Synthesis of Some C_2-Symmetric Bidentate Ligands and Their Complexes Derived from *Feist*'s Acid

by **Abdullah M. A. Al-Majid***, **Zeid A. Al-Othman**, and **Mohammad Shahidul Islam**

Department of Chemistry, College of Science, King Saud University, P.O. Box 2455, Riyadh, 11451, Kingdom of Saudi Arabia
(phone: +9661-4675889; fax: +9661-4675992; e-mail: amajid@ksu.edu.sa)

Various new C_2-symmetric bidentate ligands, bearing phosphorus, nitrogen, and sulfur, were obtained in an efficient manner, starting from (±)-*trans*-3-methylidenecyclopropane-1,2-dicarboxylic acid (*Feist*'s acid; (±)-*trans*-**3**). The structures of the new bidentate ligands, di(*tert*-butyl) (±)-[(*trans*-3-methylidenecyclopropane-1,2-diyl)dimethanediyl]biscarbamate ((±)-**9**), (±)-(*trans*-3-methyldienecyclopropane-1,2-diyl)dimethanaminium dichloride ((±)-**10**), (±)-*S*,*S*′-[(*trans*-3-methylidenecyclopropane-1,2-diyl)dimethanediyl] diethanethioate ((±)-**11**), and (±)-[(*trans*-3-methylidenecyclopropane-1,2-diyl)-dimethanediyl]bis(diphenylphosphane) ((±)-**12**), were fully characterized by standard spectroscopic techniques. These new classes of C_2-symmetric bidentate ligands have the potential to be used in asymmetric catalysis.

Introduction. – The development of novel and efficient C_2-symmetric ligands for the synthesis of various catalysts is one of the most challenging goals in modern organic chemistry [1]. As the use of ligand–metal catalysts is incrementally increasing in organic synthesis [2–4], it is important to synthesize appropriate ligands with metal-binding capacity to form metal catalysts. In this search, diamine, diphosphine, and dithiol derivatives have attracted specific attention due to their wide range of applications [3–6]. These C_2 symmetric ligands are highly capable of binding with various transition metals, such as Ti, Cu, Ni, Zr, Ru, Rh, and Pd, to form metal catalysts of varying potentials and properties [5][7–16]. These ligand–metal components have been widely used in many asymmetric catalyses, such as alkylation, *Diels–Alder* reactions, hydrogenation reactions, *etc.* [4–6][8][10][15][17]. Furthermore, these asymmetric ligands are also useful as catalysts in the addition of organozinc reagents to carbonyl compounds [8][18]. The Ti, Zr, and Hf complexes of these bidentate ligands were also found to be quite useful for the polymerization of alkenes [19–24]. In addition, these bidentate ligands can be used for the formation of metallocene complexes, which have been employed to catalyze a wide range of enantioselective reactions, including epoxidation, aziridination, sulfoxidation, as well as the *Michael* addition reaction [25–29]. In brief, both the P- and N-based ligands have broadened the scope of the new ligand architecture in transition metal catalysis [30].

During this study, we focussed on the synthesis and characterization of new classes of C_2 symmetric bidentate ligands, containing N-, S- and P- donor atoms, and some Ti-based metal complexes which can be used as catalysts for co-polymerization and polymerization of ethenes [31]. Basically, the heteroatoms are responsible of the strong

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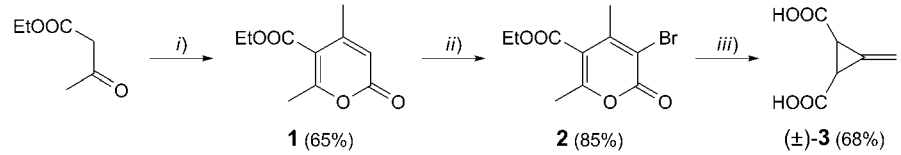
chelation with transition metals. Interestingly, these ligands can be derived directly from the well-known (±)-*trans*-3-methylidenecyclopropane-1,2-dicarboxylic acid (*Feist*'s acid; **3**). The synthesis of **3** is shown in *Scheme 1*.

Scheme 1



i) Dry HCl (g), 16 d, in a dark place. *ii*) Br_2, $CHCl_3$, 24 h, r.t. *iii*) 7M KOH, 105°, 1 h.

Results and Discussion. – (±)-*trans*-3-Methylidenecyclopropane-1,2-dicarboxylic acid ((±)-**3**) is the precursor of newly synthesized C_2 symmetric bidentate ligands in our work. *Feist*'s acid is commercially available, but expensive. We therefore prepared this acid in house, starting from cheap and readily available ethyl acetoacetate by using a procedure described by *Goss*, *Ingold*, and *Thorpe* [32]. The original method has been slightly modified, as described in the experimental section. Pyrone **1** was obtained as a slightly yellow colored liquid in 65% yield by purging freshly prepared dry HCl through neat ethyl acetoacetate for 16 d. Pyrone **1** was then treated with Br_2 in $CHCl_3$ to form the colorless and crystalline bromopyrone **2** in 85% yield. *Feist*'s acid ((±)-**3**) was obtained by the reaction of bromopyrone **2** with concentrated aqueous KOH in a good yield (68%), as crystalline product (*Scheme 1*). All analytical data of compounds **1**–**3** were in agreement with those previously reported in the literature [32]. Racemic *Feist*'s acid is the key precursor in our synthesis of new diphosphine, diamine, and dithiolate ligands, and their complexes. Thus, (±)-*trans*-(3-methylidenecyclopropane-1,2-diyl)dimethanol ((±)-**5**) was readily prepared according to the method of *Al-Majid et al.* [33] in two steps, as depicted in *Scheme 2*. The new ligands, *i.e.*, the dicarbamate (±)-**9** and the diammonium salt (±)-**10**, were synthesized in good yields in six and seven steps, respectively, starting from (±)-**3**, as shown in *Scheme 2*.

