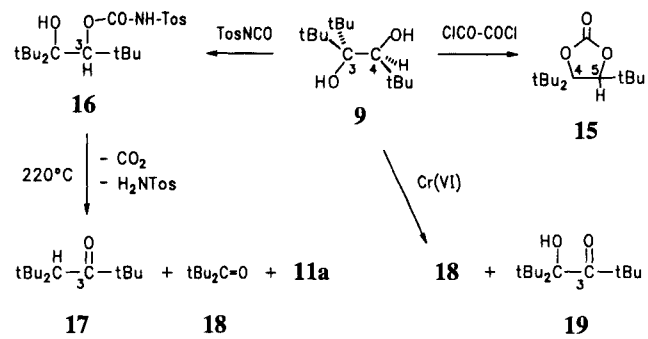


A speculative rationalization, as displayed beneath the product formulae, is based on our observation of two clearly separated phases of reagent consumption: An initial period of *tert*-butyllithium formation at −15°C appeared to terminate with the complete conversion of pivaloin to its anion **7**. A subsequent reaction period commenced well above 0°C (i.e., unlike the behaviour of preformed *tert*-butyllithium in ether), probably corresponding to production of the ketylate (radical anion) **12** which might then have participated in radical addition and hydrogen-transfer reactions to furnish **9** and **10** together with the enediolate **5** (the precursor of [D]-**2**). The more characteristic reaction mode of **12** is elimination of Li_2O to give presumably **13** as a member of a known class of radicals formed in a similar elimination from 1,2-dihydroxy radicals[17]. Under the present reductive conditions, **13** was probably converted not to the ketone **11a** (that would[15] have produced 2,2,5,5-tetramethyl-3-hexanol) but rather to the enolate **14** (and hence **11b**). This proposal is supported by the formation of *tert*-butyl neopentyl ketone[11–16] (**11a**) in the slow (hence incomplete[15]) dehydroxylation of pivaloin with lithium in ammonia.

B. Properties and Transformations of α,α,β-Tri-*tert*-butyl Glycol (9)

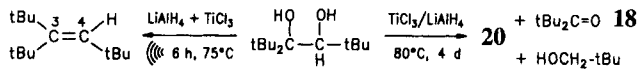
The generation in our procedure of α,β-di-*tert*-butyl glycol **10**, known[18,19] as a diastereomeric but readily separable[5] mixture, is of limited interest because pivaloin can be reduced in simpler ways[19]. However, the hitherto unknown α,α,β-tri-*tert*-butyl glycol (**9**) emerged as a useful source for three known but difficultly accessible subtances (**17**, **19**, **20**) as described below. Two of its *tert*-butyl substituents, certainly the diastereotopic ones at C-3, rotate against intramolecular repulsions with a barrier $\Delta G^{\neq} = 11.7\ (\pm 0.3)$ kcal/mol, as shown by the ^{13}C-NMR anisochronicities of their 6 methyl groups in a cooled chloroform solution. A single, sharp infrared O–H stretching vibration (3645 cm^{-1}) in CCl_4 solution and two small δ(^{1}H) values for the two hydroxy groups indicate very little intramolecular hydrogen bonding in **9**. Nevertheless, this glycol may be forced into the *O,O*-cisoid conformation of the cyclic carbonate **15**, formed as the sole product from **9** in a slow ring-closure reaction with oxalyl chloride or faster with oxalyl bromide, whereas thionyl chloride or bromide, PCl_3 (70°C, 5 h), or refluxing dimethyl carbonate (46 h with $NaOCH_3$) did not react. The monomeric constitution of carbonate **15** followed from osmometry, spectroscopic data, and hydrolysis to **9**. Restricted *tert*-butyl rotation was apparent even at ambient temperature by broadening of one of the 3 strong NMR singlets (^{1}H, ^{13}C). In contrast to the parent glycol **9**, the $^{13}CH_3$ signals of two *tert*-butyl groups remained sharp at −61°C in $CDCl_3$ solution while those of the third *tert*-butyl split into three one-carbon absorptions, this time with the slightly larger rotational barrier $\Delta G^{\neq} = 12.2\ (\pm 0.3)$ kcal/mol.

The thermal decomposition of **15** was quite sluggish at 230–260°C (reflux conditions under Ar), forming isobutene and 2-methylpropane. On the other hand, treatment of glycol **9** with tosyl isocyanate[20] provided the *N*-tosyl carbamate **16** which could not be purified completely[21] but produced 60% of the known ketone **17** rapidly at 220°C, along with small amounts of ketone **11a** and of di-*tert*-butyl ketone (**18**). The conditions of this formal dehydration of glycol **9** indicate that the carbonate **15** cannot be an intermediate. As **16** does not appear to permit a direct conversion, its thermolysis mechanism remains undefined; the constitution of **16** was based on ^{1}H- and ^{13}C-NMR comparisons with **9** (see also **25**). Our preparation of α,β,β-tri-*tert*-butylethanone **17** is short (4 steps) and productive if recrystallized carbamate **16** is used, whereas in the published multi-step syntheses[13,22–25] we could not discover b.p. or m.p. data for **17**. Our further attempts to prepare **17** even more directly by a thermal dehydration[26] of **9** led to slow decomposition.



Oxidation of the glycol **9** is prone to the undesired relief of steric congestion by scission of the central C–C bond: Di-*tert*-butyl ketone (**18**) was found as the main product after treatment of **9** with conc. nitric acid, and milder oxidants like pyridinium dichromate[27] or an attempted "co-oxidation"[28] led to incomplete conversion if the formation of **18** was avoided. A reliable procedure was developed by titration of **9** with chromium(VI)[3b] under mitigated conditions, furnishing α,β,β-tri-*tert*-butyl-β-hydroxyethanone (**19**) in crude yields above 79%, and 62–72% after purification (that is, 20–23% over 3 steps). This acyloin[29] had been isolated in low yield from the product mixture[9] of a Barbier raction with diethyl oxalate, and was postulated[8a,b] later as a liquid by-product formed with *tert*-butyllithium. It was also separated by vpc[23] as a minor component (15%) from its mixture with pivaloin (**2**) and bipivaloyl (**4**), recovered from the reaction of **4** with *tert*-butyllithium (6 equivs.) in pentane. Exploiting the latter approach, we found it more convenient to treat **4** with *tert*-butylmagnesium chloride in ether and to separate 17% of pure acyloin **19** from 43% of pure pivaloin (**2**); this short and simple method constitutes a competitive strategy to prepare **19**, provided that **4** is available.

Reduction of the glycol **9** provided tri-*tert*-butylethene (**20**) by two methods. As the shorter but more intricate alternative we can recommend the direct bis(dehydroxylation) of **9** by the low-valent titanium species ClTiH[30] wich is generally suitable[31] for this purpose. We applied first the commercial reagent, modified to a $TiCl_3/LiAlH_4$ ratio of 4:2. This method required prolonged refluxing (at least 85 h) for 90% conversion and proved somewhat unreliable[32] for our task, because less than the necessary amount of ClTiH (deliberate or in aged batches) favoured the scission of glycol **9** to form di-*tert*-butyl ketone (**18**) and some neopentyl alcohol (**21**). This cleavage was obviously promoted by the steric congestion present in **9** and may involve a redox disproportionation. The purportedly more reliable $TiCl_3$ complex of 1,2-dimethoxyethane was also used in this solvent in the presence of Zn/Cu couple[32] or of lithium metal[33] but gave only or mainly the ketone **18** after work-up. It is therefore advisable to generate the ClTiH[30] reagent in situ, and the fastest and most convenient procedure was found to be the ultrasonication[34] of **9** in hot THF with 4 equivalents of $TiCl_3$ and 2 equivalents of $LiAlH_4$ for more than 6 h, affording at least 74% of **20**.

