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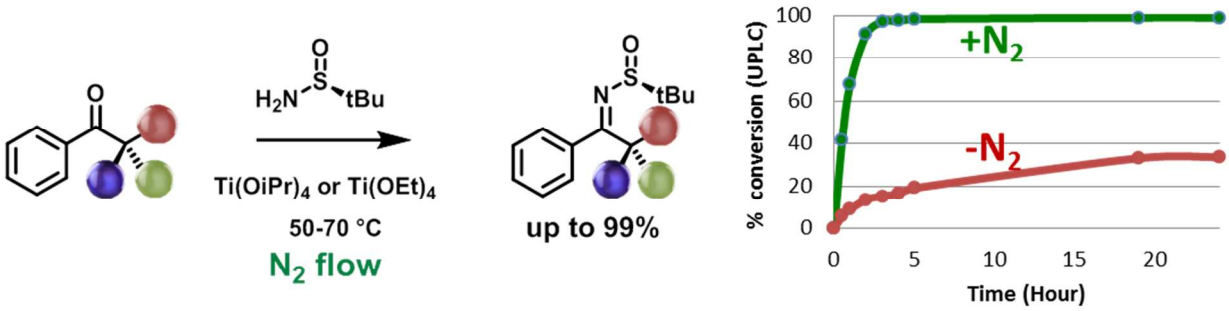


ABSTRACT An improved process for *tert*-butanesulfinyl ketimines formation using titanium(IV) alkoxides is described. This new protocol gives better results especially for sterically hindered ketones compared to classical conditions where titanium(IV) isopropoxide is found to be only moderately effective. We found that removal of isopropanol or ethanol from the reaction mixture either under a nitrogen flow or under vacuum dramatically increased reaction rate, extent of conversion and yield of the reaction. This methodology has been exemplified on several substrates reported in the literature to be difficult.

KEYWORDS : sulfinyl ketimines, hindered ketones, improved process, nitrogen flow.

tert-Butanesulfinyl ketimines are very versatile substrates providing access to a large variety of chiral secondary and tertiary amines used in chemical synthesis.[1] Indeed the chiral and electron withdrawing *tert*-butanesulfinyl group directs the addition of nucleophiles by chiral induction to the imine and can be easily cleaved under mild acidic conditions providing chiral amines. Access to *tert*-butanesulfinyl ketimines has been widely described by the Elman group and is based on the direct condensation of ketones with chiral *tert*-butanesulfinamide using titanium(IV) alkoxide as Lewis acid and water scavenger.[2] It has been determined that titanium(IV) ethoxide is usually more effective than titanium(IV) isopropoxide and elevated temperature are usually required, for hindered substrates, or for less reactive ketones. The standard procedure is to heat the mixture of ketone, chiral *tert*-butanesulfinamide and titanium(IV) ethoxide in an aprotic solvent (eg. THF or toluene) to 60 °C and increase, if necessary, the temperature until completion of the reaction.

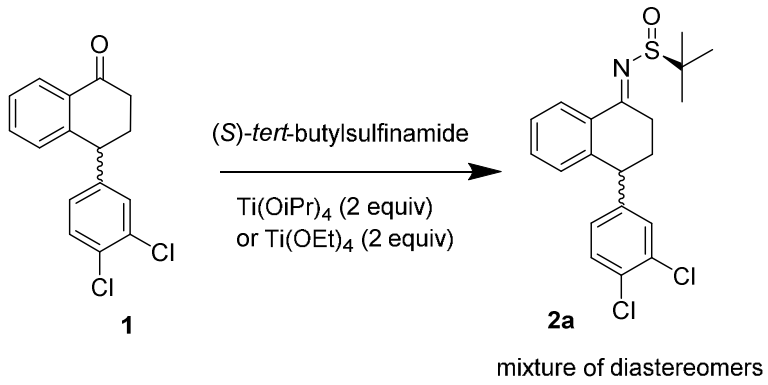
We found that titanium(IV) isopropoxide can be as efficient as titanium(IV) ethoxide for sulfonamide condensation with ketones under specific experimental conditions. During some

laboratory experiments using titanium(IV) isopropoxide and hindered ketone we noted how different extents of conversion for our substrate between a sealed tube (conv 50%) and a flask under a nitrogen flow (full conversion).[3]

