A Remarkable Cycloaddition of Bis(arylsulfonyl)iodonium Ylide with Norbornene Derivatives for the Direct Synthesis of Functionalized Indanes

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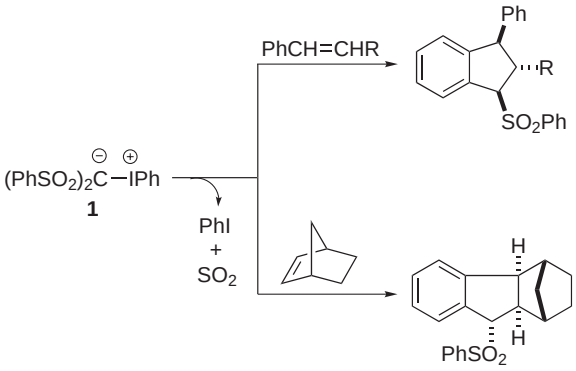
Abstract: The reaction of bis(arylsulfonyl)iodonium ylides with a variety of norbornene derivatives **3** affords functionalized indanes **4** in good yields through an unusual cycloaddition. This diastereoselective cycloaddition provides a convenient preparative route to multicyclic structures of well defined stereochemical configuration.

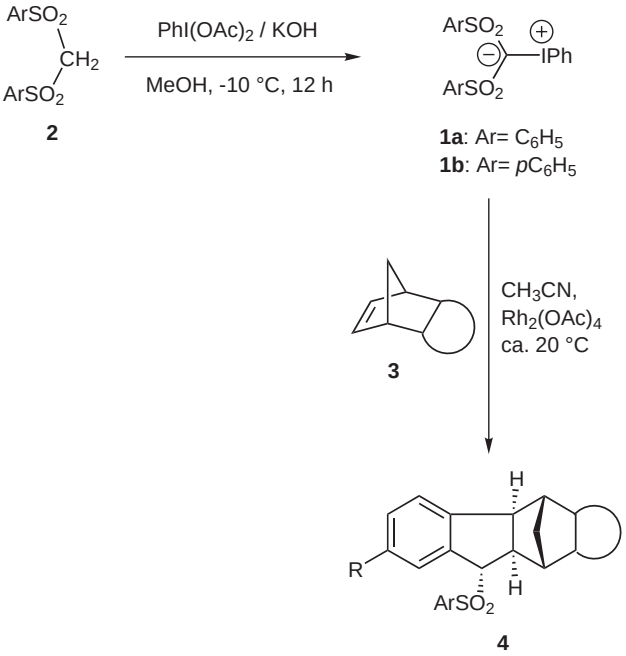
Key words: ylide, [3+2]-cycloaddition, indane

Bis(sulfonyl)iodonium ylides[1] are a versatile class of hypervalent iodine compounds,[2] which are related to the corresponding bis(sulfonyl)diazo compounds and readily prepared from bis(sulfonyl)methanes.[3] Whereas the photochemical and thermal $Cu(acac)_2$-catalyzed reaction of bis(sulfonyl)iodonium ylides with olefins affords cyclopropanes and thiosulfonates,[3] analogous to the bis(sulfonyl)diazomethanes,[4] phenylated alkenes and norbornene lead to substituted indanes (Scheme 1).[3,5] In view of the synthetic value of this unusual cycloaddition, the incentive of the present study was to examine the scope of this novel process for norbornene derivatives. Provided that the stereochemical course of this cycloaddition process is well defined and the arylsulfonyl substituent may be readily removed by reduction, a potentially useful stereoselective synthetic method would become available for the preparation of highly substituted, functionalized indanes.



Scheme 1

The bis(arylsulfonyl)iodonium ylides **1a**,**b** were prepared from the corresponding bis(arylsulfonyl)methanes **2** by treatment with iodobenzene diacetate and KOH as base at –10 °C (Scheme 2).[3] The disulfonyl iodonium ylides are labile and may be stored at –30 °C for several weeks without significant decomposition. They are practically insoluble in common organic solvents (except DMSO), so that the reaction of the ylide with the norbornene derivatives **3** was conducted under heterogeneous conditions.