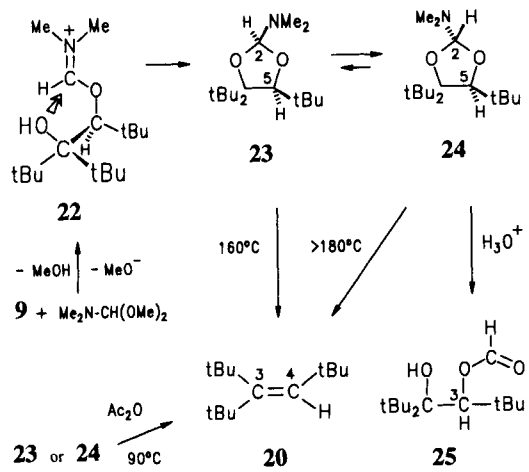


20 **9** **21**

The second route to olefin **20** is easier but requires two steps. Cyclization[35] of glycol **9** in the refluxing dimethyl acetal of dimethylformamide gave 2-dimethylamino-1,3-dioxolane as the pure *cis* isomer **23** (81%). It is the reasonable product under kinetic control if the presumed intermediate **22** cyclizes from a conformation that keeps its iminium group remote from all three *tert*-butyl substituents. Under thermodynamic control, the liquid **23** is epimerized to the more favourable *trans* isomer **24**, unpleasantly fast by a trace of acid, as observed when **23** in an aged specimen of $CDCl_3$ formed >95% of **24** overnight. At 143°C the thermal equilibrium could be established by heating either **23** or **24** for 30 min to give a 16:84 ratio.

Pure crystalline **24** was first obtained by dissolving **23** in dilute acid and quick recovery by alkalisation. However, a 30 min period in 2 M HCl was sufficient to hydrolyse **24** completely to the formate **25**. Its constitution followed from the observation of a small ^4J coupling constant between 3-H and the formyl proton. It was not possible to generate **25** independently from the glycol **9** in hot formic acid as this led to unidentified products of carbonium ion rearrangements.

The *trans* orientation in **24** was recognized from the NOESY ($^1H,^1H$) correlation of 5-H and NMe_2 with the same, central *tert*-butyl singlet (hence called the 4c-tBu). The upfield singlet was correlated with 2-H but not with 5-H and thus belongs to 4t-tBu. A HETCOR experiment identified the strongly broadened ^{13}C methyl resonance as being due to 4t-tBu.



Tri-*tert*-butylethene (**20**) was released from the *cis*-dioxolane **23** maintained at 160°C for 24 h. This known[35] mode of thermolysis was not susceptible to base catalysis (Et_3N) in our case. However, the simultaneously forming *trans*-dioxolane **24** produced **20** much more slowly even at 180°C (≥24 h), not unexpectedly in view of its thermodynamic preference. Therefore, it was more profitable to heat crude **23** or **24** in acetic anhydride[35] at 90°C and to separate **20** from the accompanying glycol **9** and formate **25** by a short-column chromatography.

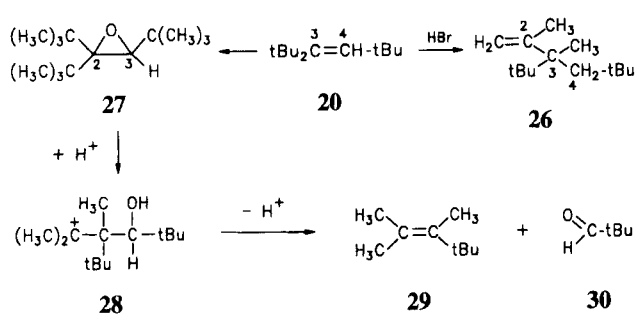
C. Tri-*tert*-butylethene and Its Epoxide

Our new syntheses outlined above afford tri-*tert*-butylethene (**20**) in 3 or 4 steps with overall yields of ca. 24%. Previous routes[23,26,36,37] have always generated mixtures of **20** with rearrangement products, demanding tedious methods of purification. Probably due to its limited availability, **20** was hardly ever investigated[23,38]; not even its b.p. was

reported, and especially the published ^{13}C-NMR shifts[39,40] show large and irregular deviations from our values which were measured at several magnetic field strengths. We observed that the *tert*-butyl groups of **20** exhibit no hint of NMR decoalescence at −63°C and hence rotate rather freely; the otherwise rigid skeleton of **20** merits an unequivocal assignment of its NMR parameters which was achieved as follows.

Designating the three methyl groups *trans* to CH_3-6 in 3-*tert*-butyl-2,2,5,5-tetramethyl-3-hexene (**20**) as CH_3-1t, and those in the *cis* position as CH_3-1c, we learned from the ^{1}H,^{1}H-NOESY interactions that the low-field methyl-proton signal belongs to CH_3-1c, because this was correlated with both upfield signals but was the only one that had no relation to the olefinic 4-H. The sequence of decreasing δ values (upfield direction) is CH_3-1c > CH_3-6 > CH_3-1t for ^{1}H and ^{13}C nuclei, as recognized by a HETCOR experiment; it became unequivocal when the CH-coupled spectrum revealed an additional ^3J (4.2 Hz) to 4-H solely for CH_3-6. Selective methyl-proton decoupling confirmed this and gave also the CH coupling constants of 4-H with the two C-2 nuclei, $^3J(cis)$=8 Hz and $^3J(trans)$=10.5 Hz, in accord with data[41,42] for similarly congested molecules. C-5 was always a singlet under selective methyl decoupling, and the δ sequence was established as C-2t > C-2c > C-5. Taking the olefinic ^1J(CH)=143.5 Hz as an indicator of steric compression[39], we conclude by comparisons with known congested models[39,42] that **20** is not excessively strained. Whilst this ^1J(CH) agrees excellently with the published[39] value, **20** does not confirm a decreased $^1J(^{13}CH_3)$ parameter as described[43] for *cis*-1,2-di-*tert*-butylethene.

Since ethene without activating substituents may be converted[44,45] to vinyllithium and lithium hydride by catalyzed addition of elemental lithium, we tried a similar addition of Li metal to **20**. However, **20** remained unchanged after prolonged ultrasonication in hot THF, even in the presence of the electron-transfer catalysts[44] biphenyl (blue solution) or naphthalene. Electrophilic bromination of **20** is known to produce an intimidating mixture[23]; we obtained similarly deterrent results by bromination of **20** in a chloroform solution saturated with Et_4NBr, by treatment with pyridinium tribromide, and with *N*-bromosuccinimide under polar conditions at −30°C or under peroxide induction at +70°C. Intractable mixtures were also formed with gaseous[46,47] bromine, whereas sodium hypobromite did not react under phase-transfer catalysis. In some of these experiments the rearranged olefin **26** was identified by its ^{1}H-NMR spectrum[23]. We could generate it as the main product from a prolonged treatment of **20** with a trace of conc. HBr in $CDCl_3$ solution, and we observed by ^{1}H and ^{13}C NMR some restriction of internal rotation in **26**.



27 **20** **26**

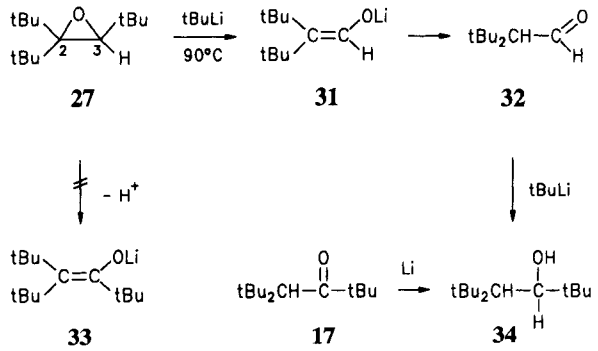
28 **29** **30**

The preceding spectral and chemical properties serve to show that **20** is not overly strained but tends to diminish internal pressure with the help of electrophilic catalysts. On the other hand, epoxidation of **20** occurred with surprising ease and reliability to give unknown oxirane **27**, provided that proper attention was paid to the product lability towards acids. Thus 3-chloroperoxybenzoic acid had to be applied at −11°C to attain 89% of undistilled **27**. It was methodically safer to use the hexahydrate of magnesium monoperoxyphthalate[48] together with Aliquat-336 as a necessary phase-transfer catalyst, whereby an excess of the oxidant should be employed at +50°C to assure an acceptably fast and almost quantitative conversion of the congested olefin **20** to **27**.