We hypothesized that removal of a volatile side-product could be implicated and decided to evaluate the importance of nitrogen flow and vacuum with reported literature results and conditions. Preliminary investigations were carried out with racemic tetralone **1** as a model compound which is reported to react poorly with chiral *tert*-butanesulfinamide and titanium(IV) isopropoxide (conversion <50%, Table 1, entry1).[4] When toluene was used as the unique solvent with titanium(IV) isopropoxide at 70 °C in a sealed tube only 33% conversion was obtained after 24 hours which was comparable with the reported conversion (entry 2).[4a] With the same reaction conditions, but in an open tube under a nitrogen flow (4 liters per minute), the reaction proceeded to 99% completion in 5 hours (entry 3). In this case, due to evaporation, toluene was added regularly to the reaction mixture to keep a constant volume. The same comparison was done replacing titanium(IV) isopropoxide by titanium(IV) ethoxide. In this case reaction completion was observed in 3 hours (entry 5), whereas literature data indicated a conversion inferior to 70% (entry 4). For practical reasons, we investigated reaction with neat titanium(IV) isopropoxide to avoid the need to recharge toluene and facilitate titanium dioxide precipitation during work up. In a sealed tube, a 70% conversion was obtained in 24 hours (entry 6) while in an open tube at the same temperature under nitrogen flow a 99% conversion was reached in just 4 hours (entry 7). We also performed the same experiment under vacuum (10 mbar) at 70 °C and after 15 hours, full conversion was also obtained (entry 8). To complete this evaluation a kinetic study was realized with the experimental conditions of entry 2 and entry 3 (Figure 1a). During the first 3 hours a first order reaction was observed that allowed us the calculation of the rate constants for

both reactions (figure 1b). When a nitrogen flow was used the reaction rate was 22 times faster than operation in a sealed tube (k_{entry3}/k_{entry2}= 22) during this early phase of the reaction.

Table 1. Condensation of racemic tetralone 1 mediated by Ti(IV) alkoxides



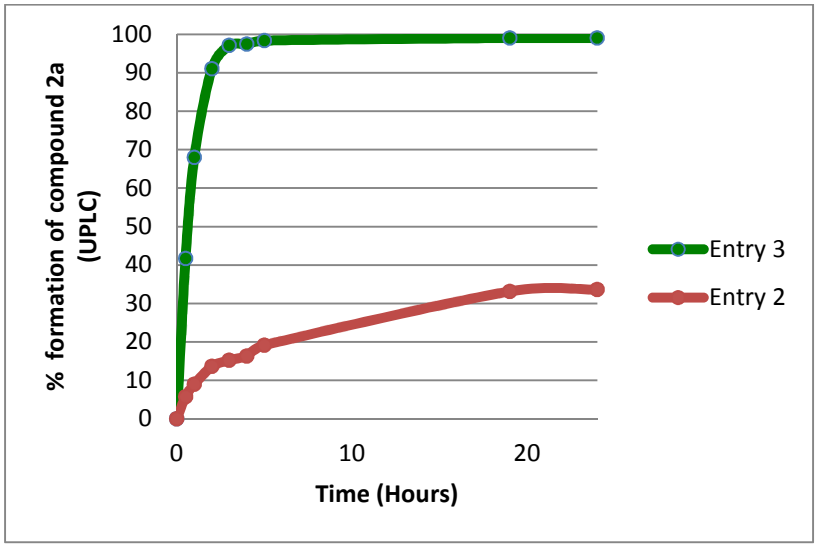
Entry	Solvent/ T °C	Reaction conditions	Nitrogen flow	Time	Conv (a% UPLC)[a]	Isolated Yield
1[b]	$Ti(OiPr)_4$/ THF / 75 °C	-	-	-	<50%[4a]	-
2	$Ti(OiPr)_4$/ Toluene/ 70 °C	Sealed Tube	No	24h	33%	-
3	$Ti(OiPr)_4$/ Toluene /70 °C	Open Tube	Yes	5h	99%	94%
4[b]	$Ti(OEt)_4$/ THF Toluene /90 °C	-	-	-	<70%[4a]	-
5	$Ti(OEt)_4$/ Toluene / 70 °C	Open Tube	Yes	3h	99%	95%
6	$Ti(OiPr)_4$/ Neat/ 70 °C	Sealed Tube	No	18h	70%	-
7	$Ti(OiPr)_4$/ Neat / 70 °C	Open Tube	Yes	4h	99%	95%
8	$Ti(OiPr)_4$/ Neat / 70 °C	Tube under Vacuum	No	15h	99%	96%

