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T-Shaped Molecular Building Blocks by Combined Bridgehead and Bridge Substitution on Bicyclo[1.1.1]pentanes

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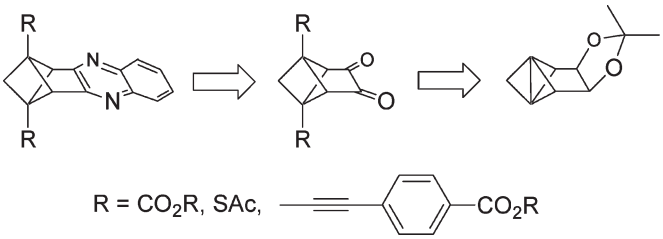

Derivatives of bicyclo[1.1.1]pentane differentially substituted in bridgehead (1,3) and bridge (2,4) positions have been synthesized. They represent a new T-shaped structural module consisting of a rigid rod with a nearly freely rotating side arm, possibly useful as a molecular building block in syntheses of more complex covalent or supramolecular scaffolds useful in bottom-up construction of molecular level devices or materials. For good chemical connectivity in the axial direction, carboxylates, ethynyls, and acetylsulfanyl groups were installed at the bridgeheads. Quinoxalines were attached in the transverse direction through a highly reactive α-diketone system located at the bridges.

Introduction

While a variety of straight molecular rods are now available, both electronically fairly conducting and highly insulating,[1] few if any T-shaped rods with a freely rotating side arm have been described. Yet, in many applications of the molecular "Tinkertoy" construction set,[2] such as molecular rotors,[3] freely rotatable T-shaped building blocks would be very useful. For some time,[4,5] a set of 1,3-substituted derivatives of bicyclo[1.1.1]pentane (**1**) and [*n*]staffanes, electronically insulating oligomeric straight-rod derivatives of **1**, has been under development as a molecular construction kit, and we now address their use for the introduction of a T-shaped element. This requires the preparation of derivatives with substituents not only in the bridgehead positions 1 and 3, but also in the bridge positions 2, 4, and/or 5 of the parent cage of **1**. Some hypothetical structures that incorporate such an element are illustrated in Chart 1.

The introduction of substituents into the bridgehead positions of **1** is easy and was realized soon after the discovery[6] of the synthesis of tricyclo[1.1.1.0^{1,3}]pentane (also called [1.1.1]propellane). This propellane is prone to a facile addition across its inner bond. Such addition reactions have afforded hundreds of 1,3-derivatives, most of which are listed in an extensive review.[5] In contrast, the installation of additional substituents into positions other than 1 and 3 proved to be a challenging task. The most frequent retrosynthetic pathways are depicted in Scheme 1.

(i) A derivatization of **1** or its suitable bridgehead derivatives is very difficult due to the high strength of the bridge

(1) Schwab, P. F. H.; Levin, M. D.; Michl, J. *Chem. Rev.* **1999**, *99*, 1863.
(2) Tinkertoy is a trademark of Playskool, Inc., Pawtucket, RI, and designates a children's toy construction set consisting of straight wooden sticks and other simple elements insertable into spool-like connectors.
(3) Michl, J.; Sykes, E. C. H. *ACS Nano* **2009**, *3*, 1042. Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281.
(4) Kaszynski, P.; Michl, J. *J. Am. Chem. Soc.* **1988**, *110*, 5225. Kaszynski, P.; Friedli, A. C.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 601. Mazières, S.; Raymond, M. K.; Raabe, G.; Prodi, A.; Michl, J. *J. Am. Chem. Soc.* **1997**, *119*, 6682–6683. Mazal, C.; Paraskos, A. J.; Michl, J. *J. Org. Chem.* **1998**, *63*, 2116. Schwab, P. F. H.; Noll, B. C.; Michl, J. *J. Org. Chem.* **2002**, *67*, 5476.
(5) Levin, M. D.; Kaszynski, P.; Michl, J. *Chem. Rev.* **2000**, *100*, 169.
(6) Wiberg, K. B.; Walker, F. H. *J. Am. Chem. Soc.* **1982**, *104*, 5239. Semmler, K.; Szeimies, G.; Belzner, J. *J. Am. Chem. Soc.* **1985**, *107*, 6410.

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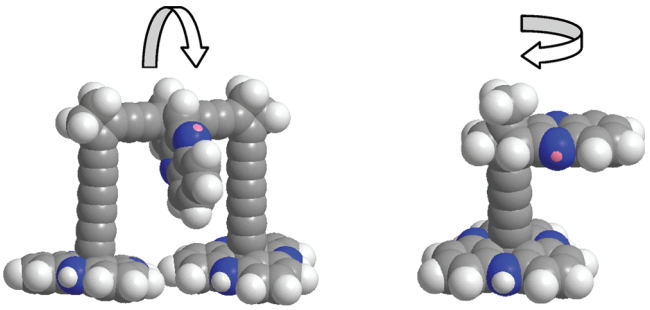
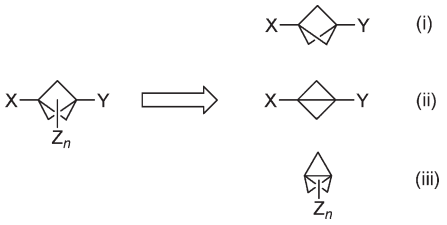
CHART 1. Molecular Rotors Designed with Bridge Substituted 1

