Thallium Trinitrate Mediated Ring Contraction of *trans*-2-Decalones: An Alternative Entry to the Hydrindane System

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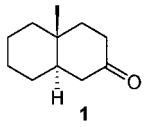
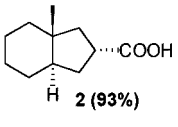
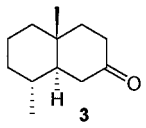
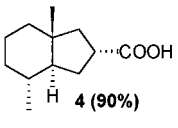
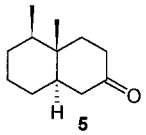
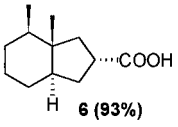
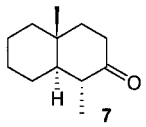
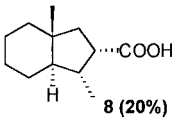
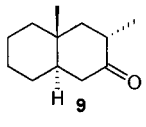
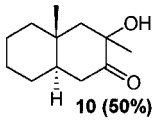
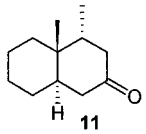
The stereocontrolled generation of either cis- or trans-fused hydrindanes is a long-standing synthetic problem which continues to receive much attention.[1,2]

In a recent paper,[3] we described the thallium trinitrate (TTN) mediated ring contraction[4] of some monocyclic ketones, leading to carboxylic acids. We also showed that the diastereoselectivity of these reactions is consistent with the mechanism proposed by McKillop et al.[4f] A preliminary experiment was also reported in which trans-fused 10-methyl-2-decalone (**1**) was found to give the carboxylic acid **2** in excellent yield.[3]

It is noteworthy that a two-step transformation of **1** into **2** (52% total yield), by treatment of the α-acyl derivative of **1** with hydrogen peroxide, has already been described by Middleton and Stock.[5] Similarly, Smissman et al.[6] converted **1** into **2** in 11% of total yield, also in two steps, by Favorskii rearrangement.

In the present paper, we report the results of our studies concerning the application of the TTN-mediated ring contraction to a series of trans-fused 10-methyl-2-decalones (Table 1), for constructing the *trans*-hydrindane system in a single stereocontrolled step.

Table 1. Reaction of Trans-Fused 2-Decalones with TTN

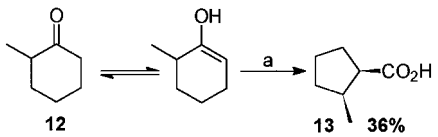
Entry	Substrate	Conditions	Product (yield)
1	 **1**	1.1 eq. TTN, 24h	 **2 (93%)**
2	 **3**	1.1 eq. TTN, 24h	 **4 (90%)**
3	 **5**	1.1 eq. TTN, 24h	 **6 (93%)**
4	 **7**	2.7 eq. TTN, 72h	 **8 (20%)**
5	 **9**	2.1 eq. TTN, 66h	 **10 (50%)**
6	 **11**	1.6 eq. TTN, 55h	complex mixture

Results and Discussion

When treated with TTN, *trans*-10-methyl-2-decalone (**1**) (entry 1) was converted into a single ring-contracted acid (**2**) in 93% yield. In the same fashion, the 2-decalones **3** and **5** (entries 2 and 3) were converted by TTN into the carboxylic acids **4** and **6**, respectively, with high diastereoselectivity and in excellent yields. The configurations of the carboxylic acids were determined by ^{1}H and ^{13}C NMR (proton-decoupled spectra and DEPT) and by comparison with the literature.[5]

The observed diastereoselectivities of the reactions are in accord with the mechanism proposed by McKillop et al.,[4f] as exemplified for substrate **1** in Scheme 1. It is noteworthy that only the thallinium ion resulting from an attack at the more hindered β-face of the molecule can generate the oxythallated adduct **1a**, as a consequence of a trans-diaxial ring-opening.

Not surprisingly, the α-methyldecalone (**7**) (entry 4) gave the acid **8** in poor yield (20%), after 72 h of reaction with 2.7 equiv of TTN. An analogous result was already observed in the contraction of 2-methylcyclohexanone (**12**),[3] which reacts through its kinetic enol form, giving the *cis*-2-methylcyclopentanecarboxylic acid (**13**) also in low yield. The failure of both substrates **7** and **12** to give good yields in the rearrangement can be probably due to steric effects, which increase the strain in the products (carboxyl and methyl groups in a cis-1,2 relationship).



12 **13** **36%**

a) 2.7 TTN.3H$_2$O; CH_2Cl_2; 72 h; r.t.