[a]Based on disappearance of ketone

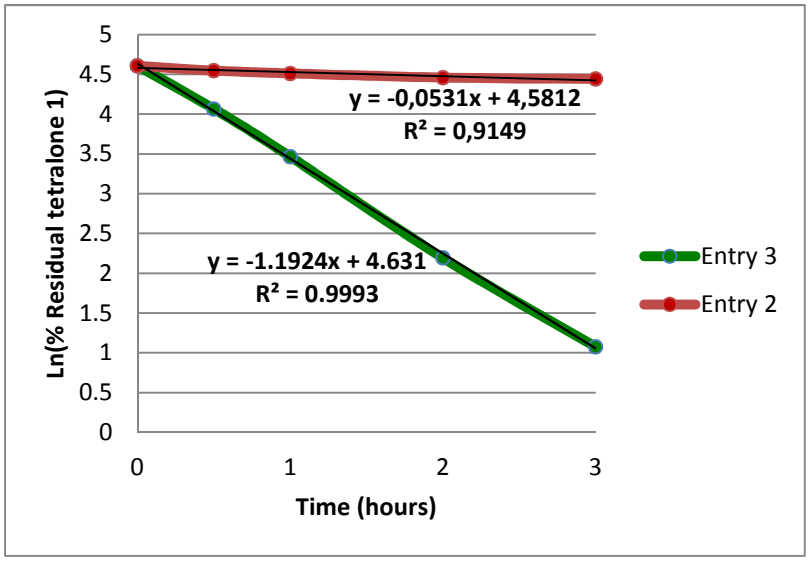
[b]Data from literature[4a]

Figure 1. Reaction rate kinetics for entry 2and entry 3 (Table 1):

a)UPLC formation of compound **2a** during 24 hours.



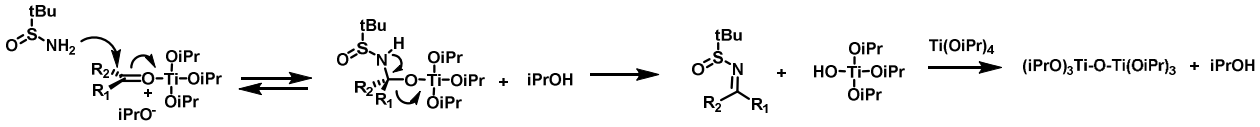
b) Ln(% residual tetralon 1) vs time



For *tert*-butanesulfinyl ketimines condensation, titanium(IV) alkoxides are known to act as Lewis acids and also as water scavengers. We postulated that the first step of the mechanism with titanium(IV) isopropoxide is displacement of one molecule of isopropanol from titanium

(Scheme 1), and in the case of hindered ketones this step might be the limiting step in the kinetics. Removing isopropanol under a nitrogen flow or with vacuum displaces this equilibrium and drives the mechanism towards ketimine formation. The monohydroxy titanate obtained reacts immediately with a second molecule of titanium(IV) isopropoxide to afford a dimeric product and isopropanol.[5]