Scheme 2

All reactions were run at room temperature (ca. 20 °C), until complete consumption of the ylide (indicated by the change from a heterogeneous mixture to a clear solution), as shown in Scheme 2. The norbornene **3a** was selected as a model substrate and tested with iodonium ylide **1a** under a variety of conditions (Table 1). In CH_2Cl_2 at 20 °C, a 54:46 mixture of the desired indane **4a** and disulfone **2a** was obtained (Table 1, entry 1). Similar results were observed in the absence of light and/or under an inert atmosphere (entries 2–4), albeit at longer reactions times (240 h to 600 h). The addition of catalytic amounts of $Rh_2(OAc)_4$ (0.1 mol%) increased dramatically (ca. 2000 times) the rate of ylide consumption, but still most of the

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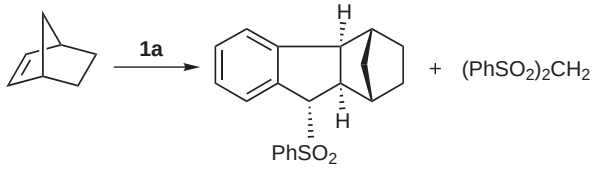
ylide was converted to its disulfonyl methane **2a** (entry 5). With CCl_4 as solvent and no rhodium catalyst, the reaction time was significantly (ca. 3 times) prolonged, with no improvement in the product ratio (entry 6).

Table 1 Optimization of Reaction Conditions[a] for the Formation of Indane **4a**



3a **4a** **2a**

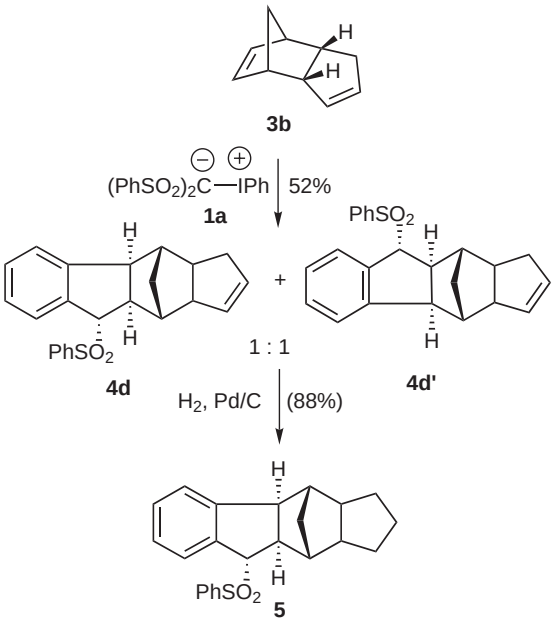
Entry	Solvent	Catalyst	T (°C)	Time[b] (h)	Product ratio[c] **4a**:**2a**
1	CH_2Cl_2		20	240	54:46
2	CH_2Cl_2[d]		20	600	45:55
3	CH_2Cl_2[d,e]		20	600	48:52
4	CH_2Cl_2[e]		20	600	42:58
5	CH_2Cl_2[e]	$Rh_2(OAc)_4$	20	0.3	44:56
6	CCl_4[e]		20	2160	45:55
7	CH_3CN[e]		20	168	70:30
8	CH_3CN	$Rh_2(OAc)_4$	20	22	70:30
9	CH_3CN	$Rh_2(OAc)_4$	80	1.5	68:32
10	CH_3CN	$PdCl_2$	20	60	75:25
11	DMSO	$Rh_2(OAc)_4$	20	24	74:26

[a] All reactions were carried out by stirring a suspension of the ylide **1a** (1.0 equiv) and norbornene **3a** (7.5 equiv) for the specified time.
[b] Time required for complete consumption of the ylide **1a**.
[c] The product ratio was determined by ^{1}H NMR-spectral analysis of the crude reaction mixture, error ±5% of the stated value.
[d] In the absence of light.
[e] Under an argon atmosphere.

