Ring Contraction of 1,2-Dihydronaphthalenes Promoted by Thallium(III) in Acetonitrile: A Diastereoselective Approach to Indanes

Helena M. C. Ferraz, Vânia M. T. Carneiro, Luiz F. Silva, Jr.*

Instituto de Química, Universidade de São Paulo, CP 26077, CEP 05513-970, São Paulo SP, Brazil
E-mail: luizfsjr@iq.usp.br

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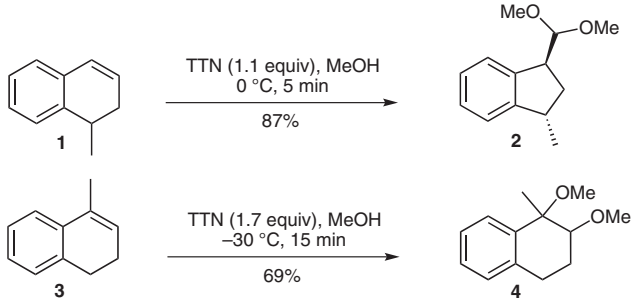
Abstract: *trans*-1,3-Disubstituted indanes are conveniently accessed by a stereoselective ring contraction of 1,2-dihydronaphthalenes upon treatment with thallium(III) nitrate (TTN) in acetonitrile. Under these conditions, the oxidative rearrangement of either di- or trisubstituted double bonds is possible.

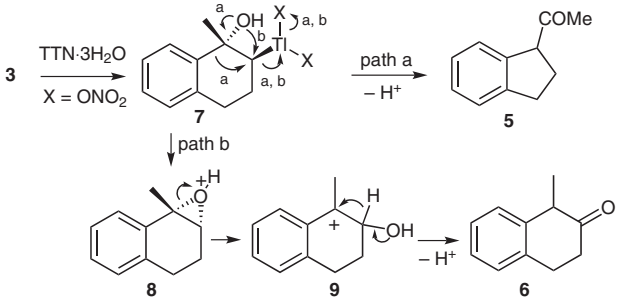
Key words: thallium(III) nitrate, carbocycles, indanes, ring contractions, oxidative rearrangements

The indane ring system is present in several compounds with remarkable biological activity.[1a] Consequently, new approaches to obtain indanes are constantly under investigation. Particularly challenging has been the stereoselective synthesis of substituted indanes.[1] To this end, we reported that *trans*-1,3-disubstituted indanes, such as **2**, are obtainable by the ring contraction of readily available 1,2-dihydronaphthalenes in the presence of thallium(III) nitrate (TTN) in methanol or in trimethyl orthoformate (TMOF) (Scheme 1).[2] However, products of addition of methanol, such as **4**, are isolated for substrates with a trisubstituted double bond (Scheme 1).[2a] Herein, we describe that indanes can be obtained from 1,2-dihydronaphthalenes bearing either di- or trisubstituted double bonds if thallium(III) nitrate is used in acetonitrile, instead of methanol, thus overcoming the drawback mentioned above.