Scheme 1. Postulated Mechanism



To confirm this hypothesis, condensation of tetralone **1** without solvent was repeated on a larger scale to trap the solvent removed from the reaction mixture. Analysis by ^{1}H NMR of the distillate confirmed the presence of isopropanol removal from the reaction. The same result was obtained repeating the experiment with titanium(IV) ethoxide and ethanol removal. In addition, we repeated entry 2 experiment (Table 1) with 2 equivalents of extra isopropanol, that considerably slowed down the kinetic of reaction and only a 3% conversion was obtained after 24 hours at 70 °C

To explore the scope of the reaction we decided to focus on titanium(IV) isopropoxide and how its use can be extended to a large variety of ketones. Moreover, on larger scale, titanium(IV) isopropoxide is easier to handle and cheaper than titanium(IV) ethoxide.

In the literature, the standard procedure is to heat reaction mixture to 60 °C, and increase the temperature above 100 °C if the conversion is sluggish.[1,2] The drawback of elevated temperatures is that some ketimine compounds are susceptible to thermal decomposition and aldol

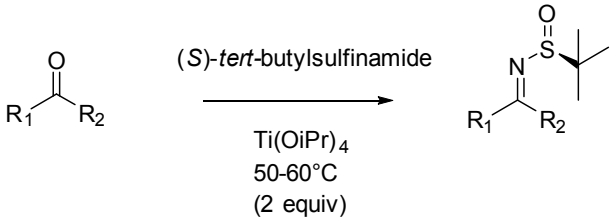
condensation.[2] To overcome this issue we chose to operate at 50 °C under a nitrogen flow and increased the temperature to 60-70 °C if the rate of the reaction was sluggish. When 95-99% conversion was reached, the mixture was diluted with THF and quenched with a saturated aqueous solution of sodium chloride. Titanium oxide was removed by filtration and after work-up the desired ketimine was isolated. A supplementary purification using silica gel chromatography was sometimes necessary depending on the ketone substrate.

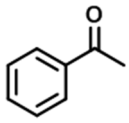
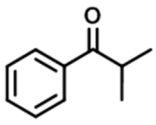
Because the protocol requires nitrogen flow and heating, we excluded volatile ketones from our study (Table 2). For all the examples, a temperature below 60 °C was sufficient to provide a complete conversion without degradation and in most cases silica gel purification was not necessary. Where data was available our isolated yields were compared to those obtained with titanium(IV) isopropoxide from the literature. Using acetophenone, **2b** (60% yield using toluene at 110 °C)[2,6] a yield of 85% was obtained at just 50 °C. Even with sterically hindered ketone such as pivalophenone **2d** a 99% conversion and a 70% isolated yield were obtained.[7] The same difference was also observed with 2-acetonaphthone **2g** giving 80% yield compared to the 50% yield in literature.[10] Interestingly, for examples **2c** and **2i,** isolated yields of respectively 80% and 84%, were better than those obtained with titanium(IV) ethoxide at higher temperature.[6a,7,12] For entries, **2d**, **2e** and **2h**, the yields obtained at 50-60 °C are comparable to those obtained with the standard titanium(IV) ethoxide Lewis acid procedure.[7,8,11] Finally, with entry **2f**, a similar yield was obtained with the titanium(IV) isopropoxide procedure compared to the microwave procedure at 120 °C from literature.[9] Examples **2h-i** were all performed at 60 °C and the reaction was complete in 4-6 hours compared to 15 hours at 50 °C using the literature protocol. The isolated yield for ketone **2i** was significantly improved (84%) compared to the 29% reported yield.[12] For the most hindered example **2j,** titanium(IV) isopropoxide was not sufficient to

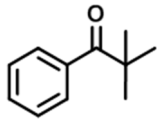
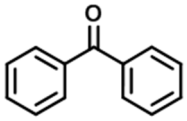
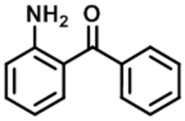
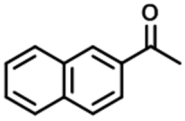
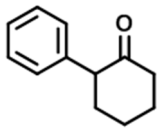
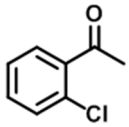
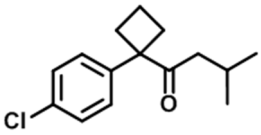
provide complete conversion (12%) in 48 hours and 70 °C. However, when we replaced titanium(IV) isopropoxide by titanium(IV) ethoxide a 60% conversion and 40% isolated yield were obtained compared to the 5% literature yield with the same Lewis acid.[13]