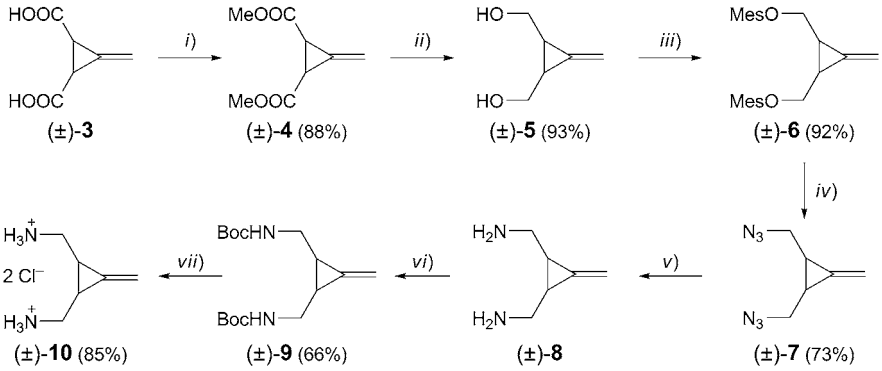
The dithiolate and diphosphine ligands **11** and **12**, respectively, were obtained in good yields from intermediate (±)-**6** in a single step, as shown in *Scheme 3*.

The titanium complexes (±)-**13** and (±)-**14** were synthesized by treating ligands (±)-**5** and (±)-**10**, respectively, with $TiCl_4$ solution in CH_2Cl_2 in rather good yields, as shown in *Scheme 4*.

Esterification of (±)-**3** gave dimethyl ester (±)-**4** in 88% yield (^{1}H-NMR ($CDCl_3$): δ(H) 3.68 (2 Me)). Compound **4** was then reduced by $LiAlH_4$ at 0° in dry THF under an inert atmosphere to afford diol (±)-**5** in 93% yield, which showed, in the ^{1}H-NMR spectrum, a characteristic *multiplet* at δ(H) 3.30–3.38 for the two CH_2 groups. Another characteristic *triplet* signal at δ(H) 4.61 was assigned to the two OH H-atoms.

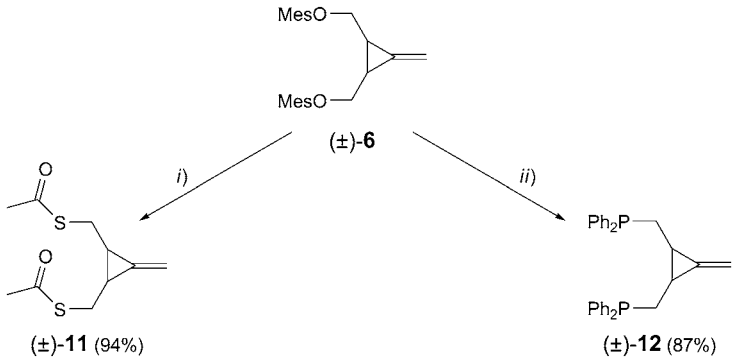
The diol (±)-**5** was protected with methanesulfonyl chloride in the presence of Et_3N in CH_2Cl_2 under dry conditions to obtain the corresponding bis[methanesulfonate] (±)-**6** in excellent yield (92%). The formation of (±)-**6** was confirmed by means of ^{1}H-NMR and IR spectroscopy. In the ^{1}H-NMR spectrum, a new *singlet* could be observed at δ(H) 3.02 for the two mesylate groups, and the OH signal of (±)-**5** at δ(H)

Scheme 2



i) MeOH, H_2SO_4 (cat.), 40°, 24 h. *ii*) THF, $LiAlH_4$ (2.0 equiv.), 0° to r.t., 4 h. *iii*) MesCl (3.0 equiv.), Et_3N (3.0 equiv.), CH_2Cl_2, 0°, 1.5 h. *iv*) DMF, NaN_3 (9.2 equiv.), 60°, 4 h. *v*) 5% Pd on $CaCO_3$ (10 wt-%), EtOH, H_2 pressure, r.t., 24 h. *vi*) DIPA (2.5 equiv.), $(Boc)_2O$ (3.0 equiv.), EtOH, r.t., 2 h. *vii*) Dioxane/HCl, r.t., 3 h.

Scheme 3

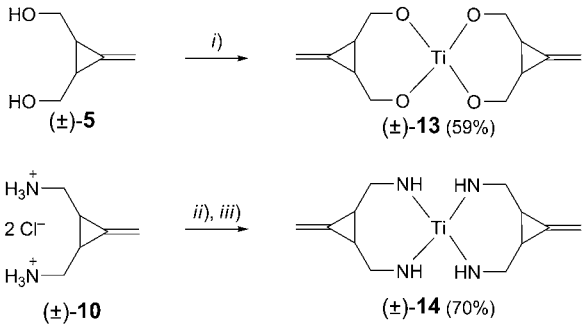


i) AcSK (2.5 equiv.), MeCN, reflux, 3 h. *ii*) Dry THF, −15°, Ph_2PLi (0.5M in THF; 6 equiv.), 2 d.