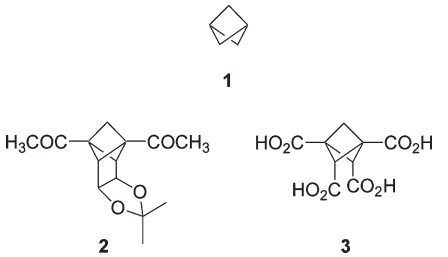


SCHEME 1. Three Main Retrosynthetic Pathways to Bridge Substituted 1



C−H bonds (due to their high s character) in the highly strained cage. Only a few procedures have succeeded such as fluorination,[7] chlorination,[8] and chlorocarbonylation.[9] (ii) A bridge substituted **1** also results from an insertion of substituted carbenes into the internal bond of bicyclo[1.1.0]butanes.[10] (iii) A third approach uses appropriate precursors for syntheses of various substituted [1.1.1]propellanes, which then afford the required derivatives of **1** by addition across the internal bond. This last method was used almost exclusively for carbon-based substituents. Szeimies' group[11] has prepared many such propellanes and developed a general procedure that was used by others subsequently. An interesting application was the preparation of C-substituted propellane homopolymers[12] and copolymers.[13] A similar approach has been used for the preparation of a tetracyclononane derivative **2**, in which an additional bridge spans the C(2) and C(4) carbon atoms of **1**.[14] The initial steps of our synthesis of bicyclo[1.1.1]pentane-1,2,3,4-tetracarboxylic acid (**3**) also employed this pathway.[15]

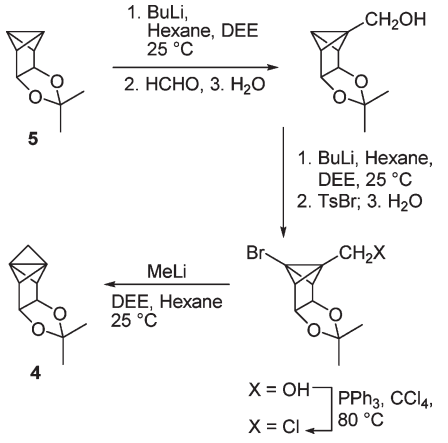
In the present paper we report the synthesis of differentially bridgehead and bridge-substituted derivatives of **1**.



Results

As a good starting material for our intended syntheses the literature[14] offered the propellane **4**, a precursor of the already known **2**, prepared by the general procedure of Szeimies (Scheme 2).[11]

SCHEME 2. Stepwise Preparation of the [1.1.1]Propellane Derivative 4[14]



Some bicyclobutane derivatives such as tricyclo[3.1.0.0^{2,6}]hexane and tricyclo[4.1.0.0^{2,7}]heptane could be doubly lithiated and the third cyclopropane ring then introduced by reaction with chloroiodomethane, yielding the corresponding propellanes in one step.[11] Since this procedure simplifies the preparation and substantially increases the yield, we attempted to use it in our case. The intermediate **5** used in the synthesis of **4**, however, could only be monolithiated, and we concluded that the third cyclopropane ring had to be constructed stepwise. We assumed that the double lithiation would most probably work in a symmetric bicyclobutane derivative and therefore designed a new intermediate **6** where the both lithiated positions are equivalent. The compound **6** is a double ketal of a known diketone **7** that was obtained by dihydroxylation of benzvalene followed by the Swern oxidation.[16] The protection of **7** was accomplished by a reaction with silylated ethylene glycol, catalyzed by silyl triflate at low temperature.[17] However, our attempts to

(7) Levin, M. D.; Hamrock, S. J.; Kaszynski, P.; Shtarev, A. B.; Levina, G. A.; Noll, B. C.; Ashley, M. E.; Newmark, R.; Moore, G. G. I.; Michl, J. *J. Am. Chem. Soc.* **1997**, *119*, 12750. Shtarev, A. B.; Pinkhassik, E.; Levin, M. D.; Stibor, I.; Michl, J. *J. Am. Chem. Soc.* **2001**, *123*, 3484.

(8) Robinson, R. E.; Michl, J. *J. Org. Chem.* **1989**, *54*, 2051. Hamrock, S. J.; Michl, J. *J. Org. Chem.* **1992**, *57*, 5027.

(9) Wiberg, K. B.; Williams, V. Z. *J. Org. Chem.* **1970**, *35*, 369.

(10) Potekhin, K. A.; Maleev, A. V.; Struchkov, Yu. T.; Surmina, L. S.; Koz'min, A. S.; Zefirov, N. S. *Dokl. Akad. Nauk SSSR Ser. Khim.* **1988**, *298*, 123. Wiberg, K. B.; Dailey, W. P.; Walker, F. H.; Waddell, S. T.; Cracker, L. S.; Newton, M. *J. Am. Chem. Soc.* **1985**, *107*, 7247. Applequist, D. E.; Renken, T. L.; Wheeler, J. W. *J. Org. Chem.* **1982**, *47*, 4985. Applequist, D. E.; Wheeler, J. W. *Tetrahedron Lett.* **1977**, 3411. Hall, H. K., Jr.; Smith, C. D.; Blanchard, E. P., Jr.; Cherkofsky, S. C.; Sieja, J. B. *J. Am. Chem. Soc.* **1971**, *93*, 121.

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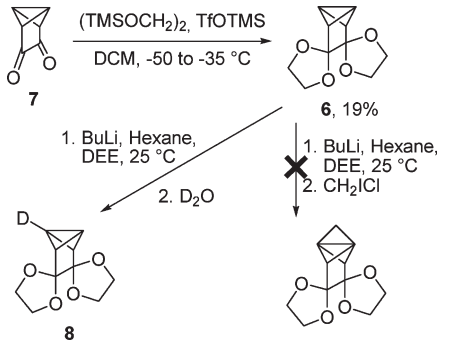
(14) Stulgies, B.; Pigg, D. P.; Kaszynski, P.; Kudzin, Z. H. *Tetrahedron* **2005**, *61*, 89.