In summary, we have developed an efficient and mild procedure for the preparation of *tert*-butanesulfinyl ketimines with titanium(IV) isopropoxide using vacuum or under a nitrogen flow to remove isopropanol from the reaction mixture. We found that removing isopropanol displaces the equilibrium of the reaction and leads to high conversions even with hindered ketones. This protocol avoids the use of high temperatures and gives better purity profile compared to classical conditions. For the most hindered ketones, when titanium(IV) isopropoxide was not efficient enough, the more expensive titanium(IV) ethoxide can be used with satisfactory to excellent results.

Table 2. Scope of the condensation of ketones mediated by titanium(IV) isopropoxide (Methode A)



Entry	Ketone	Reaction T °C	Conv. (a% UPLC)[a]	Reaction Time	Isolated Yield	Literature condition
2b		50 °C	99%	15h	85%	60%/ $Ti(OiPr)_4$/ Toluene/ 110 °C[2,6]
2c		50 °C	99%	15h	80%	45%/ $Ti(OEt)_4$/ 65 °C/ 24h[6a,7]

2d		50 °C	99%	15h	70%	69%/ $Ti(OEt)_4$/ 85 °C/ 21h[7]
2e		50 °C	99%	15h	89%	75%/ $Ti(OEt)_4$/ CH_2Cl_2/ reflux[8]
2f		50 °C	99%	5h	88%	89%/ $Ti(OEt)_4$ / THF/ MW(160W)/ 120 °C[9]
2g		60 °C	96%	15h	80%	50%/ $Ti(OiPr)_4$/ THF/ reflux[10]
2h		60 °C	95%	6h	66%	61%/ $Ti(OEt)_4$/ THF/ reflux [11]
2i		60 °C	99%	4h	84%	29%/ $Ti(OEt)_4$/ DCM/ reflux/ 2d[12]
2j		70 °C	12%	48h	Not isolated	5%/ $Ti(OEt)_4$ / THF/ reflux/ 2d[13]
		70 °C[b]	60%	48h	40%	

[a] Based on disappearance of ketone

[b] $Ti(OEt)_4$ was used

EXPERIMENTAL SECTION

General Information. All Ketones, except for example 2j[13], were obtained from commercial suppliers and used without further purification. Only anhydrous solvents were used for reaction and were purchased from Carlo Erba without further purification. Lewis acids were obtained from Sigma Aldrich , $Ti(OEt)_4$ 99% and $Ti(OiPr)_4$ 97%, and were used without purification from new bottles. (*S*)-(-)-2-methyl-2-propanesulfinamide 99% was obtained from AK Scientific. ^1H NMR and ^{13}C NMR were recorded on a 400 MHz nuclear magnetic resonance spectrometer Bruker Avance (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR). The chemical shifts (δ) and

coupling constants (J) were expressed in parts per million and hertz, respectively. Conversion were measured on a Waters UPLC Acquity system Acquity CSH C18 1.7 μm 2.1*50 mm Column, mobile phase (Acetonitrile + 0.1% formic acid) / (Water + 0.1% formic acid), flow rate 0.8 mL/min, with photodiode array detector and the following gradient: 10% to 98% acetonitrile 0 to 0.8 min, 98% acetonitrile from 0.8 min to 1.5 min and 98% to 10% acetonitrile from 1.5 to 2.0 min. HRMS (ESI) data were recorded on Thermo orbitrap QExactive. General method A, B or C were conducted on 2 g scale of the corresponding ketone.