As the oxirane **27** is not stable in commercial $CDCl_3$, its ^{13}C-NMR spectra were recorded in [D_8]toluene solution, and the ^{1}H-NMR spectrum also in CCl_4. The sequences of δ values were identical with those of the open-chain analog **9**, but in terms of the different labelling now in the order 2-*cis* > 3-tBu > 2-*trans* for the methyl groups (^{1}H as well as ^{13}C) and 2-*trans* > 2-*cis* > 3-C for the quaternary tBu-^{13}C nuclei. These assignments were made from selectively decoupled $^{13}C\{CH_3\}$ spectra by determining the following relationships. Weak irradiation of the central (δ=1.10) methyl-proton singlet (3-tBu) simplified its ^{13}C absorption to a quadruplet of narrow doublets (^3J=3.5 Hz to 3-H) and removed the ^3J splitting from C-3 (now a sharp ^1J doublet); simultaneously, the quat. 3-C became a doublet (^2J = 2.8 Hz to 3-H). The further two quat. *tert*-butyl ^{13}C multiplets were simplified to doublets with ^3J=1.8 Hz (2-*trans*) and 1.1 Hz (2-*cis*) by decoupling the upfield and downfield methyl signals, respectively. NOESY correlation with 3-H was observed for the upfield (hence *trans*, as in **9**) and the central (3-*tert*-butyl) methyl signals, but not for the downfield methyl-proton signal (hence *cis*) which showed interactions with the two other methyl signals. A ^{1}H,^{13}C-HETCOR experiment served for confirmation. Even at −96°C the *tert*-butyl rotations were still fast on the NMR (^{1}H and ^{13}C) time scales.

The epoxide ring of **27** is very easily opened by a strong anhydrous acid like TFA in catalytic amounts. This process is thought to involve a fast methyl migration with formation of **28** and subsequent fragmentation which generates the alkene **29** and pivalic aldehyde (**30**) quantitatively, as identified by ^{1}H and ^{13}C NMR in situ. Such a strong inclination toward release of steric strain is, however, not sufficient to yield a similar energetic profit by a ring-opening S_N2 attack by halide anions: We recognized this from futile treatments of **27** with lithium chloride in hot THF or *N*-methyl-2-pyrrolidone (NMP, 100°C, 18 h), lithium bromide in NMP (100°C, 90 min), or Et_4NBr in acid-free chloroform (60°C, 90 min). But when a trace of TFA was added to the latter solution with an intention of initiating the well-approved[47] nucleophilic bromination, the oxirane succumbed again to instantaneous fragmentation into **29** and **30**. Curiously, this happened also upon addition of LiBr to a stable solution of **27** in glacial acetic acid, whereas **27** remained stable in acetic anhydride solution with LiBr (4 h).

Unchanged **27** was also recovered from treatments with the strong bases lithium diisopropylamide (with HMPA), *n*-butyllithium in hexane (with or without potassium *tert*-butoxide), and *tert*-butyllithium in THF (with or without cerium trichloride[49] at 22°C for 2 d), as well as from *tert*-butyl chloride and Li metal in THF. The apparent strong resistance towards reductive or nucleophilic attack on **27** could be overcome only at +90°C with an excess of *tert*-butyllithium which after quenching with chlorotrimethylsilane surprisingly produced di-*tert*-butylacetaldehyde (**32**), readily identified by its NMR spectrum[50], along with only a trace of the *O*-trimethylsilyl derivative of enolate **31**. (Chlorotrimethylsilane reacts very slowly with **31** in hydrocarbon solution[25].) Heating the reactants in an NMR tube under the same conditions but in cyclooctane solution, we could observe a copious amount of isobutene and a developing ($t_{1/2} \approx 5$ h) ^{1}H-NMR absorption ($\delta = 6.69$) that we ascribe to enolate **31**; the final carboxylation gave again only **32**. However, when completed runs still containing residual *tert*-butyllithium were quenched in the different way of adding methanol slowly, the known[23] α,β,β-tri-*tert*-butylethanol (**34**) became a major product. While **34** at first sight was considered to arise by a reductive ring-opening of **27**, the various modes of quenching show clearly that the enolate **31** as the unique primary product had been protonated in preference to *tert*-butyllithium, which had then consumed the generated aldehyde **32**. The constitution of **34** was proven by an independent preparation from ketone **17**.



Cleavage of the 3-tBu substituent from **27** is thus the only possible reaction mode open to *tert*-butyllithium. Deprotonation of 3-H would have formed the different enolate **33**, and from that the ketone **17**, which was never found. Furthermore, since **27** is thermally stable up to at least 200°C, it cannot have isomerized in situ to the ketone **17** which would have reacted with *tert*-butyllithium in a different destructive manner as we shall show separately.

E. Conclusions

Detailed procedures for preparations of pivaloin (**2**) and for its reaction with *tert*-butyllithium enabled us to produce α,α,β-tri-*tert*-butyl compounds in sufficient amount and purity for some exploratory investigations. Three *tert*-butyl groups at a pair of adjacent sp^3-hybridized carbon atoms qualify for moderate mutual repulsion in the glycol **9** and the cyclic carbonate **15**, as expressed by restricted *tert*-butyl rotation (ca. 12 kcal/mol). Such impediment of intramolecular mobility was no longer detectable in the oxirane **27** and the alkene **20** with more sp^2-like bond hybrids and hence supposedly expanded bond angles. However, the CH acidity of oxirane **27** was insufficient for its deprotonation.

Internal pressure in the glycol **9** was apparent from accompanying or imminent fragmentation during the fast oxidation to acyloin **19** and the very sluggish deoxidation to alkene **20**. It was less surprising that some fragmentation occurred on thermolysis of the carbamate **16** of **9** to give ketone **17**. Cyclic derivatives (**15**, **23**) of glycol **9** were formed very slowly, probably due to adverse conformational preferences. Electrophilic attack on the conformationally fixed α,α,β-tri-*tert*-butyl compounds was remarkably easy for the epoxidation of alkene **20** and for the proton-catalyzed fragmentation of oxirane **27**. In contrast, the non-electrophilic opening of the oxirane ring required very harsh conditions. The chemical behaviour of acyloin **19** will also be reported subsequently.

We are very grateful to Dr. *David S. Stephenson* for measuring two-dimensional NMR spectra and to the *Deutsche Forschungsgemeinschaft* for generous support.

Experimental Section

Mol. mass: Knauer Dampfdruck-Osmometer. – IR: Bruker IFS-45 and Perkin-Elmer 125. – MS: Finnigan-MAT 90 and 95Q; Kratos MS-902. – ^{1}H NMR: Varian VXR-400S, XL-100-IL; Bruker WP-80-CW, AW-80. – ^{13}C NMR: Bruker WP-80-DS; Varian VXR-400S, XL-100-IL; internal standard TMS; coupling constants (absolute magnitudes only) obtained by gated decoupling, multiplicities by off-resonance decoupling or DEPT. – All operations with air-sensitive materials were performed with carefully dried equipment under a blanket of dry N_2 or Ar. Tetrahydrofuran (THF) was distilled from benzophenone and potassium metal, and diethyl ether from sodium. Chromatography was performed on silica gel Woelm I (100–200 μm). The use of half-saturated aqueous NaCl solution in extraction procedures with pentane was helpful in avoiding the frequently occurring phase separation problems.