(15) Mazal, C.; Škarka, O.; Kaleta, J.; Michl, J. *Org. Lett.* **2006**, *8*, 749.

(16) Christl, M.; Kraft, A. *Angew. Chem.* **1988**, *100*, 1427. *Angew. Chem., Int. Ed.* **1988**, *27*, 1369.

(17) An inspiring example was found in Rubin et al. (Rubin, Y.; Knobler, B. C.; Diederich, F. *J. Am. Chem. Soc.* **1990**, *112*, 1607), where the method was applied to strained cyclic ketones.

SCHEME 3. Attempted Direct Preparation of a [1.1.1]Propellane Derivative from 7



lithiate **6** with an excess of *n*-butyllithium did not show any evidence of the expected double lithiation, and the subsequent reaction with chloroiodomethane failed. When quenched with deuterium oxide, the reaction mixture gave only the singly deuterated product **8** (Scheme 3).

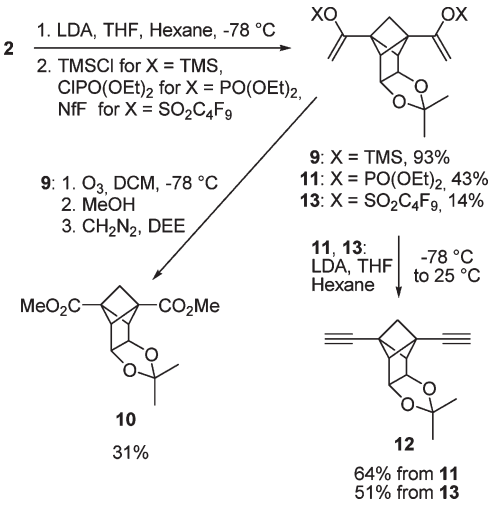
The failure of the alternative approach along with the poor yield of **6** prompted us to return to the original procedure for the preparation of **4** and then also **2**. Both compounds offer a good option to install functionalities to the bridgeheads, and to introduce a transverse functionality after removing the acetonide protection. (i) Carboxylate, (ii) ethynyl, and (iii) acetylsulfanyl were chosen as bridgehead substituents of interest.

(i) The bridgehead acetyl groups of the diketone **2** were oxidized indirectly by ozonation of the corresponding vinyl silyl ether **9**. It can be easily prepared in excellent yield by deprotonation of **2** with LDA and silylation of the resulting dilithium dienolate with chlorotrimethylsilane. Ozonation of **9** followed by diazomethane esterification afforded the dimethyl diester **10** in a reasonable yield (Scheme 4).

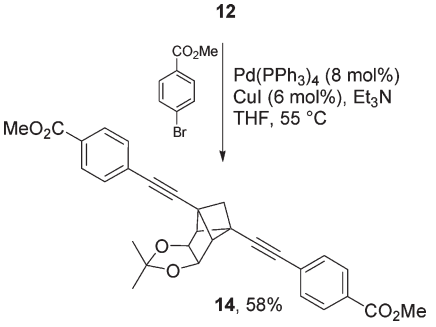
(ii) As for the bridgehead ethynyls, we again took advantage of the easy formation of the enolate and treated it with diethyl chlorophosphate obtaining the diethyl phosphate **11**. Its elimination reaction with LDA in THF yielded the diyne **12** in 64%, which means acceptable 28% overall yield from the diketone **2** (Scheme 4). The enolate of **2** was also reacted with perfluorobutanesulfonyl fluoride (NfF). A nonaflate **13**, obtained in the low yield reaction, eliminated analogously as **11** and afforded a comparable yield of the diyne **12**. The reactivity of the diyne **12** in the Sonogashira cross-coupling reaction was tested with methyl 4-bromobenzoate under standard conditions. The unoptimized isolated yield of the coupling product **14**, 58%, was very encouraging (Scheme 5).

(iii) Acetylsulfanyl groups can be introduced by an addition of diacetyl disulfide to the propellane **4**. The reaction gave a complex mixture of products where no starting **4** was detected. The only products containing the original unrearranged ring system, as proved by ^{1}H NMR, were the bisacetylsulfanyl derivative **15** and a small amount of the monoacetylsulfanyl derivative **16** (Scheme 6), which were successfully isolated by repeated column chromatography. No oligomers resulted in the reaction. The structure of **16** was assigned by means of NOESY NMR when positive NOE was found between signals of the methyl protons of the acetysulfanyl group and the protons in positions 1 and 7 of the 8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]decane skeleton of **16**.

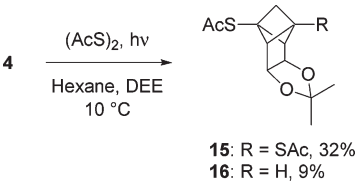
SCHEME 4. Syntheses Starting from Enolate of 2



SCHEME 5. Construction of a Laterally Substituted Molecular Rod by Sonogashira Cross-Coupling of the Diyne 12



SCHEME 6. Addition of Diacetyl Disulfide to Propellane 4



To introduce a transverse fuctionality to the previously prepared derivatives with different bridgehead substituents, their acetonide protection had to be removed and the resulting vicinal *cis*-diols transformed further. The acetonide protected compounds **10**, **14**, **15**, and **16** were deprotected by treatment with HCl in the mixture of THF and methanol yielding the corresponding diols **17**−**20**, respectively, in good yields (Scheme 7). Only in the case of **14** did chloroform have to be added to the reaction mixture to accommodate a limited solubility of the starting material.