4.61 disappeared. In the IR spectrum, two sharp bands were observed at 1344 and 1173 cm^{-1} due to the asymmetric and symmetric stretching of the SO_2 groups. Having the bismesylate (±)-**6** in hand prompted us to study its utility for the synthesis of novel C_2-symmetric bidentate ligands. Therefore, it was used as the key intermediate for the synthesis of several ligands such as **9**–**12**, as described in *Schemes 2* and *3*, respectively.

For synthesis of the diazido compound (±)-**7**, (±)-**6** was treated with an excess amount of NaN_3 (9.2 equiv.) due to the low nucleophility of N_3^- at 60° in dry DMF for 4 h. The product was isolated in a yield of 73%. The formation of (±)-**7** was confirmed by the ^{1}H-NMR and IR spectra. The ^{1}H-NMR spectrum showed the absence of the Me groups of (±)-**6**. Furthermore, the IR spectrum showed a sharp band at 2091 cm^{-1}, representing the asymmetric stretching vibration of the N=N=N group.

Scheme 4



i) $TiCl_4$ (1M in CH_2Cl_2; 0.5 equiv.), 24 h. *ii*) CH_2Cl_2, $NaHCO_3$. *iii*) $TiCl_4$ (1M in CH_2Cl_2; 0.5 equiv.), 24 h.

A new dicarbamate derivative, di(*tert*-butyl) (±)-[(*trans*-3-methylidenecyclopropane-1,2-diyl)dimethanediyl]dicarbamate ((±)-**9**) was synthesized in good yield (66%). Thus, the diamine **8** was obtained by reduction of **7** using 10 wt-% of 5% Pd on $CaCO_3$ poisoned with lead (*Lindlar* catalyst) in EtOH. The free amine is unstable to air, therefore it was immediately protected with di-*tert*-butyl dicarbonate to obtain the Boc-protected amine (±)-**9**. The overall yield in two steps was 65%. In the ^{1}H-NMR spectrum, a broad signal at δ(H) 4.8 and a sharp signal at δ(H) 1.45 appeared, which were assigned to H-atoms of the NH and *t*-Bu groups, respectively. The IR spectrum showed bands at 3331 and 1688 cm^{-1}, assigned to N–H and –HN–C=O stretching vibrations, respectively. The bisammonium salt (±)-**10** was then obtained in 85% yield as a white solid by treating (±)-**9** with a HCl/dioxane mixture. The formation of (±)-**10** was inferred from the ^{1}H-NMR spectrum, where the signal of the H-atoms of the aminium groups appeared at δ(H) 8.36. In the IR spectrum, bands at 3424 and 3029 cm^{-1} were observed due to the stretching vibrations of the NH_3^+ group. It is important to note that also the dithiolate ligand (±)-**11** could be prepared in excellent yield (94%) from (±)-**6** and AcSK under reflux conditions in MeCN, as shown in *Scheme 3*. In the ^{1}H-NMR spectra of compound (±)-**11**, a new *singlet* at δ(H) 2.33 appeared due to the thioacetate group. The IR spectra showed a band at 1691 cm^{-1} assigned to the C=O stretching vibration of thioester group (S–C=O). Consequently, the diphosphine ligand (±)-**12** was obtained in the same manner by the reaction of (±)-**6** with 3 equiv. of lithium diphenylphosphanide (Ph_2PLi) using dry THF as solvent at low temperature (–20°), as depicted in *Scheme 3*. Even after 24 h, the reaction remained incomplete, probably due to decomposition of the Li reactant. This decomposition may be attributed to the highly hygroscopic nature of Ph_2PLi. To improve the yield of the reaction, 3 equiv. of Ph_2PLi were further added, under dry conditions and the reaction was continued for additional 24 h. The desired product (±)-**12** was then obtained as viscous liquid in good yield (87%). The formation of the product was confirmed by ^{1}H-NMR spectroscopy, where the H-atoms of the two Ph groups appeared as a *multiplet* at δ(H) 7.34–7.37. The up-field shift of the signal of the CH_2 H-atoms (PCH_2) at δ(H) 1.36–1.55 can be attributed to the decreased electronegativity of the P-atom compared to S, while further splitting of the signal of the CH_2 H-atoms is due to

coupling with ^{31}P. The formation of ligand (±)-**12** was further confirmed by the ^{31}P-NMR spectrum, which showed a signal at $\delta(P)$ −16.72, which was assigned to the ^{31}P isotope of phosphorous.

The Ti complex (±)-**13** was prepared in moderate yield by treating one equiv. of the ligand (±)-**5** with 0.5 equiv. of $TiCl_4$ under dry conditions with CH_2Cl_2 as a solvent (*Scheme 4*). The proposed composition for the Ti-complex (±)-**13** is based on microanalysis, ^1H- and ^{13}C-NMR studies, and MS data. The ^1H-NMR spectrum of complex (±)-**13** showed absence of the OH signal at $\delta(H)$ 4.61, indicating that the complex (±)-**13** was really formed. Furthermore, complex (±)-**13** was also confirmed by elemental analysis. Crystallization of complex (±)-**13** was not succesful due to its highly moisture sensitivity.

Complex (±)-**14** was synthesized by the reaction of ligand (±)-**10** with 0.5 equiv. of $TiCl_4$ solution in dry CH_2Cl_2. Since the free amine is not stable in air, the reaction has been carried out under dry conditions in Ar atmosphere. The HCl salt of ligand (±)-**10** was neutralized with saturated $NaHCO_3$ solution, and the free amine was then extracted with CH_2Cl_2. The free amine solution was immediately added to the $TiCl_4$ solution at 0°. Complex (±)-**14** was obtained as a brown solid and confirmed by ^1H-NMR and IR spectra, as well as elemental analysis. In the ^1H-NMR spectrum, the intergral of the signal of the amino-H-atoms was counted only for four H-atoms, compared to eight in the free ligand (±)-**10**. In the IR spectrum, only one NH band was observed at 3332 cm^{-1} as a strong, broad stretching vibration.