4-Hydroxy-2,2,5,5-tetramethylhexan-3-one (Pivaloin, **2**). – a) *From Ethyl Pivalate:* Sodium powder was made from 69.0 g (3.00 mol) of cleaned sodium lumps with 0.5 g of stearic acid in the usual way[3], but using toluene (115 ml), in a three-necked flask (2 l) fitted with a Hershberg stirrer and a metallic condenser. The resulting suspension was cooled without stirring and the toluene removed by pipetting. The powder was washed with anhydrous ether (2 × 100 ml, 2 × 75 ml) and covered with 900 ml of ether[3a]. Ethyl pivalate (228 ml, 195 g, 1.50 mol) was added dropwise at such a rate (3 h) that the ether boiled gently. After a final 0.5 h at reflux and overnight at room temperature, a mixture of 158 g of conc. H_2SO_4 and 550 g of ice was slowly added under Ar. When the solution and precipitate had been extracted with ether (2 × 250 ml, 2 × 200 ml, 2 × 100 ml), the combined extracts were washed neutral, dried with Na_2SO_4, and concentrated at 40 Torr up to 45°C. The remaining crude crystals (126 g) were dissolved by heating in petroleum ether (55–60°C, 500 ml) contained in an Erlenmeyer flask (1 l), cooled slowly to −7°C to induce crystallization, and cooled more quickly to −70°C for total precipitation. An immersion filter stick was used to remove the yellow (due to bipivaloyl **4**)

supernatant with weak suction and to wash the precipitate with pre-cooled (−70°C) petroleum ether (2 × 200 ml). The first crop (93.0 g, 72%) had m.p. 75−77°C and was redissolved in 300 ml of petroleum ether for recrystallization in the same way. The final product was dried with Na_2SO_4 in ether solution. Filtration and removal of the solvent furnished 81.1 g (63%) of colourless pivaloin with m.p. 76−77.5°C (ref.[3a,b] 80−81°C, ref.[5] 74−75.5°C). − ^{1}H NMR (CCl_4): δ=0.94 (s, 3 CH_3-6), 1.15 (s, 3 CH_3-1), ca. 2 (variable) and 4.02 (AB system, ^3J=10.9 Hz, OH and 4-H); compare ref.[5]. − ^{13}C NMR ($CDCl_3$): δ = 26.1 (qm, 3 CH_3-1), 26.6 (qm, 3 CH_3-6), 35.4 (m, C-5), 44.6 (m, C-2), 75.8 (dm, ^1J=145 Hz, C-4), 219.1 (m, C-3).

b) *From Dimethyl Oxalate:* 20 mmol (15 ml) of *tert*-butyllithium was diluted further with 15 ml of pentane and stirred at −78°C under Ar. A solution of dimethyl oxalate (**3**, 590 mg, 5.00 mmol) in 10 ml of anhydrous ether was added dropwise and the mixture warmed up in an ice bath. After addition of water and extraction with ether (2 × 100 ml), the combined extracts were washed neutral, dried with Na_2SO_4, and concentrated to give 670 mg (78%) of almost pure (by ^{1}H NMR), solid pivaloin; m.p. 74−76°C after one recrystallization from pentane at −20°C.

2,2,5,5-Tetramethyl-3,4-hexanedione (Bipivaloyl, **4**): The mother liquors collected from **2** in method a) were distilled to give 26.6 g (21%) of yellow, liquid **4** with b.p. 79−81°C/43 Torr (ref.[3b] 66−67°C/19−20 Torr). − ^{1}H NMR (CCl_4): δ = 1.19 (s).

2,2,5,5-Tetramethyl-4-(trimethylsiloxy)-3-hexanone (**8**): A solution of pivaloin (**2**, 520 mg, 3.02 mmol) in anhydrous ether (10 ml) was stirred at −78°C during the dropwise addition (10 min) of 2.48 ml (3.30 mmol) of *tert*-butyllithium. The mixture was warmed to room temperature, recooled in ice and treated with chlorotrimethylsilane (0.40 ml, 3.2 mmol). The suspension was hydrolysed, extracted with ether (2 ×), and the organic layers were washed neutral and dried with Na_2SO_4. Evaporation of the solvent at 100 Torr yielded 787 mg (106%) of **8** with a little ether as the only visible contaminant (ref.[10] m.p. 37−39°C). − ^{1}H NMR (CCl_4): δ=0.13 (s, $OSiMe_3$), 0.92 and 1.14 (2 s, 2 *tert*-C_4H_9), 4.19 (s, CH). − Methyllithium as the base instead of *tert*-butyllithium worked equally well. An authentical sample was prepared by the very slow but quantitative literature method[10]. Methanol converted **8** quickly to pivaloin.

3-(1,1-Dimethylethyl)-2,2,5,5-tetramethylhexane-3,4-diol (**9**): The contents of a whole bottle of *tert*-butyllithium (1.40 mol) in pentane (820 ml) was employed, using the double-ended-needle technique[51,52] as follows. The bottle was securely clamped to a stable support ca. 25−40 cm above bench level, and its septum was pierced with a short cannula connected to a line of dry Ar with regulated pressure (ca. 10 Torr above atmospheric). A Dewar vessel was mounted to cool the bottle very slowly at first to 0°C and later to −70°C. Next to it, a 3-necked flask (4 l) was placed in a second Dewar vessel (vertically movable) and was fitted with a gas-tight mechanical stirrer (KPG type), an internal thermometer, and an Anschütz (Y type) head, the latter carrying a septum and (on the side arm) an nitrogen bubbler with separate Ar inlet and outlet. After charging with pivaloin (84.6 g, 491 mmol) and anhydrous ether (2 l), this reaction flask was also cooled to 0°C by adding dry ice to the acetone bath. Its septum was pierced with one end of a long (90 mm) two-tipped cannula (1.5 mm outer diameter, Aldrich Co.) that was lowered to a visible position above the ether surface. The second end of this cannula was pierced through the bottle septum but not yet dipped into the *tert*-butyllithium solution, such that a slow stream of Ar could pass from the bottle through the cannula and vent from the 4-l flask. The bottle and the flask were then cooled further very cautiously until the stirred ether soluton attained −70°C. − With both dry-ice baths kept at −72°C for the next hour, the second tip of the long cannula was now lowered to the bottom of the *tert*-butyllithium solution, which started to run through the cannula into the pivaloin solution, as controlled by weak pressurization of the bottle. Due to formation of the alkoxide **7**, the internal temperature rose to ca. −50°C during introduction of ca. one third of the organometallic and fell back to −69°C, necessitating an occasional repressurization of the flask through the bubbler. After complete *tert*-butyllithium transfer (45 min) and replacement of the septum at the reaction flask by a dry condenser (with a bubbler but no water), the dry-ice bath was lowered for warm-up of the stirred reaction mixture. If isobutane and isobutene were liberated too vigorously at +4°C, the cold bath was lifted up again for mitigation. The conversion was allowed to proceed to completion at room temperature overnight under Ar. − No significant reaction was noticed the next day when the product mixture was poured onto 500 g of ice and 500 ml of distilled water in a separatory funnel (5 l). The separated aqueous layer was shaken with ether (2 × 500 ml) which was added to the organic layer for washing with half-saturated NaCl solution (3 × 700 ml). Drying with Na_2SO_4 and concentration at 40 Torr/35°C provided 107 g of a partially solidifying product containing **9**, **10** and **2** (45:45:10). It was dissolved in 250 ml of boiling petroleum ether (55−60°C), of which 50 ml were allowed to distil off. The colourless needles deposited overnight at room temperature were washed with cold petroleum ether and dried to yield 32.1 g (38%) of racemic[5] diol **10** with m.p. 115−123°C (ref.[5] 123−124°C, ref.[18] 125−126°C). − The combined and concentrated filtrates (71.1 g) were pipetted as a warm melt on top of 300 g of silica gel in petroleum ether/ether (9:1, predried with $MgSO_4$), contained in a column of 43 mm diameter. Chromatography with the same eluent composition (total 2 l) furnished 55.4 g of the crude title compound **9**, followed by 7.03 g (8%) of pivaloin (**2**). Final elution with ether (750 ml) gave a second crop of diol **10** (mainly racemate, 6.05 g, 7%, see below). − One recrystallization of the volatile glycol **9** from 250 ml of petroleum ether at −78°C, as desdribed above for **2** but with drying at 12 Torr for only 7 h or at normal pressure over silica beads, afforded 50.7 g (45%) of practically pure material. The analytical sample was obtained with m.p. 68−69°C by a second recrystallization or by sublimation at 60°C/20 Torr. − IR (KBr): $\tilde{\nu}$=3620 cm^{-1} (w, sharp O−H), 3527 (s, br. O−H), 2960, 1485, 1394, 1367, 1204, 1054, 990. − ^{1}H NMR ($CDCl_3$): δ=1.11, 1.15 and 1.27 (3 s, 3 *tert*-C_4H_9), 1.40 (s, OH), 1.41 (d, ^3J=6 Hz, OH), 3.98 (d, ^3J=6 Hz, 4-H); similar in CCl_4 but ^3J=5.5 Hz at δ=3.92 and signal of both OH hidden under that of CH_3. − ^{13}C NMR ($CDCl_3$ at +28°C): δ=29.2 (q, 3 CH_3-1a), 30.2 (q, 3 CH_3-6), 31.5 (q, 3 CH_3-1b), 38.1 (s, C-5), 42.7 and 43.1 (2 s, C-2a,b), 83.1 (d, C-4), 86.2 (s, C-3); similar in C_6D_6[53]. − ^{13}C NMR ($CDCl_3$ at −63°C): δ=26.8, 29.2 and 29.6 (3 CH_3-1a), 30.1 (3 CH_3-6), 30.0, 30.4 and 33.7 (3 CH_3-1b), 37.8, 42.4, 42.9, 82.4, 85.4; CH_3 coalescences at −30 and −40°C/25.15 MHz. − MS: No M^+ under 70 or 15 eV at +90°C[53]. − $C_{14}H_{30}O_2$ (230.4): calcd. C 72.99, H 13.13; found C 72.70, H 12.83. − The amount of recovered starting material **2** rose to 17% when only 2.3 equivalents of *tert*-butyllithium were applied.