Scheme 1

Inspired by previous work on oxidations of olefins with thallium(III)[3] or iodine(III)[4] in acetonitrile, we decided to investigate the behavior of 1,2-dihydronaphthalene **3** in this solvent (Scheme 2). Fortunately, under these conditions, the formation of addition products was not observed, and a mixture of ketones **5** and **6** was isolated (Scheme 2, Table 1, entry 1). Presumably, ketone **5** is formed through direct rearrangement of the oxythallated adduct **7** (Scheme 2, path a),[5] while tetralone **6** might arise from competitive formation of the epoxide **8**, ring opening to the tertiary benzylic cation **9**, and finally 1,2-hydride migration[6] (path b). The result with olefin **3** prompted us to study the reaction of other 1,2-dihydronaphthalenes. To our delight, the reaction of **10** with thallium(III) nitrate in acetonitrile gave only the desired ring contraction product **11**, in 80% yield, as a 21:1 (*trans*/*cis*) mixture of diastereomers (Table 1, entry 2). The selective formation of the *trans*-isomer agrees with the mechanism previously discussed.[2c] The presence of an alkyl group at position 1 favors the ring contraction, explaining the high yield of the rearrangement product **11**.[4b] The reaction of **12** was performed in a similar manner, affording the ring contraction product **13** in 63% yield (Table 1, entry 3). However, in this case, the aromatization product **14** was also obtained as a minor component.[2b] The *trans*-1,3-disubstituted indane **16** was the main product in the oxidation of **15** (Table 1, entry 4), although the yield was lower than that from **10** and from **12**. The time required for the complete consumption of the starting olefin also varied considerably for **10**, **12**, and **15** (10 min, 6 h, and 24 h, respectively). Considering that thallium(III)-mediated ring contraction is sensitive to steric and electronic effects,[2,7] the lower yield and reactivity of **12** when compared to **10** can be explained by the higher steric hindrance of the group attached to the double bond (*i*-Pr vs Me). The difference of reactivity between **15** and **10** can be explained by both steric and electronic effects.



Scheme 2

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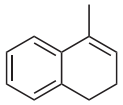
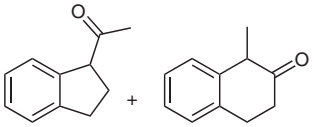
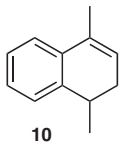
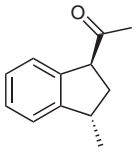
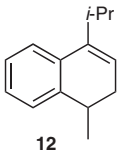
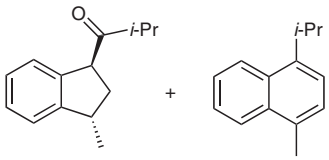
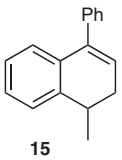
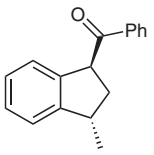
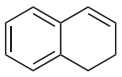
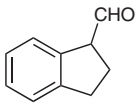
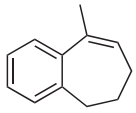
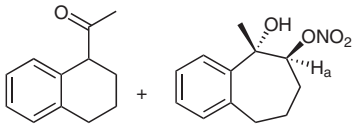
Table 1 Reactions of 1,2-Dihydronaphthalenes with Thallium(III) Nitrate Trihydrate in Acetonitrile[a]

Entry	Substrate	Product(s)	Time	Yield[b] (%)
1	 **3**	 **5** + **6**	10 min	70 (**5**/**6** = 3:1)
2	 **10**	 **11**	10 min	80 (*trans*/*cis* = 21:1)
3	 **12**	 **13** + **14**	6 h	63 (**13**), 5 (**14**)
4	 **15**	 **16**	24 h	40
5	 **17**	 **18**	10 min	97[c]
6	 **19**	 **20** + **21**	30 min	76 (**20**), 4 (**21**)

[a] Reagents and conditions: substrate (1 equiv), 3-Å MS (0.5 g/g substrate), TTN·3H_2O (1.1 equiv), MeCN, 0 °C.
[b] Isolated yield.
[c] Crude product.

After investigating the behavior of a series of trisubstituted olefins, we decided to verify if acetonitrile would also be a good solvent for the ring contraction of disubstituted substrates. Indeed, when the 1,2-dihydronaphthalene **17** was treated with thallium(III) nitrate in acetonitrile, indane **18** was obtained in high yield (Table 1, entry 5). The formation of an aldehyde (as **18**) instead of a ketal (such as **2**, cf. Scheme 1) may be an advantage, because a deprotection step is avoided.[2c] Finally, thallium(III) nitrate also induced ring contraction of a seven-membered-ring analogue,[8] as was demonstrated with the olefin **19**, which gave rise to ketone **20** in 76% yield (Table 1, entry 6). A small amount of the addition product **21** was also isolated. The relative configuration of **21** was inferred from the mechanism of the reaction.[2,9] Nitrate **21** has a characteristic signal at δ = 4.7 for H_a in the ^{1}H NMR spectrum.[2b]