Conclusions. – In conclusion, a series of new N-, S-, and P-bearing C_2 symmetrical ligands were synthesized. All these ligands were derived from (±)-*trans*-3-methylidene-cyclopropane-1,2-dicarboxylic acid (*Feist*'s acid; **3**) which served as the key precursor. The complexation of these ligands in their optical active form with different metals can lead to potential catalysts for various asymmetric inductions such as alkylation, hydrogenation, *Diels–Alder* reaction, polymerization, isomerization, *etc*. This will be investigated in near future. Our current studies were focused on the development of novel classes of chiral C_2 symmetrical bidentate, or tetradentate ligands, based on *Feist*'s acid with bulky environment. The activity of these ligands in the asymmetric induction will be studied, and we plan to report these results in due course.

Experimental Part

General. All the moisture- and air- sensitive reactions were carried out under an inert atmosphere using an Ar filled glove box and standard *Schlenk*-line techniques. All the chemicals were purchased from *Aldrich*, *Sigma–Aldrich*, and *Fluka*, *etc.*, and were used without further purification, unless otherwise stated. Pyridine, Et_3N, and DIPA were distilled over NaOH. Et_2O and THF were distilled over Na/benzophenone. Hexane, heptanes, and pentane were distilled over Na/triglyme/benzophenone. $CHCl_3$, CH_2Cl_2, benzene, toluene, and DMF were dried over CaH_2. Deuterated solvents were dried over CaH_2 and deoxygenated prior to use. Flash column chromatography (FC): silica gel (SiO_2; 100–200 mesh). IR Spectra: in KBr; *FT-IR-800* spectrophotometer; ν in cm^{-1}. ^1H-, ^{13}C-, and ^{31}P-NMR spectra: *Geol 400* spectrometer at 400 MHz (^1H), 100.6 MHz (^{13}C), and 121.5 MHz (^{31}P); in $CDCl_3$ or (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, J in Hz; δ in ppm (for ^{31}P-NMR rel. to an 85% H_3PO_4 external reference); the NMR spectra of all the intermediates, ligands, and complexes were recorded at ambient temp. unless otherwise stated. HR-ESI-MS: Mass-ESI-POS (*AGILENT Technologies 6410*–triple quad

LC/MS instrument) spectrometer; in *m/z*. Elemental analyses: *Perkin-Elmer 2400 Elemental Analyzer*; CHN mode.

*Ethyl 4,6-Dimethyl-2-oxo-2*H*-pyran-5-carboxylate* (**1**). In a threeneck 2 l round bottom flask, ethyl acetoacetate (= ethyl 3-oxobutanoate; 486.4 g, 3.74 mol) was treated with dry HCl gas for a period of 8 h at $-15°$ to 0° using an ice salt bath (HCl gas was freshly prepared by dropwise addition of 35% HCl to conc. H_2SO_4). The mixture was tightly closed and kept in a dark place for 8 d. The color turned into dark reddish. The above procedure was repeated again, and the mixture was kept in a dark place for another 8 d. Finally, the mixture was diluted with Et_2O and washed with cold H_2O. The aq. layers were extracted again with Et_2O. The combined org. phases were washed with 1M aq. Na_2CO_3 soln. and brine, dried with anh. Na_2SO_4, filtered, and concentrated in vacuum. The dark red residue was purified by fractional distillation at 160° to 190° under high vacuum to afford pure product **1** (240 g, 65%). Light yellowish liquid. IR: 2984*s*, 1725*w*, 1553*s*, 1399*s*, 1084*s*, 756*s*. ^{1}H-NMR ($CDCl_3$): 1.32 (*t*, *J* = 7.4, *Me*CH_2O); 2.15 (*s*, Me–C(4)); 2.32 (*s*, Me–C(6)); 4.28 (*q*, *J* = 7.3, Me*C*H_2O); 5.94 (*s*, H–C(3)). ^{13}C-NMR ($CDCl_3$): 14.2 (*Me*CH_2O); 19.6 (Me–C(6)); 21.2 (Me–C(4)); 61.7 (Me*C*H_2O); 111.9 (C(5)); 113.2 (C(3)); 154.4 (C(4)); 160.7 (C(2)); 164.6, 165.5 (*C*OOEt, C(6)). LC/MS (ESI): 196.1 (M^+, $C_{10}H_{12}O_4^+$). Anal. calc. for $C_{10}H_{12}O_4$ (196.20): C 61.22, H 6.16; found: C 60.81, H 7.09.