2,2,5,5-Tetramethylhexane-3,4-diol (**10**): Isolated in the course of the preceding preparation of **9** in a total yield of 45%. − ^{1}H NMR (CCl_4): δ=0.88 (s, 2 *tert*-C_4H_9), ca. 2.15 (d, ^3J = 6.5 Hz, 2 OH), 3.20 (d, ^3J=6.5 Hz, 2 CH); compare ref.[5].

2,2,5,5-Tetramethyl-3-hexanone (**11a**): Identified in product mixtures by ^{1}H NMR[12,14,16] in CCl_4; observed δ=0.98, 1.06, 2.26.

4,4,5-Tris(1,1-dimethylethyl)-1,3-dioxolan-2-one (**15**): A round-bottomed flask (25 ml) was charged with the glycol **9** (1.00 g, 4.34

mmol), CCl_4 (6 ml), oxalyl dichloride (3.0 ml, 34.4 mmol), and pyridine (0.35 ml, 4.34 mmol). The flask was connected to a double-walled reflux condenser carrying a nitrogen bubbler and was heated at +70°C for at least 2 d. The mixture was then taken up in dist. petroleum ether (120 ml) and stirred with aqueous $NaHCO_3$ until CO_2 was no longer evolved. After one further extraction with $NaHCO_3$, the organic layer was washed with water, dried with Na_2SO_4, and concentrated in vacuo. Short drying in a desiccator gave 1.10 g (99%) of **15** as s spectroscopically almost pure liquid. The pure compound (981 mg, 88%) had m.p. 40–42°C after distillation at 125–135°C (bath temp.)/0.012 mbar. – IR (KBr): $\tilde{\nu}$=2969 cm^{-1}, 1793, 1263, 1045. – ^1H NMR ($CDCl_3$): δ=1.25 and 1.27 (2 s, 2 *tert*-C_4H_9), 1.29 (br. at 400 MHz, 1 *tert*-C_4H_9), 4.81 (s, 5-H, or at 4.68 in CCl_4). – ^{13}C NMR ($CDCl_3$ at +25°C): δ=30.0 and 30.5 (2 q, 3 + 3 sharp CH_3), 30.1 (very br., 3 CH_3, sharp at +50°C), 35.2 (s, quat. 5-C), 41.4 and 41.8 (2 s, 2 4-C), 91.6 (d, CH-5), 100.3 (s, C-4), 154.4 (s, C-2). – ^{13}C NMR ($CDCl_3$ below −50°C): δ=29.6 and 30.7 (3 + 3 CH_3), 27.5, 29.8 and 32.0 (1 + 1 + 1 CH_3), 34.6, 41.2, 41.4, 91.5, 100.5, 155.0; CH_3 coalescences at ca. −23°C/25.15 MHz. – Mol. mass: 267 (osmom. in $CHCl_3$ at +37°C). – MS (15 eV at +60°C): *m/z* (%)=257 (4) [M + H^+], 141 (21), 111 (25), 85 (25), 57 (100). – $C_{15}H_{28}O_3$ (256.4): calcd. C 70.27, H 11.01; found C 70.37, H 11.03. – Formation of **15** was not facilitated with 4-(1-pyrrolidino)pyridine/triethylamine[54] in place of pyridine.

4-(1,1-Dimethylethyl)-4-hydroxy-2,2,5,5-tetramethyl-3-hexyl N-(4-Toluenesulfonyl)carbamate (**16**): A solution of the glycol **9** (15.0 g, 65.1 mmol) in 30 ml of anhydrous ether was stirred magnetically under Ar at +15°C while tosyl isocyanate (9.88 ml, 65.1 mmol), dissolved in anhydrous ether (60 ml), was added dropwise over a period of 30 min. After further stirring at room temp., the flask was tightly stoppered for overnight storage. Thereafter, the colourless solution was diluted with 150 ml of ligroin in an Erlenmeyer flask and concentrated in a steam bath to ca. 130 ml until crystallization commenced. The hard crystal cake formed overnight was crushed and washed with ligroin to leave 26.4 g (95%) of colourless **16** with m.p. 141–146°C. Repeated recrystallization from heptane or from CCl_4 gave material with m.p. 146.5–147°C. – IR (KBr): $\tilde{\nu}$=3585 cm^{-1} (sharp O–H), 3240 (br. N–H), 2965, 2920, 1748 (C=O), 1430, 1352, 1228, 1158, 1091, 878. – ^1H NMR ($CDCl_3$): δ=0.96, 1.01 and 1.11 (3 s, 3 *tert*-C_4H_9), 1.53 (s, OH), 2.39 (s, *p*-CH_3), 5.20 (s, CH-3), 7.30 (d, 2H), 7.80 (br. s, NH), 7.92 (d, ^3J=7.8 Hz, 2H). – ^{13}C NMR ([D_6]acetone): δ=21.4 (q, *p*-CH_3), 29.5, 30.1 and 31.7 (3 q, 3 × 3 CH_3), 39.3, 43.4 and 43.6 (3 s, 3 quat. C), 85.2 (d, CH-3), 86.6 (s, C-4), 128.5 (d, 2 CH), 129.7 (d, 2 CH), 137.3 (s, *p*-C), 144.7 (s, *i*-C), 151.1 (s, C=O). – $C_{22}H_{37}NO_5S$ (427.6): calcd. N 3.28; found N 3.13.