The deprotection was followed by Swern oxidation of the diols using the same protocol, which has been successfully used in the case of **7**.[16] Good yields of α-diketones **21**−**24** were obtained also this time. The reaction of the very unstable diketones **21** and **22** with 1,2-benzendiamine gave the more stable quinoxalines **25** and **26**, respectively, in moderate yield (Scheme 7).

SCHEME 7. Removal of Acetonide Protection, Oxidation of the Corresponding Diols to α-Diketones, and Syntheses of Quinoxalines

10: R = R' = CO_2Me
14: R = R' = CC-*p*-$C_6H_4CO_2Me$
15: R = R' = SAc
16: R = SAc, R' = H

17: R = R' = CO_2Me, 76%
18: R = R' = CC-*p*-$C_6H_4CO_2Me$, 87%
19: R = R' = SAc, 70%
20: R = SAc, R' = H, 79%

21: R = R' = CO_2Me, 72%[b]
22: R = R' = CC-*p*-$C_6H_4CO_2Me$
23: R = R' = SAc, 63%
24: R = SAc, R' = H, 56%

25: R = CO_2Me, 74%
26: R = CC-*p*-$C_6H_4CO_2Me$, 20%[c]

[a]Chloroform had to be used in the case of **14** due to limited solubility. [b]Yield of the crude product. [c]For two last steps.

Discussion

The syntheses described in the Results section demonstrate that the propellane **4** is a good starting material for structures that could serve as T-shaped molecular building blocks combining an essentially free rotation around an axis with a possibility to install an additional transverse functionality. Three groups that provide good connectivity in the axial direction were used: (i) carboxylate, (ii) ethynyl, and (iii) acetylsulfanyl.

(i) Carboxylates are useful in the construction of various metal−organic frameworks[18] and are readily transformed into many other functional groups. Because of the lability of the diketone **2** obtained by a known procedure from **4**, we were unable to use the haloform oxidation of bridgehead acetyls,[19] the most widely used procedure for installing carboxyls at the bridgeheads of **1**. This reaction was not fully compatible with the acetonide protection in **2**, and yielded a deprotected diacid in less than 5% yield. Fortunately the diketone **2** enolized easily and yielded the corresponding silyl enol ether **9**, permitting the use of a modified ozonation procedure successful in some other cases of sensitive compounds.[20]

(ii) Ethynyl substituents were chosen for the bridgeheads in order to permit the Sonogashira coupling reaction to be used for incorporation of the T-shaped building block. This coupling is a very popular method for construction of giant molecules such as aryleneethynylenes,[21] has a wide scope, and tolerates a wide choice of functional groups.[22] Since bridgehead halides on **1** do not undergo an oxidative addition of metal catalysts, the acetylene units need to be carried by the bridgeheads. The usual procedure for transforming a bridgehead acetyl on **1** into ethynyl is fusion with triphenylphosphine and hexachloroethane, which produces chlorovinyl derivatives, followed by treatment with sodium amide in liquid ammonia.[23] This method failed in our case since the hydrogen chloride generated in the first step is incompatible with the acetonide protection and with the presence of the strained cage. Inspired by the easy enolization and formation of the vinyl ether **9**, we decided to use Negishi's[24] elimination of vinyl phosphates, which was successful in the case of the adamantane bridgehead.[25] In our case, a satisfactory yield was obtained only when the original one-pot process was carried out stepwise. Our attempts to substitute the very toxic diethyl chlorophosphate with a less dangerous perfluorobutanesulfonyl fluoride, which was recently used in similar elimination reactions including that at the adamantane bridgehead,[26] produced poor results mainly due to a very low yield of the nonaflate **13**. The yield of the elimination step was slightly inferior, too.

(iii) Acetylsulfanyl groups were deemed useful for attachment to metal surfaces. They were introduced by photoaddition of diacetyl disulfide across the propellane **4**. In contrast to a similar reaction of [1.1.1]propellane, where reasonable yields of the first five oligomers ([*n*]staffanes with $n = 1-5$) were formed,[27] no oligomers resulted in the reaction with **4**. This process thus resembles the photoreaction of **4** with biacetyl,[14] where no oligomerization was observed, either. The presence of the singly substituted adduct **16** complicated the separation of products. An attempt to promote the oligomerization by decreasing the amount of diacetyl disulfide used in the reaction merely led to an increase in the amount of **16** formed. Not surprisingly, the structure of **16** implies that the acetylsulfanyl radical attacks the propellane from the more accessible side. An intermediate bridgehead radical is then sterically hindered and fails to react with another molecule of propellane to yield a dimer or higher oligomers. It prefers to react with another molecule of diacetyl disulfide or to abstract a hydrogen atom from the solvent or one of the other compounds present.

The compatibility of the bridgehead acetylsulfanyl groups with the deprotection and Swern oxidation in the conversion of **15** and **16** to the α-diketones **23** and **24** is important if such

(18) Perry, J. J., IV.; Perman, J. A.; Zaworotko, M. J. *Chem. Soc. Rev.* **2009**, *38*, 1400.

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(21) For some recent examples see: Blaszczyk, A.; Fischer, M.; von Haenisch, C.; Mayor, M. *Eur. J. Org. Chem.* **2007**, *16*, 2630. Wang, C.; Batsanov, A. S.; Bryce, M. R.; Sage, I. *Org. Lett.* **2004**, *6*, 2181. Kang, Y.; Wang, S. *Tetrahedron Lett.* **2002**, *43*, 3711. Wang, C.; Batsanov, A. S.; Bryce, M. R. *J. Org. Chem.* **2006**, *71*, 108.

(22) For the scope of the coupling reaction see: Sonogashira, K. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 203−229.