Method A. General solvent free procedure for the Synthesis of *tert*-butanesulfinyl ketimines with titanium alkoxide ($Ti(OiPr)_4$ or $Ti(OEt)_4$) neat under nitrogen flow. A solution or a suspension of ketone (1 equiv) in titanium alkoxide (2 equiv) was prepared under a nitrogen flow (4 liters per minute) without vapor condenser. Then (*S*)-(-)-2-methyl-2-propanesulfinamide (1.05 equiv) was added and the reaction mixture was heated to 50-70 °C. Conversion was followed by UPLC-MS. Immediately upon completion the mixture was cooled to room temperature, diluted with THF (25 vol) and treated with a solution of 24 wt % aq NaCl (0.5 vol). The resulting titanium oxide suspension was filtered through a plug of Celite, and the filter cake was washed with THF. The filtrate was concentrated under reduce pressure, diluted with ethyl acetate and transferred to a separatory funnel. The organic layer was washed with water and the aqueous phase was extracted once with ethyl acetate. The combined organic portions were dried on Na_2SO_4, filtered and concentrated under reduce pressure. When necessary the sulfinyl ketimines were purified through a pad of silica.

Method B. General procedure for the Synthesis of *tert*-butanesulfinyl ketimines with titanium alkoxide ($Ti(OiPr)_4$ or $Ti(OEt)_4$) with toluene and nitrogen flow. A solution of ketone (1 equiv) and titanium alkoxide (2 equiv) in toluene (0.35M) was prepared under a nitrogen flow (4 liters

per minute) without vapor condenser. Then (*S*)-(-)-2-methyl-2-propanesulfinamide (1.05 equiv) was added and the reaction mixture was heated to 50-70 °C. The toluene and the isopropanol from the reaction are removed with the nitrogen flow. Due to evaporation toluene was added regularly to the reaction mixture to keep a constant volume. Conversion was followed by UPLC-MS. Immediately upon completion the mixture was cooled to room temperature and work-up conducted as described in Method A.

Method C. General procedure for the Synthesis of *tert*-butanesulfinyl ketimines with titanium alkoxide ($Ti(OiPr)_4$ or $Ti(OEt)_4$) under vacuum (10 mbar) . A solution or a suspension of ketone (1 equiv) in titanium alkoxide (2 equiv) was prepared vacuum under without vapor condenser. Then (*S*)-2-methyl-2-propanesulfinamide (1.05 equiv) was added and the reaction mixture was heated to 50-70 °C. Conversion was followed by UPLC-MS. Immediately upon completion the mixture was cooled to room temperature and work-up conducted as described in Method A.

(S)-N-(4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-ylidene)-2-methylpropane-2-sulfinamide **(2a).** Method A. Pure **2a** was obtained (1.3g, 95%) as a yellow solid without purification (diastereoisiomeric mixture). Method B. Pure **2a** was obtained (1.28g, 94%) as a yellow solid without purification (diastereoisiomeric mixture). Method C. Pure **2a** was obtained (1.32g, 96%) as a yellow solid without purification (diastereoisiomeric mixture). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.15 (dd, J = 7.9, 1.5 Hz, 1H), 7.60 (dd, J = 8.3, 1.8 Hz, 1H), 7.53 – 7.33 (m, 3H), 7.10 (ddd, J = 15.5, 8.3, 2.1 Hz, 1H), 6.94 (d, J = 7.5 Hz, 0.5H), 6.87 (d, J = 7.5 Hz, 0.5H), 4.45 – 4.31 (m, 1H), 3.22 (m, 1H), 3.16 – 3.01 (m, 1H), 2.29 – 2.09 (m, 2H), 1.24 (d, J = 1.8 Hz, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.7, 175.5, 145.3, 145.1, 143.5, 143.2, 132.8, 132.8, 132.6, 132.6, 131.3, 130.8, 130.7, 130.6, 130.5, 129.4, 129.4, 129.3, 129.3, 128.9, 128.8, 127.4,

127.3, 126.5, 56.9, 56.9, 43.1, 42.9, 30.2, 30.0, 30.0, 29.1, 22.1. HRMS calcd for $C_{20}H_{22}Cl_2NOS^+$ $[M + H]^+$ m/z 394.0799, found m/z 394.0787.