4-(1,1-Dimethylethyl)-2,2,5,5-tetramethyl-3-hexanone (**17**): A round-bottomed flask (25 ml) charged with recrystallized carbamate **16** (5.00 g, 11.7 mmol) was connecte by a short (15 cm) distillation pipe to a two-necked receptacle cooled in an ice bath and carrying a reflux condenser. After flushing with dry Ar, the flask was immersed in a hot salt bath (195°C), heated to 220°C until the vigorous CO_2 evolution slowed down after 10 min, heated to 230–240°C for another 5 min, and then cooled under Ar. The whole apparatus was rinsed with pentane, and the hard residue was pulverized in a mortar with exhaustive extraction with pentane, leaving the expected amount of pure tosylamide (NMR, m.p.). The combined and filtered pentane extracts (ca. 150 ml) were washed with 2 M NaOH (30 ml) and with aqueous NaCl solution (3 × 20 ml), then dried with $MgSO_4$ and concentrated at 75 Torr. The remaining colourless liquid (2.06 g) was distilled at 12 Torr to give a forerun (0.28 g) of di-*tert*-butyl ketone (**18**) and *tert*-butyl neopentyl ketone (**11a**) at 30–43°C as an 80:20 mixture, followed by 1.48 g (60%) of pure **17** with b.p. 98–105°C/12 Torr and m.p. 25–27°C (long colourless lancets). – ^1H NMR (CCl_4): δ=1.03 (s, 2 *tert*-C_4H_9), 1.15 (s, 1 *tert*-C_4H_9), 2.85 (s, 4-H); compare ref.[23]. – ^{13}C NMR ($CDCl_3$): δ = 29.0 (q, 3 C-1), 31.7 (q, 6 C-6), 35.7 (s, 2 C-5), 44.7 (s, C-2), 62.2 (d, C-4), 222.5 (s, C-3). – The distillation residue was 200 mg of glycol **9** (8%). More efficient cooling of the emanating CO_2 was necessary in larger runs (tried with 26.2 g of **16**), and thermolysis at very low pressure is not advisable as the tosylamide tends to sublime.

4-(1,1-Dimethylethyl)-4-hydroxy-2,2,5,5-tetramethyl-3-hexanone (**19**): a) *By Oxidation of* **9**: The recrystallized glycol **9** (9.15 g, 39.7 mmol) was suspended in an ice-cooled mixture of dist. water (4 ml), glacial acetic acid (16 ml), and conc. H_2SO_4 (2 ml). Without delay, 2 ml of a previously prepared solution of CrO_3 (3.42 g, 34.2 mmol) in 4 ml of dist. water and 8 ml of glacial acetic acid was added dropwise with vigorous stirring. The addition was interrupted until the suspension turned green, and was then continued at such a rate that the green colour remained visible (10 min). With final manual stirring with a glass rod, the thick brown mass was treated with 100 g of ice and then with 2.5 g of $Na_2S_2O_5$ (13.1 mmol) dissolved in 25 ml of water. After extraction with dist. petroleum ether (40–80°C, 150 and 2 × 60 ml), the combined extracts were washed with half-saturated aqueous NaCl (170 ml), 2 M NaOH, once more with NaCl solution (170 ml), and dried with $MgSO_4$. Di-*tert*-butyl ketone (**18**) was partially removed in a rotary evaporator at 40°C/80 Torr to furnish 7.30 g (80%) of the volatile acyloin **19** with m.p. 93–105°C. One recrystallization at +4°C from an ether/pentane (1:1) mixture (or at −78°C from 10 ml of petroleum ether per 1 g of **19**) afforded 6.50 g (72%) of colourless needles with m.p. 111–114°C (ref.[9] 113–113.5°C; ref.[23] 112–116°C). – IR (Nujol): $\tilde{\nu}$=3526 cm^{-1} (sharp O–H), 1672, 1372, 1096. – ^1H NMR (CCl_4): δ=1.07 (s, 2 *tert*-C_4H_9), 1.22 (s, 1 *tert*-C_4H_9), 1.76 (s, OH); in $CDCl_3$: δ=1.11, 1.29, 1.94; compare ref.[23]. – ^{13}C NMR ($CDCl_3$): δ = 29.6 (q, 6 CH_3-6), 30.0 (q, 3 CH_3-1), 42.1 (s, 2 C-5), 47.1 (s, C-2), 92.7 (s, C-4), 219.9 (s, C-3); low solubility but no change at −60°C.

b) *From Bipivaloyl* (**4**): A solution of *tert*-butylmagnesium chloride (564 mmol) in 300 ml of anhydrous ether was cooled to −70°C under Ar. With magnetic stirring, 48.0 g (282 mmol) of **4** in 100 ml of anhydrous ether was added dropwise (30 min), and the chocolate-brown suspension was kept at −50°C for 1 h, then warmed up in an ice-bath. Cautious addition of water (100 ml) and subsequently of 2 M HCl (150 ml) caused vigorous foaming. After extraction with pentane (3 × 100 ml), the combined organic layers were washed neutral, dried with Na_2SO_4, and concentrated to give 54.7 g of a yellow mixture of **2**, **4** and **19** (4:1:2). On chromatographic separation on silica gel (220 g) with ether admixed to petroleum ether (boiling range 40–80°C, 1:9), the first 225 ml eluted **4** and the major part of **19**. This material (22.9 g) gave 10.7 g (17%) of **19** with m.p. 110–113°C (ether/pentane, 1:1; at +4°C). Further elution (100 ml) of the adsorbent delivered a mixture of **19** with **2**, followed (with $CHCl_3$ eluent) by 21.0 g (43%) of pure pivaloin (**2**) with m.p. 74–77°C.

3-(1,1-Dimethylethyl)-2,2,5,5-tetramethyl-3-hexene (**20**). – a) *From* **9** *and* Ti^{II} *with Ultrasonication:* A two-necked flask (250 ml), equipped with a magnetic stirring bar and a double-walled reflux condenser carrying a nitrogen bubbler, was charged with lithium aluminium hydride (1.65 g, 43.4 mmol) and anhydrous THF (100 ml) and cooled in an ice bath under Ar. When solid titanium(III) chloride (13.4 g, 86.7 mmol) was added cautiously under Ar, an exothermic reaction was observed with H_2 evolution and formation

of a black suspension[30]. The flask was heated to reflux in an ultrasound cleaning bath for 1 h (perhaps[30] an unnecessary operation) and then recooled in ice. With magnetic stirring, 5.00 g (21.7 mmol) of the glycol **9** in 20 ml of anhydrous THF was added dropwise. Ultrasonication of the slurry was continued for 6 h at +75°C to attain 91% conversion. The flask was cooled in ice and flushed with Ar during the cautious addition of water until the slow H_2 evolution ceased. The black mixture was transferred with pentane (200 ml) and water (200 ml) to a separatory funnel, and the aqueous layer was shaken with more pentane (3 × 200 ml). The combined pentane extracts were washed with aqueous NaCl (half-saturated, 2 × 100 ml) and aqueous $NaHCO_3$ (100 ml), dried with Na_2SO_4, and concentrated in a rotary evaporator to afford 4.22 g (99%) of **20** containing ca. 8% of the starting material **9** and only a trace of di-*tert*-butyl ketone (**18**). These impurities were retained by silica gel on short-column chromatography with low-boiling petroleum ether which furnished 3.15 g (74%) of spectroscopically pure **20**; b.p. 82–83°C/12 Torr (no b.p. in refs.[23,26,36,37]). – IR (film): $\tilde{\nu}$ = 3067 cm^{-1} (w), 3006, 2958, 2920, 2872, 1482, 1470, 1392, 1365, 1223, 1200. – ^{1}H NMR (CCl_4, or $CDCl_3$ at +25° and −63°C): δ = 1.18 (s, 3 CH_3-1t), 1.20 (s, 3 CH_3-6), 1.32 (s, 3 CH_3-1c), 5.33 or 5.38 (s, 4-H); compare ref.[36]. – ^{13}C NMR ($CDCl_3$ at +25°C): δ = 32.87 (qm, ^1J = 125.3 Hz, ^3J = 5.0 Hz, 3 CH_3-1t), 33.45 (qdm, ^1J = 125.3 Hz, ^3J = 4.2 and 5 Hz, 3 CH_3-6), 33.58 (m, $^2J \approx 3.6$ Hz, C-5), 34.47 (qm, ^1J = 125.3 Hz, ^3J = 5.0 Hz, 3 CH_3-1c), 36.58 (dm, ^3J = 10.5, ^2J = 3.5 Hz, C-2c), 40.20 (dm, ^3J = 8, ^2J = 3.5 Hz, C-2t), 134.50 (dm, ^1J = 143.5, ^3J = 4.3 Hz, C-4), 151.92 (m, ^3J = 3.2 Hz, C-3); at −63°C δ = 32.5, 33.3, 33.4, 34.1, 36.5, 40.1, 133.8, 151.5. – MS (70 eV): *m/z* (%) = 196.2197 (2) [$C_{14}H_{28}$], 139.1487 (72) [$C_{10}H_{19}$], 83.0819 (100) [C_6H_{11}].