In summary, indanes can be obtained diastereoselectively by the reaction of 1,2-dihydronaphthalenes with thallium(III) in acetonitrile. This solvent appears to be more efficient than methanol for the rearrangement of olefins. Finally, these conditions lead to higher isolated yields than obtained in an analogous protocol using iodine(III).[4b]

Warning: Thallium salts are toxic and must be handled with care. TTN was used as received. MeCN was distilled from CaH_2 and stored over molecular sieves. Melting points are uncorrected. Column chromatography was performed using silica gel 200–400 mesh. TLC analysis was performed on silica gel plates, using phosphomolybdic acid, vanillin or *p*-anisaldehyde solution for visualization. IR spectra were measured on a Perkin-Elmer 1750-FT. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra of samples in $CDCl_3$ were obtained on a Bruker spectrometer. Gas chromatography was carried out on HP 6890 series II and Shimadzu 2010 instru-

ments. HRMS analysis was conducted on a Bruker Daltonics Microtof Electrospray apparatus. Compounds **3**, **10**, and **17** were prepared by literature procedures.[2b,c,4b]

4-Isopropyl-1-methyl-1,2-dihydronaphthalene (12); Typical Procedure for Grignard Reactions To Prepare the Substrates

A soln of 4-methyl-1-tetralone (2.40 g, 15.0 mmol) in anhyd Et_2O (6 mL) was added to a soln of *i*-PrMgBr [prepared from *i*-PrBr (7.38 g, 60.0 mmol), Mg (1.44 g, 59.2 mmol), and I_2 (some crystals) in anhyd Et_2O (18 mL)]. The mixture was stirred for 20 h at reflux. After that, a soln of 6 M HCl was added dropwise at 0 °C until the pH was 2–3. The soln was stirred for 1 h. The organic layer was extracted with Et_2O (90 mL), washed with a sat. aq soln of $Na_2S_2O_3$ (30 mL) and brine (30 mL) and dried ($MgSO_4$). The soln was concentrated under reduced pressure and the residue was purified by flash chromatography (hexanes); this gave **12**[10] as a colorless oil; yield: 1.08 g (39%). (The NMR data of **12** were not previously reported.[10])

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 6.6 Hz, 3 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 1.20 (d, *J* = 6.9 Hz, 3 H), 2.01–2.11 (m, 1 H), 2.35–2.45 (m, 1 H), 2.82 (sext, *J* = 6.9 Hz, 1 H), 2.90–3.02 (m, 1 H), 5.79 (td, *J* = 4.7, 1.2 Hz, 1 H), 7.16–7.23 (m, 3 H), 7.30–7.34 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 22.1, 22.3, 28.0, 30.9, 32.3, 119.7, 122.6, 126.0, 126.2, 126.6, 134.1, 141.9, 142.0.

1-Methyl-4-phenyl-1,2-dihydronaphthalene (15)

The reaction was performed as described above for **12**. A mixture of 4-methyl-1-tetralone (0.641 g, 4.00 mmol) and PhMgBr [prepared from PhBr (0.819 g, 5.22 mmol), Mg (0.125 g, 5.21 mmol), and I_2 (some crystals) in anhyd Et_2O (2 mL)] was stirred for 2 h at reflux. The crude product was purified giving **15**[11] as a colorless oil; yield: 0.704 g (80%). (The NMR data of **15** were not previously reported.[11])