(S)-2-methyl-N-(1-phenylethylidene)propane-2-sulfinamide **(2b)**. Method A. Pure **2b** was obtained (3.16 g, 85%) as a yellow solid from silica pad purification (4:1 heptane / ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 – 7.89 (m, 2H), 7.60 – 7.46 (m, 3H), 2.73 (s, 3H), 1.23 (s, 9H).^{13}C NMR (101 MHz, DMSO-d_6) δ 176.6, 138.4, 131.9, 128. 7, 127.2, 56.8, 40.0, 22.1, 19.7. HRMS calcd for $C_{12}H_{18}NOS^+$ $[M + H]^+$ m/z 224.1109, found m/z 224.1104.

(S)-2-methyl-N-(2-methyl-1-phenylpropylidene)propane-2-sulfinamide **(2c)**. Method A. Pure **2c** was obtained (2.73 g, 80%) as a yellow solid from silica pad purification (4:1 heptane / ethyl acetate).^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (m, 3H), 7.39 – 7.30 (m, 2H), 3.08 (s, 1H), 1.12 (m, 15H).^{13}C NMR (101 MHz, DMSO-d_6) δ 189.5, 137.7, 129.4, 128.2, 126.7, 55.5, 40.0, 21.7, 19.9, 19.6. HRMS calcd for $C_{14}H_{22}NOS^+$ $[M + H]^+$ m/z 252.1422, found m/z 252.1416.

(S)-N-(2,2-dimethyl-1-phenylpropylidene)-2-methylpropane-2-sulfinamide **(2d)**. Method A. Pure **2d** was obtained (2.30 g, 70%) as a white solid from heptane trituration. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 – 7.32 (m, 3H), 7.18 – 7.03 (m, 2H), 1.17 (s, 9H), 1.10 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 192.1, 136.6, 128.4, 127.8, 126.4, 55.1, 42.0, 27.8, 21.7. HRMS calcd for $C_{15}H_{24}NOS^+$ $[M + H]^+$ m/z 265.1579, found m/z 266.1573

(S)-N-(diphenylmethylene)-2-methylpropane-2-sulfinamide **(2e)**. Method A. Pure **2e** was obtained (2.80 g, 89%) as a white solid from heptane trituration. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.18 (m, 10H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.0, 132.6, 128.5, 56.1, 21.9. HRMS calcd for $C_{17}H_{20}NOS^+$ $[M + H]^+$ m/z 285.1266, found m/z 286.1260

(S)-N-((2-aminophenyl)(phenyl)methylene)-2-methylpropane-2-sulfinamide **(2f)**. Method A. Pure **2f** was obtained (2.7 g, 88%) as a yellow solid from diisopropyl ether trituration. ^{1}H NMR (400 MHz, MeOD) δ 7.77 (d, *J* = 35.4 Hz, 0.3 H), 7.53 (d, *J* = 4.3 Hz, 3H), 7.23 (dd, *J* = 15.4, 7.2 Hz, 2.7H), 6.92 – 6.74 (m, 2H), 6.42 (t, *J* = 7.7 Hz, 1H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, MeOD) δ 184.7, 152.2, 137.3, 134.7, 134.0, 128.9, 128.1, 127.5, 116.7, 115.9, 114.8, 55.1, 21.1. HRMS calcd for $C_{17}H_{21}N_2OS^+$ $[M + H]^+$ m/z 301.1375, found m/z 301.1372

(S)-2-methyl-N-(1-(naphthalen-2-yl)ethylidene)propane-2-sulfinamide **(2g)**. Method A. Pure **2g** was obtained (2.6 g, 80%) as a yellow oil from silica pad purification (4:1 heptane / ethyl acetate): Z/E isomers mixture. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 – 8.11 (m, 0.66H), 8.09 – 7.91 (m, 2H), 7.75 – 7.48 (m, 4H), 7.37 (dd, *J* = 18.2, 7.0 Hz, 0.39H), 2.82 (s, 2H), 2.59 (s, 1H), 1.22 (s, 6H), 1.09 (s, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 181.3, 138.6, 133.4, 132.8, 130.1, 128.9, 128.8, 128.7, 128.6, 127.0, 126.5, 126.3, 125.5, 125.2, 125.1, 124.9, 124.6, 124.2, 123.7, 123.3, 56.3, 54.5, 24.8, 22.0, 21.6. HRMS calcd for $C_{16}H_{20}NOS^+$ $[M + H]^+$ m/z 274.1266, found m/z 274.1250