The yield of indane **4a** was improved when the more polar solvent CH_3CN was employed. The reaction time was now shorter and the product ratio was 70:30 (entry 7). On addition of catalytic amounts of $Rh_2(OAc)_4$ (0.1–0.2 mol%) in CH_3CN, the reaction times were again much shorter (entry 8); a similar improvement was achieved in DMSO and with catalytic amounts of $Rh_2(OAc)_4$ (entry 11). Also at the elevated temperature of 80 °C (entry 9), the reaction time was shortened considerably. The use of catalytic amounts of $PdCl_2$ as additive (entry 10) did not significantly shorten the reaction times. When $Cu(acac)_2$ or CuI was employed as additive, a rather complex reaction mixture was obtained, in which the thiosulfonate was the major product (data not shown in Table 1). Thus, the optimal reaction conditions consist of CH_3CN as solvent and $Rh_2(OAc)_4$ as additive, since the reaction times are shortest and the proportion of the indane **4** cycloadduct highest, that is, the decomposition of the ylide is minimal under these conditions.

The scope of this remarkable cycloaddition was explored by using other norbornene derivatives. The cycloadducts **4** (Table 2) were isolated by flash chromatography on silica gel in moderate yields (up to 64%, relative to the consumed ylide). It should be emphasized that when referred to the amount of consumed alkene, high yields (up to 98%) of the adducts **4** were registered. This indicates that an efficient and clean process operates, except that substantial amounts (up to 49%) of the ylide decompose to the bis(arylsulfonyl)methane **2**.

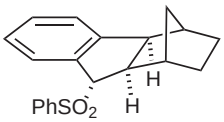
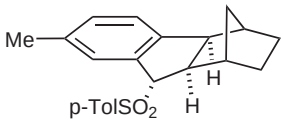
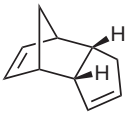
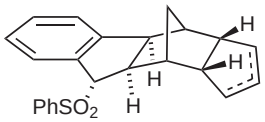
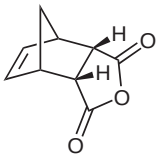
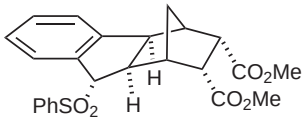
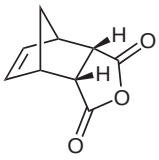
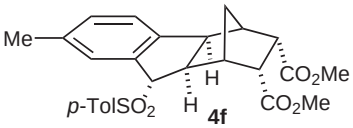
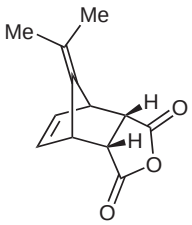
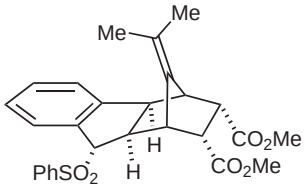
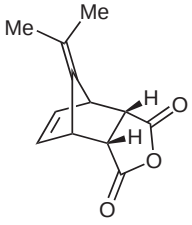
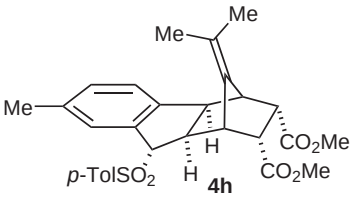
The reaction of the ylide **1a** with norbornene (**3a**) afforded exclusively the indane **4a**[3,6] in 64% yield (Table 2, entry 1). Unexpectedly, a complex non-separable reaction mixture was isolated upon reaction with norbornadiene, while no reaction was observed with 5-methylene-2-norbornene (data not shown in Table 2). Dicyclopentadiene (**3b**) reacted exclusively at the norbornene double bond to give a 1:1 mixture of the two regioisomers **4d** and **4d′** in 52% yield (entry 3). The assigned structures were established by catalytic hydrogenation of this mixture to afford only one product, namely the indane **5** in 88% yield (Scheme 3).



Scheme 3

The cycloaddition of substrate **3a** was conducted also with the iodonium ylide **1b** (entry 2), whose *p*-methyl substituent of the phenyl-sulfonyl group permitted the determination of the regioselectivity of the cycloaddition process in regard to the substitution pattern in the benzo ring of the indane product (see later). The reaction of the ylide **1b** with all norbornene derivatives was much faster and afforded the corresponding indane cycloadducts **4** in good yields.