*Ethyl 3-Bromo-4,6-dimethyl-2-oxo-2*H*-pyran-5-carboxylate* (**2**). To a soln. of **1** (430 g, 2.19 mol) in dry $CHCl_3$ (870 ml) was added a soln. of Br_2 (430.26 g, 2.52 mol) in dry $CHCl_3$ at 0°. The mixture was allowed to warm up to r.t., and then stirred for 24 h until complete consumption of **1** was observed by TLC (R_f = 0.6, 50% AcOEt in hexane). The mixture was poured into crushed ice and extracted with AcOEt. The combined org. phases were washed with 10% Na_2CO_3 and brine, dried ($MgSO_4$), filtered, and concentrated in vacuum. The crude residue was purified by crystallization from cold MeOH to give **2** (515 g, 85%). White crystals. M.p. 83°. IR: 3426*s* (br.), 2976*m*, 2942*m*, 1724*w*, 1630*s*, 1529*s*, 1371*s*, 1096*s*, 748*s*, 516*s*. ^{1}H-NMR ($CDCl_3$): 1.30 (*t*, *J* = 7.4, *Me*CH_2O); 2.26 (*s*, 2 Me); 4.28 (*q*, *J* = 7.3, Me*C*H_2O). ^{13}C-NMR ($CDCl_3$): 14.2 (Me); 19.0 (Me); 21.9 (Me); 62.2 (Me*C*H_2O); 110.1 (C(3)); 114.2 (C(5)); 152.0 (C(4)); 157.4 (C(2)); 161.1, 165.0 (*C*OOEt, C(6)). LC/ESI-MS: 275 (M^+, $C_{10}H_{11}{}^{79}BrO_4^+$), 277 ($M^+$, $C_{10}H_{11}{}^{81}BrO_4^+$). Anal. calc. for $C_{10}H_{11}BrO_4$ (275.10): C 43.66, H 4.03; found: C 43.48, H 4.61.

*(±)-*trans*-3-Methylidenecyclopropane-1,2-dicarboxylic Acid* (= Feist*'s Acid*; (±)-*trans*-**3**). To a soln. of KOH (7M, 514 ml) at 105° was added a soln. of compound **2** (100 g, 0.36 mol) in dioxane (200 ml) over a period of 20 min. The mixture was then further heated at 105° until complete consumption of **2** (determined by TLC, R_f = 0.2 in pure AcOEt; 30 min), and cooled to 0°. The mixture was then acidified with 50% H_2SO_4 (200 ml), a solid precipitate was formed, filtered off through a sintered funnel and washed with Et_2O. The aq. layers were also extracted with Et_2O, and the combined org. phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuum. The crude residue was purified by crystallization from cold Et_2O to give (±)-**3** (35 g, 68%). Off-white crystal. M.p. 201–204°. IR: 3500–2500*s* (br., OH stretching), 1700*s* (br., CO stretching), 1470*s*, 1320*s*, 1300*s*, 1210*s*, 1100*s*, 980*s*, 920*s*, 790*s*, 660*m*. ^{1}H-NMR ((D$_6$)DMSO): 2.85 (*s*, 2 H–C); 5.9 (*s*, CH_2=C); 12.9–13.2 (br. *s*, 2 COOH). ^{13}C-NMR ((D$_6$)DMSO): 29.5 (2 CH); 110 (C=*C*H_2); 133.5 (*C*=CH_2); 174.0 (2 COOH). LC/ESI-MS: 141.02 ([*M* – H]$^+$, $C_6H_6O_4^+$). Anal. calc. for $C_6H_6O_4$ (142.11): C 50.71, H 4.26; found: C 50.52, H 4.33.

Dimethyl trans*-3-Methylidenecyclopropane-1,2-dicarboxylate* ((±)-**4**). In a 100 ml single-neck round-bottom flask equipped with condenser, compound **3** (10 g, 70.4 mmol) was dissolved in MeOH (150 ml). A cat. amount of H_2SO_4 was added, and the mixture was held at 35–40° for 24 h. The progress of the reaction was monitored by TLC (R_f (20% AcOEt/hexane) 0.6). The solvent was then removed under reduced pressure and diluted with H_2O. The aq. layers were extracted with AcOEt. The org. phase was washed with 10% $NaHCO_3$ soln. and brine, and dried ($MgSO_4$). The combined org. extracts were concentrated in vacuum. The residue was purified by SiO_2 chromatography, eluted with 5–10% AcOEt in hexane, to provide (±)-**4** (10.5 g, 88%). Colorless liquid. IR: 2955*s*, 1733*s* (CO stretching), 1437*s*, 1309*s*, 1165*s*, 790*s*, 1000*m*, 917*s* (CH_2), 661*s*. ^{1}H-NMR ($CDCl_3$): 2.85 (*s*, 2 H–C); 3.68 (*s*, 2 COOMe); 5.64 (*s*, CH_2=C). ^{13}C-NMR ($CDCl_3$): 25.6 (2 CH); 52.5 (2 COO*Me*); 106.7 (C=CH_2); 128.9 (*C*=*C*H_2); 169.7 (2 *C*OOMe). LC/ESI-MS: 170.05 (M^+, $C_8H_{10}O_4^+$). Anal. calc. for $C_8H_{10}O_4$ (170.16): C 56.47, H 5.92; found: C 56.51, H 6.01.

*(±)-(*trans*-3-Methylidenecyclopropane-1,2-diyl)dimethanol* ((±)-**5**). To a suspension of $LiAlH_4$ (2.6 g, 67.85 mmol) in dry THF (40 ml) was added dropwise a soln. of compound (±)-**4** (5.7 g,

33.9 mmol) in THF (40 ml) at $-10°$ during 20 min under Ar. The mixture was warmed to r.t., and stirred for 4 h until complete consumption of (±)-**4** (determined by TLC, R_f (pure AcOEt) 0.3). The mixture was cooled to $-10°$, and the reaction was quenched with 10% HCl. The precipitate (a white solid) was filtered off through a pad of *Celite* and washed with Et_2O. The org. phases were separated, and the aq. layers were further extracted with AcOEt. The combined org. extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuum to give (±)-**5** (3.6 g, 93%). Colorless liquid. IR: 3348*s* (br., OH stretching), 1760*s* (br.), 1422*w*, 1135*s*, 1033*s*, 896*s*, 695*m*, 594*s*. ^{1}H-NMR ((D$_6$)DMSO): 1.44 (*t*, *J* = 5.2, 2 H–C); 3.30–3.38 (*m*, 2 C*H*$_2$OH); 4.6 (*t*, *J* = 5.8, 2 CH$_2$O*H*); 5.37 (*s*, CH$_2$=C). ^{13}C-NMR ((D$_6$)DMSO): 24.0 (2 CH); 63.3 (2 CH$_2$OH); 104.2 (C=*C*H$_2$); 137.9 (*C*=CH$_2$). LC/MS (ESI): 140.1 (M^+, $C_6H_{10}O_2^+$). Anal. calc. for $C_6H_{10}O_2$ (114.14): C 63.14, H 8.83; found: C 59.51, H 8.91.