(23) Schwab, P. F. H.; Noll, B. C.; Michl, J. *J. Org. Chem.* **2002**, *67*, 5476. Gleiter, R.; Pfeifer, K.-H.; Szeimies, G.; Bunz, U. *Angew. Chem.* **1990**, *102*, 418. *Angew. Chem., Int. Ed.* **1990**, *29*, 413. Bunz, U.; Szeimies, G. *Tetrahedron Lett.* **1990**, *31*, 651.

(24) Negishi, E.; King, A. O.; Klima, W. L. *J. Org. Chem.* **1980**, *45*, 2526.

(25) Stulgies, B.; Prinz, P.; Magull, J.; Rauch, K.; Meindl, K.; Rühl, S.; de Meijere, A. *Chem.—Eur. J.* **2005**, *11*, 308.

(26) Lyapkalo, I. M.; Vogel, M. A. K.; Boltukhina, E. V.; Vavřík, J. *Synlett* **2009**, 558.

(27) Friedli, A. C.; Kaszynski, P.; Michl, J. *Tetrahedron Lett.* **1989**, *30*, 455. Kaszynski, P.; Michl, J. *J. Am. Chem. Soc.* **1988**, *110*, 5225. Kaszynski, P.; Friedli, A. C.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 601.

derivatives are needed for metal surface applications. The α-diketone moiety can be used for construction of additional functionalities in a direction perpendicular to the axis of the expected rotation of the T-shaped building block. α-Diketones are rather unstable in general, particularly when strained, as is the case here. However, they can be easily transformed into various heterocycles. The quinoxalines **25** and **26** yielded the first examples of T-shaped molecular building blocks with a heterocyclic unit in the bridge plane of **1**. The rod-like **26** represents a good example of a molecular rod with an essentially freely rotatable transverse rigid arm attached alongside a rod. It promises to be useful for the construction of more complex covalent scaffolds.

The limited stability of the strained α-diketone is responsible for the difficulties encountered in the attempts to protect the intermediate **7** on the alternative pathway to the propellane analogous to **4**. The intermediate **7** was very sensitive to acidic conditions generally needed to protect a carbonyl group,[28] and a very mild procedure had to be used. Only a low yield of **6** resulted in the reaction of **7** with silylated ethylene glycol under silyl triflate catalysis, which is mild enough and runs fast enough even at low temperature, and this route had to be abandoned.

Conclusions

We have prepared an electronically insulating T-shaped molecular connector with a nearly freely rotating side arm, based on a bridge-substituted bicyclo[1.1.1]pentane cage. We have provided an illustration of the ways in which this unit can be extended, through carboxylate, thiol, or acetylene chemistry at the bridgehead position, and through a highly reactive α-diketone moiety in the transverse direction, as demonstrated with quinoxaline.

Experimental Section

All reactions were carried out under argon atmosphere with dry solvents, freshly distilled under anhydrous conditions, unless otherwise noted. Standard Schlenk and vacuum line techniques were employed for all manipulations of air or moisture sensitive compounds. Yields refer to isolated, chromatographically and spectroscopically homogeneous materials, unless otherwise stated. 3,5-Diacetyl-9,9-dimethyl-8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]decane (**2**),[14] tricyclo[3.1.0.0^{2,6}]hexane-3,4-dione (**7**),[16] diacetyl disulfide,[29] and an ethereal solution of diazomethane[30] were prepared according to previously published procedures.

1,2-Benzenediamine was purchased and sublimed prior to use. Trimethylsilyl chloride, perfluorobutanesulfonyl fluoride, diethyl chlorophosphate, oxalyl chloride, dimethyl sulfoxide, diisopropylamine, $Pd(PPh_3)_4$, and methyl 4-bromobenzoate were purchased and used without further purification. Triethylamine and dichloromethane were distilled from CaH_2 under argon immediately prior to use.

Melting points were determined with a standard apparatus and are uncorrected. ^{1}H, ^{13}C, ^{19}F, and ^{31}P spectra were acquired at 25 °C with 300 and 500 MHz (^{1}H frequencies) spectrometers. ^{1}H and ^{13}C spectra were referenced to residual solvent peaks. IR spectra were recorded for neat samples on NaCl plates. GC-MS spectra were measured on an instrument with a fused silica capillary column (cross-linked 5% phenyl methyl silicone).

Dispiro[(1,3-dioxolane)-2,3′-tricyclo[3.1.0.0^{2,6}]hexane-4′,2″-(1,3-dioxolane)] (6). A flame-dried Schlenk flask was charged with diketone **7** (287 mg, 2.652 mmol) in dry dichloromethane (60 mL) and with 1,2-bis[(trimethylsilyl)oxy]ethane (3.00 mL, 12.237 mmol). The solution was cooled to −50 °C and trimethylsilyl trifluoromethanesulfonate (235 μL, 1.300 mmol) was added. The cooling was interrupted and the reaction mixture was slowly heated to −30 °C in 30 min and then stirred at that temperature for 30 min. Subsequently, dry triethylamine (350 μL) was added, which turned the color of the reaction mixture yellow immediately. The mixture was heated to room temperature. Then, volatiles were evaporated under reduced pressure. Column chromatography (alumina, CH_2Cl_2/hexanes 1:2, then CH_2Cl_2/hexanes 1:1) yielded **6** as a colorless oil (97 mg, 0.494 mmol, 19%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.20 (t, J = 1.93 Hz, 2H), 2.46 (t, J = 1.93 Hz, 2H), 3.82−3.91 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 2.8, 39.7, 60.2, 98.4. MS (ESI+, CH_3CN), m/z: 197.1 ([M + H]$^+$), 203.1 ([M + Li]$^+$), 219.1 ([M + Na]$^+$).