(S)-2-methyl-N-(2-phenylcyclohexylidene)propane-2-sulfinamide **(2h)**. Method A. Pure **2h** was obtained (2.1 g, 66%) as a yellow oil from silica pad purification (4:1 heptane / ethyl acetate) : diasteroisomers mixture. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.29 (m, 2H), 7.23 – 7.13 (m, 3H), 3.77 (m, 1H), 3.49 (dt, *J* = 13.3, 4.3 Hz, 0.5H), 3.35 (m, 0.5H), 2.59 – 2.44 (m, 0.5H), 2.34 (td, *J* = 12.7, 5.0 Hz, 0.5H), 2.16 – 1.92 (m, 3H), 1.87 (m, 1H), 1.80 – 1.51 (m, 2H), 0.94 (s, 4.5H), 0.91 (s, 4.5H). 13C NMR (101 MHz, DMSO-d_6) δ 188.3, 188.1, 140.6, 140.5, 128.8, 128.7, 128.5, 127.9, 127.7, 126.3, 56.2, 55.8, 54.5, 54.5, 34.5, 34.3, 33.7, 33.3, 27.8, 27.2, 24.9, 24.8, 21.7, 21.6. HRMS calcd for $C_{16}H_{24}NOS^+$ $[M + H]^+$ m/z 278.1579, found m/z 278.1573

(S)-N-(1-(2-chlorophenyl)ethylidene)-2-methylpropane-2-sulfinamide **(2i)**. Method A. Pure **2i** was obtained (2.8 g ,84%) as a yellow oil from silica pad purification (4:1 heptane / ethyl acetate) : Z/E isomers mixture (M major and m minor). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 – 7.28 (m, 4H), 2.65 (s, 2H), 2.44 (s, 1H), 1.22 (s, 6H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.8(M+m), 140.3(M+m), 131.0 (M), 130.4(m), 130.0(M), 129.3 (M+m), 129.1(m), 128.9(M), 127.8(m), 127.6(M), 127.0(m), 56.9(M+m), 23.9(M+m), 22.0(M), 21.8(m) HRMS calcd for $C_{12}H_{17}ClNOS^{+}$ $[M + H]^{+}$ m/z 258.0719, found m/z 258.0715

(S)-N-(1-(1-(4-chlorophenyl)cyclobutyl)-3-methylbutylidene)-2-methylpropane-2-sulfinamide **(2j)**. Method A with titanium ethoxide instead of titanium isopropoxide. Pure **2j** was obtained (1.2 g ,42%) as a yellow oil from silica pad purification (4:1 heptane / ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 – 7.41 (m, 2H), 7.38 (d, J = 8.3 Hz, 2H), 2.82 – 2.58 (m, 3H), 2.51 – 2.32 (m, 2H), 2.22 (dd, J = 13.5, 8.1 Hz, 1H), 1.92 – 1.66 (m, 3H), 1.22 (s, 9H), 0.70 (d, J = 6.6 Hz, 3H), 0.55 (d, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.0, 142.6, 131.4, 128.8, 128.4, 57.2, 56.5, 40.3, 40.2, 40.1, 40.0, 32.2, 32.1, 25.8, 22.5, 22.1, 22.1, 15.5. HRMS calcd for $C_{19}H_{29}ClNOS^{+}$ $[M + H]^{+}$ m/z 354.1658, found m/z 354.1655

ASSOCIATED CONTENT

Supporting Information.

Copies of ^{1}H NMR, ^{13}C NMR of all compounds (PDF)

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ABBREVIATIONS

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