Table 2 Cycloaddition[a] of Bis(arylsulfonyl)iodonium Ylides **1a**,**b** with Norbornene Derivatives **3** to Afford the Functionalized Indanes **4**

Entry	Ylide	Alkene	Time(h)[b,c]	Conversion(%)[d]	Product	Yield (%)[e]
1	**1a**	 **3a**	22	nd	 **4a**	64
2	**1b**	 **3a**	240	nd	 **4b**	30
3	**1a**	 **3b**	84	nd	 **4d**,**4d′**	52
4	**1a**	 **3c**	2	22	 **4e**	61
5	**1b**	 **3c**	0.3	24	 **4f**	58
6	**1a**	 **3d**	1.3	25	 **4g**	41
7	**1b**	 **3d**	0.5	23	 **4h**	45

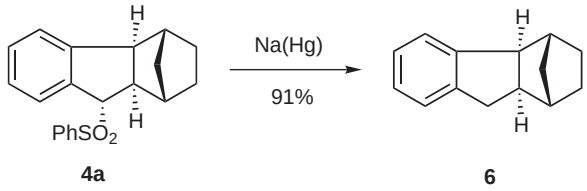
[a] All reactions were carried out by stirring a suspension of ylide **1** (1 equiv) and alkenes **3** (excess) in CH_3CN for the required time.
[b] Time required for complete consumption of the ylide.
[c] The reaction was carried out in the presence of a catalytic amount (0.1 mol%) of $Rh_2(OAc)_4$, except entry 2 (no additive, CH_2Cl_2).
[d] Conversion of the norbornene derivative **3**, as determined after isolation by silica-gel chromatography.
[e] Yield of isolated product (relative to 100% consumption of the ylide) after silica gel chromatography.

This unusual cycloaddition of the bis(arylsulfonyl)-iodonium ylide was extended to the norbornene anhydrides **3c**, **3d** (entries 4–7), which gave the corresponding indane derivatives in high yields. Since these anhydride products could not be directly purified by silica gel chromatography, they were converted to the respective diesters **4e**, and **4f** and fully characterized. For the 7-methylenenorbornene anhydride **3d** (entries 6 and 7), again the ylides

1a and **1b** reacted exclusively with the norbornene double bond to give after esterification the diesters **4g** (41%) and **4h** (45%).

The structural assignment of the indanes is exemplified for the **4b** derivative. The ^{1}H NMR spectrum of the **4b** cycloadduct displays for the indane ring a doublet at δ 4.31 ppm (J = 2.2 Hz for the proton at the C-1 position), a doublet at δ 2.76 ppm (J = 7.3 Hz for the proton at the C-3 position), and a doublet of doublets at δ 2.58 ppm (J = 2.2 Hz and 7.3 Hz for the proton at the C-2 position). The lack of a ROESY signal between the protons at the C-1 and C-3 sites and the ROESY signal between the protons at C-2 and C-3 positions indicate the *trans*/*cis* configuration of the three substituents in the five-membered ring, as was previously established by X-ray analysis of the cycloadduct **4a**.[3a] Furthermore, HMBC signals reveal that the methyl group of the aryl ring and the sulfonyl-bearing C-1 position of the five-membered ring are located *meta* to one another in the product,[5] although originally this methyl substituent occupied the *para* position in the *para*-toluenesulfonyl group of the iodonium ylide.

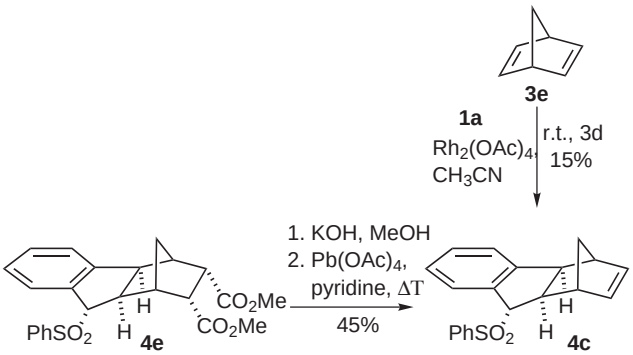
Clearly, these diverse examples of the norbornene derivatives in Table 2 demonstrate that the scope of this remarkable cycloaddition is broad for the indane synthesis. Since the required iodonium ylide is readily accessible by condensation of bis(arylsulfonyl)methane with the commercially available iodobenzene diacetate, this novel process constitutes an attractive diastereoselective route for the preparation of functionalized indanes, in which the three adjacent stereocenters of the cyclopentane ring are generated in one step. Moreover, the arylsulfonyl functionality may be readily removed reductively, as exemplarily illustrated for the cycloadduct **4a** by treatment with sodium amalgam to afford the indane **6** in 91% yield (Scheme 4).