(1) For some recent examples of *trans*-hydrindanes, see: (a) Uenishi, J.; Kawahama, R.; Yonemitsu, O. *J. Org. Chem.* **1997**, *62*, 1691. (b) Ishii, S.; Helquist, P. *Synlett* **1997**, 508. (c) Saha, A.; Bhattacharjya, A. *J. Chem. Soc., Chem. Commun.* **1997**, 495. (d) Batey, R. A.; Lin, D.; Wong, A.; Hayhoe, C. L. S. *Tetrahedron Lett.* **1997**, *38*, 3699.

(2) For some recent examples of *cis*-hydrindanes, see: (a) Lee, Y.-K.; Singleton, D. A. *J. Org. Chem.* **1997**, *62*, 2255. (b) Sha, C.-K.; Chiu, R.-T.; Yang, C.-F.; Yao, N.-T.; Tseng, W.-H.; Liao, F.-L.; Wang, S.-L. *J. Am. Chem. Soc.* **1997**, *119*, 4130. (c) Vonwiller, S. C.; Warner, J. A.; Mann, S. T.; Haynes, R. K. *Tetrahedron Lett.* **1997**, *38*, 2363. (d) Huart, C.; Ghosez, L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 634. (e) Rönn, M.; Andersson, P. G.; Bäckvall, J.-E. *Tetrahedron Lett.* **1997**, *38*, 3603. (f) Mehta, G.; Reddy, D. S. *Synlett* **1997**, 612.

(3) Ferraz, H. M. C.; Silva, L. F., Jr. *Tetrahedron Lett.* **1997**, *38*, 1899.

(4) For thallium(III) salt mediated ring contraction of ketones, see: (a) Grisar, J. M.; Bolkenius, F. N.; Petty, M. A.; Verne, J. *J. Med. Chem.* **1995**, *38*, 453. (b) Singh, O. V.; Khanna, M. S.; Garg, C. P.; Kapoor, R. P. *Synth. Commun.* **1993**, *23*, 585. (c) Mincione, E.; Bovicelli, P.; Gil, J. B.; Forcellese, M. L. *Gazz. Chim. Ital.* **1985**, *115*, 37. (d) Irwin, A. J.; Jones, J. B. *J. Org. Chem.* **1977**, *42*, 2176. (e) Taylor, E. C.; Chiang, C. S.; McKillop, A.; White, J. F. *J. Am. Chem. Soc.*, **1976**, *98*, 6750. (f) McKillop, A.; Hunt, J. D.; Taylor, E. C. *J. Org. Chem.* **1972**, *37*, 3381. (g) Wiberg, K. B.; Koch, W. *Tetrahedron Lett.* **1966**, 1779. (h) References cited in 3 and 4a−g.

(5) Middleton, S.; Stock, L. E. *Aust. J. Chem.* **1980**, *33*, 2467.

(6) Smissman, E. E.; Lemke, T. L.; Kristiansen, O. *J. Am. Chem. Soc.* **1966**, *88*, 334.

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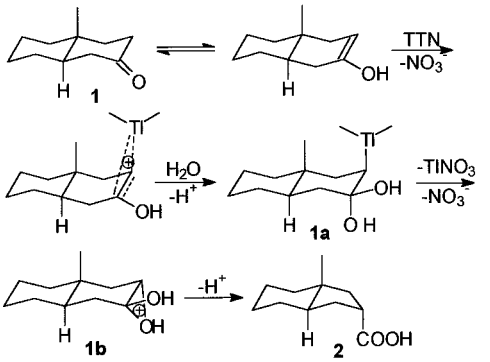
Scheme 1

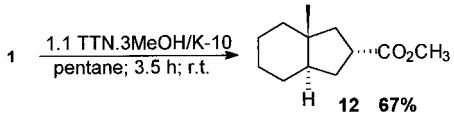


Despite the low yield, the ring contraction of **7** provides additional information about the stereochemical course of the reaction: it suggests that the contraction proceeds with retention of configuration at the migrating center, similar to other Wagner−Meerwein rearrangements[7] and also in accord with the mechanism proposed by McKillop et al.[4f]

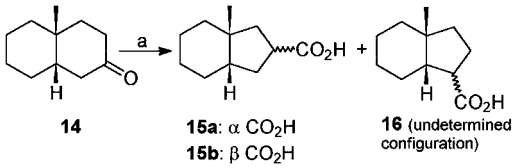
On the other hand, the decalone **9** (entry 5) did not undergo ring contraction, the main product being the α-hydroxy derivative **10**, together with 19% of the starting material, even after 66 h of reaction. This result might be expected, as anticipated by Wiberg,[4g] since enolization will occur toward the methyl group and loss of Tl(I) from the oxythallated adduct will give a better stabilized tertiary carbocation, decreasing the driving force for rearrangement. An analogous result was observed in the reaction of 2,6-dimethylcyclohexanone with TTN.[3]

In striking contrast to the results obtained with substrates **1**, **3**, and **5**, the reaction of decalone **11** (entry 6) with TTN gave a complex mixture of products. This somewhat surprising result is presumably a consequence of the axial position of the 4-methyl substituent, which may hinder the rearrangement.