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 7.2 Hz, 3 H), 2.20 (ddd, *J* = 16.8, 7.8, 4.6 Hz, 1 H), 2.54 (ddd, *J* = 16.8, 6.6, 4.6 Hz, 1 H), 2.91–3.03 (m, 1 H), 5.99 (t, *J* = 4.6 Hz, 1 H), 7.04 (dd, *J* = 7.6, 1.0 Hz, 1 H), 7.09 (td, *J* = 7.2, 1.5 Hz, 1 H), 7.15–7.22 (m, 2 H), 7.24–7.36 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8, 31.5, 32.2, 125.7, 126.0, 126.0, 126.2, 127.0, 127.3, 128.2, 128.2, 128.7, 128.7, 134.3, 139.4, 140.9, 141.6.

9-Methyl-6,7-dihydro-5*H*-benzocycloheptene (19)

The reaction was performed as described for **12**. A mixture of α-benzosuberone (0.991 g, 6.22 mmol) and MeMgI [prepared from MeI (2.513 g, 17.7 mmol), Mg (0.407 g, 16.7 mmol), and I_2 (some crystals) in anhyd Et_2O (6 mL)] was stirred for 5 h at reflux. The crude product was purified giving **19**[12] as a colorless oil; yield: 0.708 g (72%). (The NMR data of **19** were not previously reported.[12])

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.81 (q, *J* = 7.2 Hz, 2 H), 2.02–2.11 (m, 2 H), 2.09 (s, 3 H), 2.56 (t, *J* = 6.9 Hz, 2 H), 5.96 (tq, *J* = 7.2, 1.5 Hz, 1 H), 7.08–7.29 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6, 24.9, 32.6, 34.5, 125.9, 126.1, 126.4, 126.5, 128.8, 136.8, 140.9, 141.9.

Oxidation of 4-Methyl-1,2-dihydronaphthalene (3); Typical Procedure for TTN Reactions

To a stirred soln of **3** (0.144 g, 1.00 mmol) and 3 Å MS (0.072 g, 0.5 g/g of substrate) in MeCN (5.0 mL) under N_2 was added TTN·$3H_2O$ (0.463 g, 1.10 mmol) at 0 °C. The reagent promptly dissolved. The mixture was stirred for 10 min and abundant precipitation was observed. The resulting mixture was filtered through a silica gel pad (200–400 mesh, ca. 10 cm, CH_2Cl_2). The filtrate was washed with brine and dried ($MgSO_4$). The soln was concentrated under reduced pressure and the residue was purified by flash chromatography (Et_2O–hexanes, 1:9); this gave a 3:1 mixture of **5**[13] and **6**[14] as a colorless oil; yield: 0.112 g (70%).

1-(*trans*-1-Methyl-2,3-dihydro-1*H*-inden-3-yl)ethanone (11)

The typical procedure was followed, but **10** (0.158 g, 1.00 mmol) was used in place of **3**. The residue was purified by flash chromatography (EtOAc–hexanes, 0–5% gradient); this gave **11**[4b] as a *cis*/*trans* mixture (1:21, by ^{1}H NMR after purification). Yield: 0.139 g (80%); colorless oil.

2-Methyl-1-(*trans*-1-methyl-2,3-dihydro-1*H*-inden-3-yl)propan-1-one (13)

The typical procedure was followed, but **12** (0.186 g, 1,00 mmol) was used in place of **3**. The mixture was stirred for 6 h at 0 °C. The residue was purified by flash chromatography (EtOAc–hexanes, 0–5% gradient) giving **13** and 1-isopropyl-4-methylnaphthalene (**14**),[15] both as colorless oils; yield (**13**): 0.127 g (63%); yield (**14**): 0.009 g (5%).