*(±)-(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanediyl Dimethanesulfonate* ((±)-**6**). To a soln. of (±)-**5** (3.6 g, 31.6 mmol) in CH_2Cl_2 (105 ml) at 0° was added Et_3N (13 ml, 9.6 g, 94.7 mmol) under Ar and stirred for 5 min. MsCl (7.36 ml, 10.85 g, 94.73 mmol) was then added dropwise over 15 min and the mixture was then stirred for 1.5 h until complete consumption of (±)-**5** (determined by TLC, R_f (pure AcOEt) 0.5). The reaction was quenched with 10% soln. of Na_2CO_3, and the product was extracted with CH_2Cl_2. The combined org. layers were washed with 10% soln. of Na_2CO_3, dried (Mg_2SO_4), filtered through a pad of *Celite*, and concentrated in vacuum. The residue was purified by FC (70% AcOEt in hexane) to give (±)-**6** (7.8 g, 92%). White viscous liquid. IR: 1344*s* (SO_2 asym. stretching), 1173*s* (sym. stretching), 1053*s*, 975*m*, 831*s*, 528*s*. ^{1}H-NMR ($CDCl_3$): 1.96 (*t*, *J* = 5.9, 2 H–C); 3.02 (*s*, 2 SO$_2$Me); 4.02–4.05 (*m*, CH$_2$O); 4.28–4.31 (*m*, CH$_2$O); 5.64 (*s*, CH$_2$=C). ^{13}C-NMR ((D$_6$)DMSO): 21.10 (2 SO$_2$Me); 38.0 (2 CH); 70.8 (2 CH$_2$); 106.8 (C=*C*H$_2$); 130.9 (*C*=CH$_2$). LC/ESI-MS: 270.03 (M^+, $C_8H_{14}O_6S_2^+$). Anal. calc. for $C_8H_{14}O_6S_2$ (270.32): C 35.54, H 5.22; found: C 35.39, H 5.43.

(±)-trans-*1,2-Bis(azidomethyl)-3-methylidenecyclopropane* ((±)-**7**). To a soln. of (±)-**6** (1.8 g, 6.67 mmol) in dry DMF (40 ml) under Ar was added NaN_3 (4 g, 61.5 mmol) portionwise and heated to 60° for 4 h until complete consumption of (±)-**6** (confirmed by TLC, R_f (50% AcOEt/hexane) 0.8). The mixture was cooled to r.t., and poured into H_2O. The product was extracted with Et_2O, and the combined org. phases were washed with H_2O, brine, dried (Mg_2SO_4), filtered, and concentrated in vacuum. The residue was purified by FC (SiO_2, 100–200 mesh; 5–10% AcOEt in hexane) to provide (±)-**7** (0.80 g, 73%). Yellow liquid. IR (neat): 3077*w* (HC=C stretching), 2991*w*, 2927*w*, 2872*s* (CH alkene stretching), 2091*s* (N_3 stretching), 1724*s* (CH–CH$_2$ stretching), 1451*s*, 1258*s*, 903*s*. ^{1}H-NMR ($CDCl_3$): 1.69 (*m*, 2 H–C); 3.2 (*s*, 2 CH$_2$); 5.61 (*s*, CH$_2$=C). ^{13}C-NMR ($CDCl_3$): 21.3 (2 CH); 53.0 (2 CH$_2$); 108.2 (C=*C*H$_2$); 133.2 (*C*=CH$_2$). LC/ESI-MS: 164.1 (M^+, $C_6H_8N_6^+$). Anal. calc. for $C_6H_8N_6$ (164.17): C 43.90, H 4.91, N 51.19; found: C 44.36, H 5.13, N 49.58.

*(±)-(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanamine* ((±)-**8**). To a soln. of diazide (±)-**7** (0.5 g, 3.05 mmol) in abs. EtOH (15 ml) was added Pd on $CaCO_3$ poisoned with lead (10 wt-%, 5% *Lindlar* catalyst) under an inert atmosphere of Ar. The mixture was degassed by purging dry Ar through the suspension for 10 min, and was then hydrogenated under atmospheric H_2 pressure (H_2 balloon) for 24 h at r.t., until complete consumption of (±)-**7** (determined by TLC, R_f = 0.05 in pure AcOEt). The mixture was filtered through a pad of *Celite* and washed with EtOH (2 × 5 ml) to afford (±)-**8** (0.334 g, 98% yield, crude) as a colorless crude product. This amine product is very unstable, so without isolating the crude mixture was immediately taken for next step.