4a **6**

Scheme 4

We mentioned already, that the reaction of iodonium ylide **1a** with norbornadiene (**3e**) leads to a complex reaction mixture after stirring at room temperature for 3 days, in which β-disulfone **1a** is the major product, whereas only a small amount (15%) of the desired cycloadduct **4c** was obtained. Such a cycloadduct **4c** could, however, be readily produced (Scheme 5) by the hydrolysis of the diester **4e** with hot KOH in MeOH, followed by decarboxylation[7] with $Pb(Oac)_4$ in hot pyridine (overall 45% yield).



Scheme 5

As for the mechanism of this remarkable cycloaddition of iodonium ylide, a carbene route is unlikely.[8] For example, under conditions that generate carbenes,[3] such as catalysis with copper complexes, the reaction of the ylide with norbornene (**1a**) led to a complex reaction mixture. From the latter only the phenyl benzenethiosulfonate ($PhSO_2SPh$), the typical product derived from the bis(phenylsulfonyl)carbene,[3,4,9] was isolated in moderate yield (ca. 40%). Also a metal-carbenoid intermediate is unlikely to be involved, since the bis(arylsulfonyl)iodonium ylide reacts with the norbornene (**1a**) in the absence of metal catalysts to afford the same indane products, but much longer reaction times are required (Table 1, entry 1). The mechanism should be analogous to the cycloaddition of the iodonium ylide to stilbenes.[5] The *exo* configuration is expected and well documented for cycloadditions with norbornene,[10] while the exclusive *trans* arrangement of the phenylsulfonyl group with respect to the norbornene ring is in accord with that found for the stilbenes.[5]

In summary, the work described herein provides a simple and efficient method for the direct diastereoselective synthesis of functionalized indanes **3** through the cycloaddition of the bis(benzenesulfonyl)iodonium ylide with a variety of norbornene derivatives **2**. Therewith, complex multicyclic ring skeletons of well defined configurations become conveniently accessible.