9,9-Dimethyl-3,5-bis(1-(trimethylsilyloxy)vinyl)-8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]decane (9). A solution of diketone **2** (533 mg, 2.130 mmol) in THF (10 mL) was slowly added to a stirred solution of LDA at −78 °C, freshly prepared from diisopropylamine (848 μL, 6.0 mmol) in THF (20 mL) and *n*-butyllithium in hexane (2.5 M, 2.04 mL, 5.1 mmol). After 2 h of stirring at this temperature, the reaction mixture was slowly heated to room temperature and stirred for an additional 15 min. Then it was cooled back to −78 °C and trimethylsilyl chloride (1.39 mL, 11.0 mmol) was added. The reaction mixture was stirred for an additional 1 h, then slowly warmed to room temperature and stirred for 1.5 h. Volatiles were removed under reduced pressure and the crude product **9** was extracted with pentane (3 × 20 mL) as a colorless oil (781 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (s, 18H), 1.31 (s, 3H), 1.44 (s, 3H), 2.01 (s, 2H), 2.89 (s, 2H), 3.99 (d, J = 1.37 Hz, 1H), 4.05 (d, J = 1.37 Hz, 1H), 4.17 (d, J = 0.77 Hz, 1H), 4.37 (d, J = 0.77 Hz, 1H), 4.87 (br s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.04, 0.3, 23.9, 24.0, 42.7, 45.6, 52.9, 63.4, 82.2, 90.0, 92.2, 113.9, 154.8, 155.6. IR (neat): 2966, 2902, 1630, 1535, 1456, 1373, 1309, 1255, 1223, 1198, 1053, 1016, 847, 752 cm^{-1}. GC-MS, m/z (%): 394 (M, 1), 379 (M − CH_3, 1), 336 (8), 308 (7), 293 (11), 279 (7), 246 (8), 217 (9), 203 (7), 180 (5), 156 (7), 147 (9), 117 (5), 73 (100), 43 (4).

9,9-Dimethyl-8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]decane-3,5-dicarboxylic Acid Dimethyl Ester (10). Ozone was introduced into a solution of silyl enol ether **9** (781 mg, 1.98 mmol) in dichloromethane (50 mL) at −78 °C until a slightly blue color of the solution indicated the end of the reaction (∼40 min). An excess of ozone was purged off with a stream of argon at −78 °C. Methanol (1.20 mL) and then an excess of an ethereal diazomethane solution was added (until the reaction mixture turned yellow). The solution was stirred for 12 h at room temperature. Column chromatography on silica gel (ethyl acetate/hexane 1:1) yielded diester **10** as a white crystalline solid (173 mg, 31%). Mp 95.4−96.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 6H), 2.43 (s, 2H), 3.35 (s, 2H), 3.68 (s, 3H), 3.71 (s, 3H), 4.92 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.0, 24.5, 42.30, 42.34, 49.4, 51.6, 51.8, 65.9, 81.1, 114.6, 168.1, 168.5. IR (KBr): 3442, 2985, 2948, 2902, 1730, 1630, 1435, 1377, 1313, 1288, 1269, 1198, 1153, 1101, 1051, 980, 858 cm^{-1}. GC-MS, m/z (%): 283 (M + H, < 1), 267 (M − CH_3, 100), 251 (M − OCH_3, 5), 207 (6), 193 (51), 165 (62), 133 (19), 105 (15), 91 (10), 77 (12), 59 (14), 43 (34). HRMS, (ESI+) for ($C_{14}H_{18}O_6$ + H$^+$): calcd 283.1173, found 283.1176.

Enol Phosphate 11. A solution of diketone **2** (1.150 g, 4.59 mmol) in THF (15 mL) was slowly added to the cold (−78 °C)

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solution of LDA freshly prepared from diisopropylamine (1.623 mL, 11.49 mmol) in THF (30 mL) and *n*-butyllithium in hexane (2.5 M, 4.227 mL, 10.57 mmol). The mixture was stirred at this temperature for 2 h, slowly warmed to −30 °C, and cooled again to −78 °C. A yellowish solid precipitated. Subsequently, diethyl chlorophosphate (1.660 mL, 11.49 mmol) was added and the mixture was stirred for 2 h at −78 °C, and then slowly warmed to room temperature. The yellowish precipitate disappeared leaving a brown-orange solution. Volatiles were removed under reduced pressure yielding brown oil that was dissolved in ether (140 mL) and washed with water (2 × 30 mL). Combined water layers were extracted with ether (2 × 20 mL) and the organic extract was dried over Na_2SO_4. Evaporation of solvents followed by the column chromatography on silica gel with ethyl acetate yielded enol phosphate **11** as a colorless oil (1.032 g, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (s, 3H), 1.28−1.34 (m, 12 H), 1.37 (s, 3H), 2.18 (s, 2H), 3.06 (s, 2H), 4.07−4.17 (m, 8H), 4.43−4.44 (m, 1H), 4.76−4.78 (m, 1H), 4.83 (s, 2H), 4.88−4.90 (m, 1H), 4.95−4.96 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.9 (d, J = 2.93 Hz), 16.0 (d, J = 2.89 Hz), 23.9, 43.8, 44.6 (d, J = 7.62 Hz), 51.7 (d, J = 7.49 Hz), 64.0, 64.1 (d, J = 6.13 Hz), 64.4 (d, J = 6.11 Hz), 81.6, 98.1 (d, J = 3.23 Hz), 98.9 (d, J = 3.24 Hz), 114.4, 150.5 (d, J = 2.82 Hz), 150.6 (d, J = 2.80 Hz). ^{31}P NMR (300 MHz, $CDCl_3$): δ −5.34, −5.52. IR (neat): 2983, 2937, 2912, 1651, 1479, 1444, 1371, 1271, 1225, 1192, 1163, 1032, 995, 949, 858 cm^{-1}. MS, m/z (%): 523 (M + H, 19), 507 (M − CH_3, 8), 447 (11), 310 (17), 291 (20), 263 (58), 235 (34), 207 (28), 179 (33), 161 (53), 155 (69), 127 (51), 99 (92), 81 (35), 45 (28). HRMS, (ESI+) for ($C_{22}H_{36}O_{10}P_2$ + Na^+): calcd 545.1676, found 545.1674.