Indane 13

IR (film): 2964, 2929, 2871, 1709, 1466, 1052, 755 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 6.5 Hz, 3 H), 1.13 (d, *J* = 7.0 Hz, 3 H), 1.28 (d, *J* = 7.0 Hz, 3 H), 1.83 (dt, *J* = 12.5, 8.7 Hz, 1 H), 2.55 (ddd, *J* = 12.5, 7.5, 3.5 Hz, 1 H), 2.93 (sept, *J* = 7.0 Hz, 1 H), 3.38–3.46 (m, 1 H), 4.26 (dd, *J* = 8.7, 3.5 Hz, 1 H), 7.15–7.18 (m, 1 H), 7.20–7.25 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 18.4, 18.9, 20.2, 38.1, 38.4, 38.9, 54.9, 123.8, 124.5, 126.4, 127.5, 140.8, 149.4, 214.5.

MS: *m*/*z* (%) = 131 (100), 202 (8) $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{19}O$: 203.1430; found: 203.1434.

(*trans*-1-Methyl-2,3-dihydro-1*H*-inden-3-yl)(phenyl)methanone (16)

The typical procedure was followed, but **15** (0.222 g, 1.01 mmol) was used in place of **3**. The mixture was stirred for 6 h at 0 °C and for 18 h at r.t. The residue was purified by flash chromatography (EtOAc–hexanes, 1:9) giving **16** as a colorless oil; yield: 0.095 g (40%).

IR (film): 3066, 2958, 1682, 1447, 1218, 755, 699 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (d, *J* = 7.2 Hz, 3 H), 2.01 (ddd, *J* = 12.8, 8.8, 7.2 Hz, 1 H), 2.71 (ddd, *J* = 12.8, 7.2, 4.0 Hz, 1 H), 3.50 (sext, *J* = 7.2 Hz, 1 H), 5.06 (dd, *J* = 8.8, 4.0 Hz, 1 H), 7.05–7.11 (m, 2 H), 7.22–7.25 (m, 2 H), 7.48–7.53 (m, 2 H), 7.57–7.63 (m, 1 H), 8.03–8.06 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 38.5, 38.6, 51.1, 123.8, 125.1, 126.4, 127.5, 128.7, 128.7, 128.9, 128.9, 133.0, 136.8, 140.8, 149.4, 200.4.

MS: *m*/*z* (%) = 91 (27), 104 (100), 132 (82), 145 (52), 236 (41) $[M^+]$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{17}O$: 237.1274; found: 237.1271.

2,3-Dihydro-1*H*-indene-1-carbaldehyde (18)

The typical procedure was followed, but **17** (0.132 g, 1.01 mmol) was used in place of **3**. Evaporation of the solvent afforded the crude aldehyde **18**[16] as a light yellow oil; yield: 0.144 g (97%).

1-(1,2,3,4-Tetrahydro-1-naphthyl)ethanone (20)

The typical procedure was followed, but **19** (0.158 g, 1.00 mmol) was used in place of **3**. The mixture was stirred for 30 min. The residue was purified by flash chromatography (EtOAc–hexanes, 1:9)

giving **20**[16] and **21**, both as colorless oils; yield (**20**): 0.132 g (76%); yield (**21**): 0.009 g (4%).

Compound 21

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50–1.65 (m, 1 H), 1.83 (s, 3 H), 2.07–2.18 (m, 1 H), 2.34–2.43 (m, 1 H), 2.48–2.62 (m, 1 H), 2.82–2.89 (m, 1 H), 2.99–3.08 (m, 1 H), 4.70 (dd, *J* = 12.3, 3.3 Hz, 1 H), 7.11 (dd, *J* = 7.5, 1.2 Hz, 1 H), 7.21 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.29 (td, *J* = 7.5, 1.2 Hz, 1 H), 7.81 (dd, *J* = 7.5, 1.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5, 25.7, 32.1, 36.0, 75.7, 94.0, 124.9, 127.2, 128.2, 131.4, 138.1, 143.3.

MS: *m*/*z* (%) = 43 (100), 131 (34), 145 (55), 191 (1) [$M^+ - NO_2$].

ESI-HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{15}NO_4Na$: 260.0893; found: 260.0889.

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