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(6) **Representative Experimental Procedure. Synthesis of 4a**: To a suspension of the ylide **1a** (1.00 g, 2.0 mmol) and norbonene **3a** (1.40 g, 15.0 mmol) in acetonitrile (10 mL) was added a catalytic amount (0.1 mol%) of $Rh_2(OAc)_4$ and the mixture was stirred at 20 °C for 22 h until a clear solution was produced. The solvent was evaporated (40 °C at 10 torr) and the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to yield 419 mg (64%) of the indane derivative **4a**; colorless plates, mp 140–141 °C (lit.[3] 140–141 °C). IR (KBr): 3050 cm^{-1}, 2940, 2860, 1580, 1470, 1440, 1330, 1300, 1280, 1250, 1230, 1210, 1200, 1185, 1160, 1120, 1080, 1020, 990, 940, 910, 880, 870, 840, 820. ^{1}H NMR (250 MHz, $CDCl_3$) : δ = 0.82 (d, *J* = 10.4 Hz, 1 H), 0.93 (d, *J* = 10.4 Hz, 1 H), 1.24–1.29 (m, 2 H), 1.48–1.52 (m, 2 H), 2.13 (s, 1 H), 2.62 (dd, *J* = 1.9 Hz, 7.3 Hz, 1 H), 2.78 (d, *J* = 7.3 Hz, 1 H), 4.38 (d, *J* = 1.9 Hz, 1 H), 7.04 (d, *J* = 7.3 Hz, 1 H), 7.15–7.29 (m, 2 H), 7.35–7.45 (m, 3 H), 7.51–7.59 (m, 3 H). ^{13}C NMR (63 MHz, $CDCl_3$) : δ = 28.1 (t), 28.9 (t), 32.7 (t), 42.7 (d), 42.9 (d), 47.8 (d), 53.6 (d), 76.2 (d), 112.6 (s), 124.5 (d), 126.1 (d), 126.8 (d), 128.6 (d), 129.2 (d), 129.5 (d), 133.4 (d), 135.5 (s), 136.7 (d), 148.2 (s).
Synthesis of 4b: A suspension of the ylide **1b** (1.0 g, 1.9 mmol)and norbonene **3a** (2.0 g, 21.0 mmol) in dichloromethane (10 mL) was stirred for 240 h until a clear solution was produced. The solvent was evaporated (40 °C at 10 torr) and the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to yield 200 mg (30%) of the indane derivative **4b**; colorless plates, mp 181–182 °C. IR (KBr): 2955cm^{-1}, 2920, 2860, 1590, 1490, 1450, 1305, 1285, 1250, 1220, 1210, 1200, 1190, 1175, 1150, 1130, 1120, 1085, 890, 855, 830, 820. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 0.83 (d, *J* = 10.4 Hz, 1 H), 0.91–0.94 (m, 1 H), 1.19–1.30 (m, 2 H), 1.34–1.57 (m, 2 H), 2.10 (dd, *J* = 3.0 Hz, 12.6 Hz, 2 H), 2.33 (s, 3 H), 2.39 (s, 3 H), 2.58 (dd, *J* = 2.2 Hz, 7.3 Hz, 1 H), 2.76 (d, *J* = 7.3 Hz, 1 H), 4.31 (d, *J* = 2.2 Hz, 1 H), 6.94 (d, *J* = 7.7 Hz, 1 H), 7.09 (d, *J* = 7.7 Hz, 1 H), 7.20 (d, *J* = 8.2 Hz, 2 H), 7.28 (s, 1 H), 7.47 (d, *J* = 8.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 21.2 (q), 21.6 (q), 28.1 (t), 29.0 (t), 32.8 (t), 42.7 (d), 53.3 (d), 76.1 (d), 124.1 (d), 126.6 (d), 129.2 (d), 129.3 (d), 130.4 (d), 134.0 (s), 135.7 (s), 136.5 (s), 144.3 (s), 145.3 (s). Anal. Calcd for $C_{22}H_{24}O_2S$ (352.5): C, 74.96; H, 6.86; S, 9.10. Found: C, 74.66; H, 6.85; S, 9.11.
Synthesis of 5: To a solution of the indane derivative **4a** (118 mg, 0.36 mmol)in methanol (10 mL), was added in portions Na_2HPO_4 (180 mg) and 6% sodium amalgam (1.50 g) and the resulting mixture was stirred at 20 °C for 48 h. The solvent was evaporated (40 °C at 10 torr), the residue was dissolved in dichloromethane (30 mL), and extracted with brine (2 × 50 mL). The organic layer was dried over magnesium sulfate, the solvent evaporated (20 °C at 10 torr), and the residue was purified by silica gel chromatography (CH_2Cl_2 as eluent) to yield 61 mg (91%) of the indane **5** as colorless oil. IR (Neat): 2930 cm^{-1}, 2850, 1475, 1450, 830. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 0.98–1.02 (m, 1 H), 1.11–1.15 (m, 1 H), 1.24–1.30 (m, 1 H), 1.37–1.43 (m, 1 H), 1.50–1.65 (m, 2 H), 2.10 (d, *J* = 3.8 Hz, 1 H), 2.29 (d, *J* = 3.8 Hz, 1 H), 2.36–2.41 (m, 1 H), 2.61 (dd, *J* = 3.8 Hz, 17.2 Hz, 1 H), 3.14 (d, *J* = 7.8 Hz, 1 H), 3.26 (dd, *J* = 10.2 Hz, 17.2 Hz, 1 H), 7.10–7.20 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 28.8 (t), 29.0 (t), 32.4 (t), 39.3 (t), 43.4 (d), 43.7 (d), 44.9 (d), 55.5 (d), 124.0 (d), 124.5 (d), 126.1 (d), 126.2 (d), 144.8 (s), 146.3 (s). HRMS (EI): Calcd for $C_{14}H_{16}$ 184.1252 Found: 184.1252.

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