b) *Thermally from* **9** *and* Ti^{II} *with Formation of Side-products* **18** *and* **21**: If an unsufficient amount or if aged batches of the commerical $TiCl_3$/$LiAlH_4$ reagent (modified for a 4:2 ratio) were applied for 4 d at +80°C without ultrasonication, typically only 31% of **20** was isolated but up to 51% of pure di-*tert*-butyl ketone (**18**: IR: $\tilde{\nu}$ = 1687 cm^{-1}; ^{1}H NMR: δ = 1.20) and 22% of neopentyl alcohol (**21**: ^{1}H NMR: δ = 0.86 and 3.14) were obtained. The latter contaminants were almost absent when the fresh commercial reagent was modified (4:2 ratio) and used under the same conditions, to provide 94% of crude **20** after chromatography.

c) *From Dioxolanes* **23** *or* **24**: The crude dioxolane (3.30 g, 11.5 mmol) in 9.0 ml of acetic anhydride was heated to 90°C for at least 3.5 h under inert gas. The cooled mixture was shaken with pentane (50 ml) and sufficient amounts of iced 2 N NaOH to remain alkaline. The washed and dried pentane layer furnished 2.33 g of crude material which was separated by chromatography on 15 g of silica gel (column length 22 mm). The first 50 ml of petroleum ether sufficed to elute the pure olefin **20** (1.36 g, 60%). The by-products **9** (15%) and then **25** (18%) were eluted with ether. Distillation at 83–85°C/12 Torr with severe losses due to volatility gave an analytically pure[36] sample.

cis-2-Dimethylamino-4,4,5-tris(1,1-dimethylethyl)-1,3-dioxolane (**23**): The glycol **9** (3.00 g, 13.0 mmol) was refluxed in DMF dimethyl acetal (at least 20.0 ml, 150 mmol) for 96 h at 120°C ($t_{1/2}$ ca. 9 h). After solvent stripping, the residue (3.54 g) containing 15% of **9** was used for conversion to **20**. Pure liquid **23** (81% yield) distilled at 80–88°C/0.02 mbar. – ^{1}H NMR (CCl_4): δ = 1.15, 1.18 and 1.21 (3 s, 3 *tert*-C_4H_9), 2.31 (s, NMe_2), 3.99 (s, 5-H), 4.88 (s, 2-H). – ^{13}C NMR (deacidified $CDCl_3$): δ = 30.9 (3 CH_3 of 4c-tBu), 31.2 (br., 3 CH_3 of 4t-tBu), 31.3 (3 CH_3 of 5-tBu), 38.6 (q, NMe_2), 35.3, 40.5 and 43.3 (3 s, 3 quat. C), 88.5 (d, C-5), 94.2 (s, C-4), 109.3 (d, C-2); assigned by comparison with **24**. – $C_{17}H_{35}NO_2$ (285.5): calcd. C 71.53, H 12.36, N 4.91; found C 71.53, H 12.15, N 4.73.

trans-2-Dimethylamino-4,4,5-tris(1,1-dimethylethyl)-1,3-dioxolane (**24**): This isomer was detected in an unsuccessful attempt to prepare the olefin **20** by heating 22.5 mmol of **23** for 48 h at 160°C. The resulting mixture was dissolved in 150 ml of pentane and shaken with 2 N HCl (20 ml). The aqueous layer was quickly made alkaline and re-extracted with pentane (3 ×) which was washed neutral, dried with Na_2SO_4, and concentrated. The solid residue (2.56 g, 40%) of almost pure **24** was recrystallized from petroleum ether (10 ml) to yield colourless, glistening needles with m.p. 75–76.5°C. – IR (KBr): $\tilde{\nu}$ = 2998 cm^{-1}, 2958, 2820, 1487, 1390, 1357, 1135. – ^{1}H NMR ($CDCl_3$): δ = 1.18 (s, 4t-*tert*-C_4H_9), 1.21 (s, 4c-*tert*-C_4H_9), 1.22 (s, 5-*tert*-C_4H_9), 2.20 (s, NMe_2), 4.28 (s, 5-H), 4.61 (s, 2-H); in CCl_4 δ = 1.15, 1.20, 1.20, 2.13, 4.22, 4.47. – ^{13}C NMR ($CDCl_3$): δ = 30.9 (3 CH_3 of 4c-tBu), 31.1 (br., 3 CH_3 of 4t-tBu), 31.7 (3 CH_3 of 5-tBu), 39.5 (2 CH_3 of NMe_2), 33.7, 40.6 and 41.1 (3 s, 3 quat. C), 87.1 (d, C-5), 96.7 (s, C-4), 110.3 (d, C-2). – $C_{17}H_{35}NO_2$ (285.5): calcd. C 71.53, H 12.36, N 4.91; found C 71.81, H 12.41, N 4.94.

4-(1,1-Dimethylethyl)-4-hydroxy-2,2,5,5-tetramethyl-3-hexyl Formate (**25**): A mixture of the *trans*-dioxolane **24** (200 mg, 0.70 mmol) with 4 ml of 2 N aqueous HCl was stirred for 30 min and then extracted with ether (3 × 10 ml). The combined and washed extracts were dried with Na_2SO_4 and concentrated to leave 160 mg (88%) of the pure solid **25**. The analytical sample crystallized from 1 ml of petroleum ether as colourless blocks with m.p. 71–73°C. – IR (KBr): $\tilde{\nu}$ = 3594 cm^{-1} (sharp O–H), 2970, 2917, 1717 (s), 1487, 1395, 1364, 1211, 1183 (s), 906. – ^{1}H NMR ($CDCl_3$): δ = 1.10, 1.12 and 1.24 (3 s, 3 *tert*-C_4H_9), 1.61 (s, OH), 5.44 (br. s, 3-H), 8.13 (d, ^4J = 0.9 Hz, formate H, s when irradiating 3-H); in CCl_4 δ = 1.08, 1.10, 1.22, 1.62, 5.42, 8.01. – ^{13}C NMR ($CDCl_3$): δ = 29.3, 30.4 and br. 31.5 (3 × 3 CH_3), 38.5 (quat. C-2), 43.0 and 43.4 (2 quat. C-5), 82.8 (br., CH-3), 86.1 (quat. C-4), 160.7 (d, formate C). – $C_{15}H_{30}NO_3$ (258.4): calcd. C 69.72, H 11.70; found C 69.67, H 11.44.

3-(1,1-Dimethylethyl)-2,3,5,5-tetramethyl-1-hexene (**26**): Formed from **20** in $CDCl_3$ solution (0.6 ml) under the action of conc. HBr (48%, 0.01 ml) with $t_{1/2}$ ca. 30 h at 22°C. – ^{1}H NMR ($CDCl_3$): δ = 0.85 and 0.93 (2 s, 2 *tert*-C_4H_9), 1.11 (s, 3-CH_3), 1.32 and 1.86 (AB system, ^2J = 14.5 Hz, 2 4-H), 1.80 (d, ^4J = 1.1 Hz, 2-CH_3), 4.79 (d, ^2J = 1.6 Hz, 1-H), 4.96 (m, 2nd 1-H); but compare ref.[23]. – ^{13}C NMR ($CDCl_3$): δ = 20.6 (br., 3-CH_3), 24.2 (2-CH_3), 26.2 (3 CH_3 of 3-*tert*-C_4H_9), 31.9 (quat. C-5), 32.2 (3 CH_3-6), 37.7 (br., quat. C of 3-*tert*-C_4H_9), 45.4 (br., CH_2-4), 46.4 (quat. C-3), 113.4 (CH_2-1), 149.7 (br., C-2). – At −42°C most of these resonances became split in a 2:1 ratio.