3,5-Diethynyl-9,9-dimethyl-8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]-decane (12). The enol phosphate **11** (427 mg, 0.817 mmol) in THF (5 mL) was slowly added to the stirred solution of LDA, prepared from diisopropylamine (1.39 mL, 9.804 mmol) in THF (15 mL) and *n*-butyllithium (2.5 M, 3.59 mL, 8.987 mmol) in hexane at −78 °C. The reaction mixture turned red immediately. The dark red solution was stirred at that temperature for 1 h, then slowly warmed to room temperature and stirred for 3 h. Then it was poured into pentane (120 mL) and washed with water (3 × 20 mL). The combined water layers were extracted with pentane (2 × 20 mL) and the organic extract was dried over Na_2SO_4. Volatiles were removed under reduced pressure and the resulting yellowish solid was purified by the column chromatography on silica gel (diethyl ether/pentane 2:1) providing diacetylene **12** as white needles (112 mg, 64%). Mp 111.2−113.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.59 (s, 3H), 2.17 (s, 1H), 2.18 (s, 1H), 2.43 (s, 2H), 3.18 (s, 2H), 4.90 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.2, 24.3, 34.2, 41.3, 47.3, 70.0, 70.1, 71.6, 78.7, 81.5, 81.8, 115.0. IR (KBr): 3251, 2985, 2935, 2897, 1379, 1342, 1265, 1219, 1201, 1157, 1068, 1047, 972, 850 cm^{-1}. GC-MS, m/z (%): 215 (M + H, 2), 199 (M − CH_3, 79), 155 (11), 139 (54), 127 (97), 105 (49), 77 (28), 43 (100). HRMS, (EI) for ($C_{14}H_{13}O_2^+$): calcd 213.0916, found 213.0918.

Sonogashira Cross-Coupling Reaction of Diyne 12 with Methyl 4-Bromobenzoate. A flame-dried Schlenk flask was charged with diyne **12** (112 mg, 0.523 mmol), methyl 4-bromobenzoate (337 mg, 1.569 mmol), $Pd(PPh_3)_4$ (49 mg, 0.042 mmol, 8 mol %), and CuI (6 mg, 0.031 mmol, 6 mol %). After three successive vacuum/argon cycles, dry and degassed THF (7 mL) and triethylamine (6 mL) were added via syringe. The yellow reaction mixture was stirred for 16 h at 55 °C. A white solid precipitated. The solution was cooled to room temperature, diluted with ether (75 mL), and washed with water (3 × 15 mL). The yellow organic phase was dried over Na_2SO_4. After evaporation of volatiles, the pure product **14** was isolated as a white solid (146 mg, 58%) by chromatography on silica gel ($CHCl_3$/ethyl acetate 35:1). Mp 227.6−229.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.55 (s, 3H), 2.58 (s, 2H), 3.34 (s, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 4.97 (s, 2H), 7.41−7.46 (m, 4H), 7.91−7.95 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 24.6, 35.2, 42.3, 47.7, 52.0, 52.1, 70.8, 80.8, 81.8, 82.8, 87.2, 90.6, 114.9, 126.9, 127.8, 129.29, 129.34, 129.7, 131.5, 131.6, 166.2, 166.3. IR (KBr): 3440, 2983, 2933, 2893, 2222, 1722, 1603, 1437, 1377, 1281, 1200, 1111, 1074, 968, 854, 766 cm^{-1}. MS, m/z (%): 482 (M, 2), 467 (M − CH_3, 9), 451 (M − OCH_3, 18), 424 (43), 407 (12), 395 (100), 382 (19), 365 (51), 337 (58), 307 (37), 289 (33), 276 (56), 239 (19), 223 (22), 202 (20), 163 (25), 59 (58), 43 (39). HRMS (APCI) for ($C_{30}H_{26}O_6$ + H^+): calcd 483.1802, found 483.1797.

Addition of Diacetyl Disulfide to Propellane 4. Freshly distilled $(AcS)_2$ (2.000 g, 13.314 mmol) was added to a solution of propellane **4** in ether/hexanes (30 mL, 1:2) prepared from 3-bromo-4-chloromethyl-8,8-dimethyl-7,9-dioxatetracyclo[4.3.0.0^{2,4}.0^{3,5}]-nonane (Scheme 2) (554 mg, 1.982 mmol). The solution was stirred in a quartz reactor in an ice−water bath and irradiated by 450 W medium-pressure mercury lamp for 4.5 h under argon. Solvents were distilled under reduced pressure and the excess of $(AcS)_2$ was removed from the remaining reddish oil by distillation in a Kugelrohr apparatus (60 °C, 0.5 Torr). Separation of the distillation residue by column chromatography on silica gel (CH_2Cl_2, then ethyl acetate/hexane 1:4) provided two non-rearranged products, the bis- and monoacetylsulfanyl derivatives **15** (198 mg, 32%) and **16** (41 mg, 9%), respectively, as white solids.