*Di(*tert-*butyl)* (±)-*[(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanediyl]biscarbamate* ((±)-**9**). Under Ar, DIPA (= 1,1′-iminodipropan-2-ol; 1.44 ml, 10.2 mmol) and di(*tert*-butyl) dicarbonate (2 ml, 10.2 mmol) were added to a soln. of (±)-**8** (crude 3.05 mmol in EtOH), and the mixture was stirred at ambient temp. for 2 h, until complete consumption of (±)-**8** was observed by TLC (R_f in (30% AcOEt/hexane) 0.8). The solvent was then removed under reduced pressure to afford a crude product which was purified by FC (SiO_2, 100–200 mesh; 5–10% AcOEt in hexane) to provide (±)-**9** (0.63 g, 66%). Low-melting solid. IR: 3331*s* (br., NH stretching), 2982*s* (br.), 1688*s* (C=O stretching), 1542*s*, 1365*s*, 1180*s*, 942*s*, 891*s*, 648*s*. ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 2 H–C); 1.45 (*s*, 2 Me$_3$C); 2.94–2.98 (*m*, CH$_2$N); 3.18–3.22 (*m*, CH$_2$N); 4.81 (*s*, 2 CH$_2$N*H*); 5.45 (*s*, CH$_2$=C). ^{13}C-NMR ($CDCl_3$): 21.9 (2 CH); 28.5 (2 *Me*$_3$C); 42.8 (2 CH$_2$N); 79 (2 Me$_3$*C*); 105.3 (C=*C*H$_2$); 135.7 (*C*=CH$_2$); 156.1 (2 CONH). LC/ESI-MS : 313 ($[M+H]^+$, $C_{16}H_{29}N_2O_4^+$), 213 ($[M+H-COOCMe_3]^+$), 113 ($[M+H-2\,COOCMe_3]^+$). Anal. calc. for $C_{16}H_{28}N_2O_4$ (313.40): C 61.51, H 9.03, N 8.97; found: C 61.07, H 9.18, N 9.23.

*(±)-(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanaminium Dichloride* ((±)-**10**). A dioxane/HCl mixture (5 ml) was added to a soln. of (±)-**9** (600 mg, 1.92 mmol) in CH_2Cl_2 (5 ml), and the mixture was then stirred for 3 h at ambient temp. Total consumption of (±)-**9** was determined by TLC (R_f (pure AcOEt) 0.05). A white precipitate was formed. The solvent was removed under reduced pressure, and the residue was washed with Et_2O to afford the HCl salt of (±)-**10** (302 mg, 85%). White solid. IR: 3424*s* (br., NH stretching), 3029*s* (br., NH stretching), 1594, 1557*s*, 1506*s*, 1160*s*, 906*s*, 852*s*, 576*s*. ^{1}H-NMR ((D$_6$)DMSO): 1.82 (*s*, 2 H–C); 2.63 (br. *s*, CH_2N); 3.03 (br. *s*, CH_2N); 5.64 (*s*, CH_2=C); 8.36 (br. *s*, 2 $NH_3^+Cl^-$). ^{13}C-NMR ((D$_6$)DMSO): 19.9 (2 CH); 40.7 (2 CH_2N); 108.0 (C=*C*H$_2$); 133.9 (*C*=CH$_2$). LC/ESI-MS : 113 ([M – 2 HCl + H]$^+$, $C_6H_{13}N_2^+$). Anal. calc. for $C_6H_{14}Cl_2N_2$ (185.09): C 38.93, H 7.62, N 15.13; found: C 39.17, H 7.90, N 15.29.

*(±)-*S,S′*-[(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanediyl] Diethanethioate* ((±)-**11**). The bismesylate (±)-**6** (2 g, 7.4 mmol) and AcSK (2.12 g, 18.5 mmol) were charged into a double-neck round-bottom flask and dissolved in MeCN (40 ml). The mixture was heated to reflux for 3 h, and it was then left under stirring at ambient temp. overnight. Complete consumption of (±)-**6** was confirmed by TLC (R_f (20% AcOEt/hexane) 0.6). The solvent was then removed under reduced pressure to afford a crude product which was dissolved in $CHCl_3$ and washed with dist. H_2O. The aq. layers were further extracted with $CHCl_3$. The combined org. phases were dried ($MgSO_4$), filtered, and concentrated in vacuum. The residue was purified by FC (SiO_2, 100–200 mesh; 5–10% AcOEt in hexane) to give (±)-**11** (1.6 g, 94%). Low-melting solid. IR: 1691*s* (C=O stretching), 1134*s*, 627*s*. ^{1}H-NMR ($CDCl_3$): 1.52 (*t*, J = 6.24, 2 H–C); 2.33 (*s*, 2 Me); 2.78–2.97 (*m*, 2 CH_2S); 5.45 (*s*, CH_2=C). ^{13}C-NMR ($CDCl_3$): 11.9 (2 CH); 22.6 (2 Me); 30.7 (2 CH_2S); 105.2 (C=*C*H$_2$); 138.3 (*C*=CH$_2$); 195.72 (2 C=O). LC/ESI-MS: 230.1 (M^+, $C_{10}H_{14}O_2S_2^+$). Anal. calc. for $C_{10}H_{14}O_2S_2$ (230.35): C 52.14, H 6.13; found: C 49.29, H 6.08.