2,2,3-Tris(1,1-dimethylethyl)oxirane (**27**). – a) *With 3-Chloroperoxybenzoic Acid:* A solution of the peracid (1.18 g, 85%, 5.81 mmol) in 5 ml of anhydrous dichloromethane was stirred at −12°C during the dropwise addition of alkene **20** (750 mg, 3.82 mmol) in 3 ml of CH_2Cl_2. After further stirring at −11°C for 2 h, the mixture was diluted with pentane (30 ml) and filtered. The precipitate was washed with pentane (30 ml), and the combined solutions were extracted with 2 M aqueous NaOH (20 ml) and with dist. water (4 × 20 ml), then dried with Na_2SO_4. The almost pure residue (720 mg, 89%) obtained by solvent stripping was distilled for combustion analysis in a split-column apparatus: Colourless liquid (596 mg, 73%) with b.p. 94.5–95.5°C/12 Torr. – IR (film): $\tilde{\nu}$ = 1477 cm^{-1}, 1393, 1369, 1216, 1152, 945, 892. – ^{1}H NMR ([D_8]toluene; at +25°C): δ = 1.07 (s, 3 2t-CH_3), 1.10 (s, 3 3-CH_3), 1.16 (s, 3 2c-CH_3), 2.73 (s, 3-H); at −96°C: δ = 1.05, 1.06, 1.14, 2.74; in CCl_4:

δ = 1.06, 1.13, 1.15, 2.61. – ^{13}C NMR ([D$_8$]toluene; at +25°C): δ = 30.2 (qm, ^1J = 125.9 Hz, ^3J = 4.9 Hz, 3 2t-CH$_3$), 30.7 (qdm, ^1J = 125.9 Hz, ^3J = 3.5 and 4.9 Hz, 3 3-CH$_3$), 31.5 (qm, ^1J = 125.9 Hz, ^3J = 4.9 Hz, 3 2c-CH$_3$), 32.0 (dm, ^2J = 2.8 Hz to 3-H, quat. 3-C), 36.0 (dm, ^3J = 1.1, ^2J = 3.7 Hz, 2c-C), 39.2 (dm, ^3J = 1.8, ^2J = 3.6 Hz, 2t-C), 71.3 (dm, ^1J = 157.5, ^3J = 5.2 Hz, C-3), 74.2 (m, C-2); at −96°C: δ = 29.9, 30.5, 31.1, 31.9, 35.9, 39.1, 71.1, 73.6. – $C_{14}H_{28}O$ (212.4): calcd. C 79.18, H 13.29; found C 79.65, H 13.29.

b) *With Peroxyphthalate:* The alkene **20** (2.50 g, 12.7 mmol) and tricapryl(methyl)ammonium chloride (Aliquat-336, 175 mg) in 80 ml of $CHCl_3$ (de-acidified with $NaHCO_3$ solution) were stirred at +50°C and treated with a solution of fresh magnesium monoperoxyphthalate hexahydrate (85%, 14.8 g, 25 mmol) in 80 ml of dist. water. After 90 min of stirring, a second portion (7.45 g in 40 ml) of the peroxy reagent was added at once, and finally a third portion after 90 min (3.75 g in 20 ml). Stirring at +50°C was continued for another 90 min, whereafter the $CHCl_3$ layer was separated, the solvent removed in a rotary evaporator, and the residue taken up in pentane (200 ml). This organic layer was washed with aqueous $NaHCO_3$ (80 ml) and water (3 × 50 ml), dried with Na_2SO_4, and concentrated to leave 2.69 g (99%) of the practically pure product **27**.

2,3,4,4-Tetramethyl-2-pentene (**29**): Addition of trifluoroacetic acid (0.004 ml, 0.052 mmol) to the oxirane **27** (44 mg, 0.21 mmol) in 0.5 ml of $CDCl_3$ caused the quantitative formation of **29** and pivalic aldehyde (**30**) with a reaction half-life of 30 min at +22°C. – ^{1}H NMR of **29** ($CDCl_3$ or CCl_4): δ = 1.15 (s, 1 *tert*-C$_4$H$_9$), 1.63 (m, 3 H), 1.66 (br. q, J = 0.8 Hz, 3 H), 1.80 (q, ^{5}J = 1.4 Hz, 3 H); compare refs.[55,56]. – ^{13}C NMR of **29** ($CDCl_3$): δ = 17.2, 23.3 and 24.1 (3 q, 3 CH$_3$), 30.9 (3 q, 3 CH$_3$-5), 35.9 (s, C-4), 124.1 and 135.1 (2 s, C-2/C-3). – ^{1}H NMR of **30** ($CDCl_3$): δ = 1.08 (s, 9 H), 9.47 (s, 1 H). – ^{13}C NMR of **30** ($CDCl_3$): δ = 23.4 (3 CH$_3$), 42.6 (quat. C), 206.9 (CH=O); compare ref.[40].

Conversion of the Oxirane **27** *to 2-(1,1-Dimethylethyl)-3,3-dimethylbutanal* (**32**): A pentane solution (2.77 ml) of **27** (200 mg, 0.94 mmol) and *tert*-butyllithium (4.71 mmol) was heated under Ar while all volatile components escaped through a small distillation bridge. After 3 h at +90°C, the flask was cooled to −78°C for the introduction of chlorotrimethylsilane (0.95 ml in 5 ml of pentane). The warmed-up mixture with precipitated lithium hydride was cautiously hydrolysed with aqueous 1 N NaOH (10 ml) and diluted with pentane (25 ml). The pentane layer was washed neutral, dried with Na_2SO_4, and concentrated at 80 Torr to leave 200 mg of a crude liquid, consisting only of **32** (by ^{1}H NMR[50]) and small amounts of trimethylsilylated impurities.

4-(1,1-Dimethylethyl)-2,2,5,5-tetramethyl-3-hexanol (**34**): Anhydrous ethylamine (6 ml) was distilled into a Schlenk flask (25 ml) with magnetic stirring bar, kept at −25°C under Ar. The ketone **17** (480 mg, 2.26 mmol) was added, followed by metallic lithium (140 mg, 20 mmol) in small pieces which formed a dark blue solution on stirring for 25 min. The solvent was removed in a stream of dry Ar without cooling, and the residue was covered with pentane (20 ml). After manual removal of residual lithium pieces and cautious protolysis of the remaining lithium powder with cooling under Ar, the mixture was taken up in more pentane (40 ml) and water. The pentane layer was washed with NaCl solution (3 × 10 ml) and with aqueous $NaHCO_3$, then dried with Na_2SO_4 and concentrated at 80 Torr to afford 420 mg (87%) of almost pure **32**. A sample distilled at 120–130°C (bath temp.)/12 Torr. – ^{1}H NMR ($CDCl_3$): δ = 1.00, 1.09 and 1.18 (3 s, 3 *tert*-C$_4$H$_9$), 1.31 (br. d, $^3J \approx 5$ Hz, OH, removed with D_2O), 1.48 (d, ^3J = 0.9 Hz, 4-H), 3.74 (d, ^3J = 5.2 Hz, 3-H, collapsed with D_2O); similar in CCl_4, compare ref.[23]. – ^{13}C NMR ($CDCl_3$): δ = 29.6 (3 CH$_3$-1), 31.7 and 33.9 (2 × 3 CH$_3$-6), 35.7 and 36.3 (2 × C-5), 37.4 (C-2), 54.4 (CH-4), 81.9 (CH-3); assigned by comparisons with **9** and **17**.

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