Two other reaction conditions for promoting the ring contraction were also examined using decalone **1** as substrate. The first of these was Wiberg's condition,[4g] which gave the acid **2** in 84% yield. Using TTN adsorbed on K-10 and pentane as solvent, following a McKillop and Taylor procedure,[4e] the methyl ester **12**[8] was obtained in 67% yield.



Two important characteristics make the thallium(III)-mediated ring contractions of *trans*-2-decalones **1**, **3**, and **5** proceed with a high degree of regio- and diastereoselectivity: the rigidity of the trans-fused system and the formation of a regiodefined $\Delta^{2,3}$ enol.[9] If these characteristics are not present in the molecule, the reaction occurs without selectivity. Actually, when the *cis*-10-methyl-2-decalone (**14**) was treated with TTN/CH_2Cl_2, three isomeric acids **15a**, **15b**, and **16** were obtained in a 4:2:3 ratio, respectively. The proportion was determined by gas cromatography and ^{13}C NMR (inverse gated decoupling). The configurations of acids **15a** and **15b** were tentatively assigned as α and *β*, respectively, by NMR (DEPT, HETCOR), using the chemical shifts values of C2, in analogy with other cyclopentanecarboxylic acids.[3]



a) 2.2 TTN.3H_2O; CH_2Cl_2; 24 h; r.t.

In conclusion, we believe the facile ring contraction here described should be useful for constructing the trans-fused hydrindane system in a single step, from a 1,3,4-unsubstituted *trans*-2-decalone system.

Experimental Section

General. The decalones **1**, **3**, and **5** were prepared by reduction of the corresponding α,*β*-unsaturated ketones[10,11,12] with lithium in liquid ammonia.[13] The decalone **7** was prepared by reduction of the corresponding α,*β*-unsaturated ketone[10] with lithium in liquid ammonia, followed by trapping the enolate with methyl iodide.[14] The decalone **9** was prepared by alkylation of **1**, using LDA as base. The decalone **11** was prepared by reduction of the corresponding α,*β*-unsaturated ketone with lithium in liquid ammonia.[13] This α,*β*-unsaturated ketone was prepared using the procedure described by Scanio and Starrett,[15] followed by HPLC purification, for separating the other diastereoisomer. The decalone **14** was prepared by hydrogenation[16] of the corresponding α,*β*-unsaturated ketone.[10] The TTN·3H_2O and K-10 (acidic montmorillonite clay) were used as received from Aldrich. The TTN·3MeOH/K-10 was prepared by following the procedure described by Taylor et al.[4f]

Warning. Thallium and its derivatives are toxic and must be handled with care.[17]

Preparation of (2α,3a*β*,7aα)-3a-Methyloctahydro-1*H*-indene-2-carboxylic Acid (2) (Method A: Reaction in CH_2Cl_2).[18] To a solution of the decalone **1** (0.332 g, 1.98 mmol) in CH_2Cl_2 (10 mL) was added TTN·3H_2O (0.98 g, 2.2 mmol). The mixture was stirred at room temperature for 24 h and then filtered through Celite. The filtrate was washed with brine and dried over magnesium sulfate, and the solvent was evaporated to give 0.335 g (1.8 mmol, 93%) of **2** as an oil. The NMR and IR spectral data of **2** were identical with those reported in the literature.[5]

Preparation of (2α,3a*β*,7aα)-3a-Methyloctahydro-1*H*-indene-2-carboxylic Acid (2) (Method B: Reaction in 35% $HClO_4$). A solution of TTN·3H_2O (0.40 g, 0.90 mmol) in 35% $HClO_4$ was added to the decalone **1** (0.128 g, 0.77 mmol). The

(7) (a) Borodkin, G. I.; Panova, E. B.; Shakirov, M. M.; Shubin, V. G. *J. Org. Chem. USSR* **1983**, *19*, 103 and references therein. (b) Shono, T.; Fujita, K.; Kumai, S. *Tetrahedron Lett.* **1973**, 3123.

(8) The H_2O of hydration of TTN were changed by MeOH during the preparation of TTN/K-10.[4e]

(9) Mundy, B. F. *J. Chem. Educ.* **1972**, *49*, 91.

(10) Heathcook, C. H.; Ellis J. E.; McMurry, J. E.; Coppolino, A. *Tetrahedron Lett.* **1971**, 4995.

(11) Still, W. C.; VanMiddlesworth, F. L. *J. Org. Chem.* **1977**, *42*, 1258.

(12) Zoretic, P. A.; Golen, J. A.; Saltzman, M. D. *J. Org. Chem.* **1981**, *46*, 3554.