*(±)-[(*trans-*3-Methylidenecyclopropane-1,2-diyl)dimethanediyl]bis(diphenylphosphane)* ((±)-**12**). A soln. of $LiPPh_2$ (0.5M in THF; 24 ml, 3 equiv.) was added dropwise to a soln. of (±)-**6** (1.1 g, 4 mmol) in dry THF (15 ml) at −15° under Ar atmosphere, and the mixture was slowly allowed to warm to r.t. and stirred for 24 h. TLC showed that only 50% of the starting material was consumed. An extra amount of $LiPPh_2$ (3 equiv.) was then added at −15° and the mixture was stirred at r.t. for further 24 h until total consumption of (±)-**6** was confirmed by TLC (R_f (10% AcOEt/hexane) 0.5). The reaction was then quenched with NH_4Cl soln., and the mixture was extracted with Et_2O. The Et_2O phase was washed with brine, dried ($MgSO_4$), filtered through a pad of *Celite*, and concentrated in vacuum to afford crude (±)-**12**. The residue was purified by FC (SiO_2, 100–200 mesh; 5% AcOEt in hexane) to afford pure (±)-**12** (1.6 g, 87%). Oil. IR: 3366*s* (br.), 2932*s*, 1434*s*, 1068*s*, 695*s*. ^{1}H-NMR ($CDCl_3$): 1.36–1.55 (*m*, 2 CH_2P); 2.06 (*t*, J = 8.1, 2 H–C); 4.37 (*t*, J = 5.1, CH_2=C); 7.34–7.37 (*m*, 20 arom. H). ^{13}C-NMR ($CDCl_3$): 22.8 (2 CH_2P); 27.2 (2 H–C); 34.5 (C=*C*H$_2$); 60.9 (*C*=CH$_2$); 129.1 (each 4 C(3), C(4), C(5) of Ph); 132.9 (4 C(2) and 4 C(6) of Ph); 139.2 (4 C(1) of Ph). ^{31}P-NMR ($CDCl_3$): −16.72 (PPh_2). LC/MS (ESI): 450.2 (M^+, $C_{30}H_{28}P_2^+$). Anal. calc. for $C_{30}H_{28}P_2$ (450.49): C 79.98, H 6.26; found: C 79.65, H 6.02.

Preparation of the Diol–Titanium Complex (*Bis[(*trans-*3-methylidenecyclopropane-1,2-diyl)dimethanolato-*κO*(2–)]titanium*; (±)-**13**). A soln. of $TiCl_4$ (1M in CH_2Cl_2; 0.875 ml, 0.875 mmol) was added dropwise to the soln. of diol (±)-**5** (200 mg, 1.75 mmol) at 5°, and the resulting mixture was stirred for 14 h at r.t. A dark white solid precipitated. The solvent was removed under vacuum to give crude (±)-**13**. This crude product was dissolved in anh. CH_2Cl_2 (40 ml), and the resulting mixture was stirred for 20 min, and then filtered through a sintered funnel, followed by washing with CH_2Cl_2 (10 ml). The filtrate was then concentrated in vacuum to afford a light yellow solid, which was further recrystalized from toluene to afford desired (±)-**13** (140 mg, 59%). IR: 3350*s* (br., OH str.), 1632*s* (br.), 1400*w*, 1135*s*, 1026*s*, 896*s*, 904*m*, 831*s*, 581*s*. ^{1}H-NMR ((D$_6$)DMSO): 1.43 (*s*, 4 H–C); 3.26–3.35 (*m*, 4 CH_2O); 5.35 (*s*, 2 CH_2=C). ^{13}C-NMR ((D$_6$)DMSO): 24.1 (4 H–C); 63.3 (4 CH_2O); 104.2 (2 C=*C*H$_2$); 137.96 (2 *C*=CH$_2$). Anal. calc. for $C_{12}H_{16}O_4Ti$ (272.12): C 52.97, H 5.93; found: C 53.21, H 6.07.

Synthesis of Diamine–Titanium Complex (*Bis[(*trans-*3-methylidenecyclopropane-1,2-diyl)dimethanaminato-*κN*(2–)]titanium*; (±)-**14**). Compound (±)-**10** (330 mg, 1.78 mmol) was dissolved in CH_2Cl_2 (10 ml) into a single-neck round-bottom flask (50 ml). Na_2CO_3 soln. (10%, 7.5 mmol) was added to the mixture and stirred for 20 min. The CH_2Cl_2 layer containing free amine was separated out and dried ($MgSO_4$). The free amine soln. in CH_2Cl_2 was then taken into another single-neck round-bottom flask under inert conditions and cooled to 5°. A soln. of $TiCl_4$ (1M soln. in CH_2Cl_2, 0.875 ml, 0.875 mmol) was

added dropwise to the mixture. The mixture was then stirred for 14 h at ambient temp., and a white solid precipitated. The solvent was removed under vacuum to give a crude product. This crude product was dissolved in anh. CH_2Cl_2 (40 ml), and the resulting mixture was stirred for 20 min and filtered through a sintered funnel, followed by washing with CH_2Cl_2 (10 ml). The filtrate was then concentrated under reduced pressure to afford a light yellow solid, which was further recrystalized from toluene to give (±)-**14** (165 mg, 70% yield). IR: 3332*s* (br., NH stretching), 2982 (CH stretching, alkene), 1542*s*, 1365*s*, 1180*s*, 942*s*, 891*s*, 648*s*. ^{1}H-NMR ((D$_6$)DMSO): 1.84 (*s*, 4 H–C); 2.60–2.61 (*m*, 2 CH_2N); 3.00–3.02 (*m*, 2 CH_2N); 5.64 (*s*, 3 CH_2=C); 8.48 (br. *s*, 4 NH_2). ^{13}C-NMR ((D$_6$)DMSO): 20.0 (4 H–C); 40.7 (4 CH_2N); 108.0 (2 C=*C*H$_2$); 134.0 (2 *C*=CH$_2$). Anal. calc. for $C_{12}H_{20}N_4Ti$ (268.18): C 53.74, H 7.52, N 20.89; found: C 53.51, H 7.72, N 21.06.

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