***S*-(5-Acetylsulfanyl-9,9-dimethyl-8,10-dioxatetracyclo[5.3.0.0^{2,5}.0^{3,6}]decane-3-yl) thioacetate (15):** Mp 72.3−73.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.56 (s, 3H), 2.25 (s, 3H), 2.26 (s, 3H), 2.82 (s, 2H), 3.58 (br s, 2H), 4.73 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.9, 24.9, 31.0, 31.1, 44.7, 48.8, 51.3, 68.3, 81.2, 114.7, 194.3, 195.4. MS (ESI+, $CHCl_3$), m/z: 315.1 ([M + H]$^+$), 321.1 ([M + Li]$^+$), 337.1 ([M + Na]$^+$).

***S*-(1*RS*,2*SR*,6*RS*,7*SR*)-(9,9-Dimethyl-8,10-dioxatetracyclo-[5.3.0.0^{2,5}.0^{3,6}]decane-3-yl) thioacetate (16):** Mp 59.5−60.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.43 (s, 3H), 2.25 (s, 3H), 2.35 (s, 2H), 3.01 (s, 1H), 3.22 (br s, 2H), 4.72 (br s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.4, 26.0, 31.3, 34.5, 43.4, 52.6, 66.1, 81.6, 113.9, 195.3. MS (ESI+, $CHCl_3$), m/z: 241.1 ([M + H]$^+$), 247.1 ([M + Li]$^+$), 263.1 ([M + Na]$^+$).

Liberation of Diol 18 from Acetonide 14. The acetonide **14** (115 mg, 0.238 mmol) was dissolved in a mixture of chloroform (5 mL), methanol (6 mL), and concentrated hydrochloric acid (1.3 mL). The yellowish reaction mixture was stirred at room temperature for 22 h. Then the solution was diluted with ether (75 mL) and washed with 10% $NaHCO_3$ (3 × 15 mL). Water layers were extracted with ether (3 × 15 mL) and the combined organic layers were dried over Na_2SO_4. Evaporation of solvents followed by column chromatography on silica gel (chloroform/ethyl acetate 4:3) provided a white solid that was dissolved in chloroform and precipitated with pentane yielding an analytically pure sample of diol **18** in the form of long white needles (91 mg, 87%). Mp 235.5−237.3 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.58 (s, 2H), 2.66−2.68 (m, 2H), 3.36 (s, 2H), 3.90 (s, 3H), 3.91 (s, 3H), 4.52 (d, J = 4.25 Hz, 2H), 7.41−7.46 (m, 4H), 7.92−7.97 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.4, 35.7, 48.2, 52.19, 52.22, 72.7, 73.5, 81.3, 81.9, 87.4, 89.8, 127.0, 127.3, 129.37, 129.43, 129.6, 129.8, 131.7, 166.4, 166.5. IR (KBr): 3533, 3423, 3321, 2978, 2949, 2891, 2222, 1714, 1603, 1404, 1284, 1178, 1105, 1014, 858, 769 cm^{-1}. MS, m/z (%): 442 (M, < 1), 424 (4), 411 (M − OCH_3, 4), 395 (16), 382 (5), 365 (8), 337 (11), 323 (5), 277 (15), 265 (14), 252 (9), 240 (9), 237 (9), 203 (15), 187 (9), 163 (100), 149 (19), 135 (11), 115 (11), 64 (15), 59 (36). HRMS (ESI+) for ($C_{27}H_{22}O_6$ + Na^+): calcd 465.1309, found 465.1307.

Swern Oxidation of the Diol 18 and the Reaction of Resulting Diketone 22 with 1,2-Benzenediamine to Quinoxaline 26. To a solution of DMSO (51 μL, 0.724 mmol) in dichloromethane

(2 mL) was added oxalyl chloride (48 μL, 0.543 mmol) at −78 °C. After 5 min, the diol **18** (80 mg, 0.181 mmol) in dichloromethane (18 mL) was slowly introduced, and the resulting milky solution was stirred for 1 h at −78 °C. Then triethylamine (151 μL, 1.086 mmol) was added. The mixture was stirred for 10 min and then warmed to room temperature. The solution became yellow. Volatiles were removed under reduced pressure and the resulting yellowish solid was dissolved in a mixture of chloroform and ethyl acetate (2:1) and filtered through a short silica gel column. A careful evaporation of solvents yielded the crude diketone **22** (58 mg) as an unstable yellowish solid, which was immediately dissolved in THF (6 mL). Freshly sublimed 1,2-benzenediamine (20 mg, 0.185 mmol) was added, and the brownish reaction mixture was stirred at room temperature for 2 h. Volatiles were removed under reduced pressure and the resulting brown solid was chromatographed on silica gel (chloroform/ethyl acetate 1:1) yielding the quinoxaline **26** as a yellowish solid (19 mg, 20%). Mp 243 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.05 (s, 2H), 3.84 (s, 6H), 4.24 (s, 2H), 7.32−7.34 (m, 4H), 7.62−7.65 (m, 2H), 7.86−7.88 (m, 4H), 7.99−8.02 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.6, 49.2, 52.1, 73.7, 85.5, 85.9, 126.2, 128.8, 129.0, 129.2, 129.9, 131.7, 140.5, 163.0, 166.1. IR (KBr): 2981, 2949, 2896, 2214, 1724, 1602, 1436, 1371, 1291, 1193, 1103, 1056, 851, 763. HRMS (ESI+) for ($C_{33}H_{22}N_2O_4 + H^+$): calcd 511.1658, found 511.1652.

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Supporting Information Available: Experimental procedures for compounds **13**, **17**, **19**−**21**, and **23**−**25** and NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.