(13) (a) House, H. O.; Giese, R. W.; Kronberger, K.; Kaplan, J. P.; Simeone J. F. *J. Am. Chem. Soc.* **1970**, *92*, 2800. (b) Caine, D.; Smith, T. L., Jr. *J. Org. Chem.* **1978**, *43*, 755.

(14) Stork, G.; Rosen, P.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275.

(15) Scanio, C. J. V.; Starrett, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 1539.

(16) (a) Rao, H. S. P.; Reddy, K. S. *Tetrahedron Lett.* **1994**, *35*, 171. (b) See also ref 13b.

(17) Markó, I. E.; Leung, C. W. *J. Am. Chem. Soc.* **1994**, *116*, 371.

(18) The conditions were different from those described in the previous paper.[3] A shorter time (24 h instead of 48 h) and a smaller amount of TTN (1.1 equiv instead of 1.5 equiv) were required to perform the reaction.

mixture was stirred at room temperature for 3.5 h and then extracted three times with hexane. The organic layer was washed with brine and dried over magnesium sulfate, and the solvent was evaporated, giving 0.118 g (0.65 mmol, 84%) of **2**.

Preparation of (2α,3a*β*,7α,7aα)-3a,7-Dimethyloctahydro-1*H*-indene-2-carboxylic Acid (4). The acid **4** was synthesized from **3** (0.100 g, 0.56 mmol) and TTN·$3H_2O$ (0.27 g, 0.61 mmol) using the procedure described above for **2** (method A). Yield: 90% (0.099 g, 0.50 mmol).

Preparation of (2α,3a*β*,4*β*,7aα)-3a,4-Dimethyloctahydro-1*H*-indene-2-carboxylic Acid (6). The acid **6** was synthesized from **5** (0.330 g, 1.83 mmol) and TTN·$3H_2O$ (0.90 g, 2.03 mmol) by following the procedure described above for **2** (method A). Yield: 93% (0.336 g, 1.71 mmol).

Preparation of (1α,2α,3a*β*,7aα)-1,3a-Dimethyloctahydro-1*H*-indene-2-carboxylic Acid (8). The preparation of **8** was performed following the procedure described above for **2** (method A), using decalone **7** (0.096 g, 0.53 mmol) and TTN·$3H_2O$ (0.64 g, 1.4 mmol) and stirring for 72 h. The crude product (0.089 g) was further purified by column chromatography (ethyl acetate−hexane, gradient elution 0−30%, silica gel 230−400 mesh), and the acid **8** was obtained in 20% (0.021 g, 0.11 mmol).

Reaction of Decalone 9 with TTN. The decalone **9** (0.071 g, 0.39 mmol) and TTN·$3H_2O$ (0.36 g, 0.82 mmol) were stirred for 66 h (method A). The analysis by ^{1}H and ^{13}C NMR and gas chromatography of the crude product showed that the α-hydroxy ketone **10** was formed in 50%, together with 19% of the starting material.

Reaction of Decalone 11 with TTN. The decalone **11** (0.052 g, 0.29 mmol) and TTN·$3H_2O$ (0.21 g, 0.46 mmol) were stirred for 55 h (method A). Gas chromatographic analysis indicated at least 15 products (from 2% to 16%) with very similar retention times, besides 18% of starting material.

Preparation of Methyl (2α,3a*β*,7aα)-3a-Methyloctahydro-1*H*-indene-2-carboxylate (12) (Method C: Reaction with TTN/K-10 in Pentane). To a solution of the decalone **1** (0.111 g, 0.67 mmol) in pentane (10 mL) was added 1.09 g of TTN·3MeOH/K-10. The mixture was stirred at room temperature for 3.5 h and then filtered. The filtrate was evaporated giving 0.089 g (0.45 mmol, 67%) of ester **12**: oil; IR n (C=O) 1735 cm^{-1}; ^{1}H NMR (*δ*) 0.74 (s, 3H), 1.04−1.87 (m, 13H), 2.86−2.91 (m, 1H), 3.67 (s, 3H); ^{13}C NMR (*δ*) 16.6, 21.5, 25.4, 26.4, 32.2, 38.7, 39.2, 41.7, 45.2, 47.4, 51.5, 178.1.

Reaction of decalone 14 with TTN. The decalone **14** (0.048 g, 0.29 mmol) and TTN·$3H_2O$ (0.28 g, 0.64 mmol) were stirred for 24 h (method A). The analysis by ^{1}H and ^{13}C NMR and gas chromatography of the crude product showed the formation of the acids **15a**, **15b**, and **16** in a 4:2:3 ratio, respectively. Global yield: 82% (0.043 g, 0.24 mmol).

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Supporting Information Available: NMR spectra for **2**, **4**, **6**, **8**, **10**, **12**, **15a**, **15b**, and **16** and characterization data for **4**, **6**, **8**, **10**, **15a**, **15b**, and **16** (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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