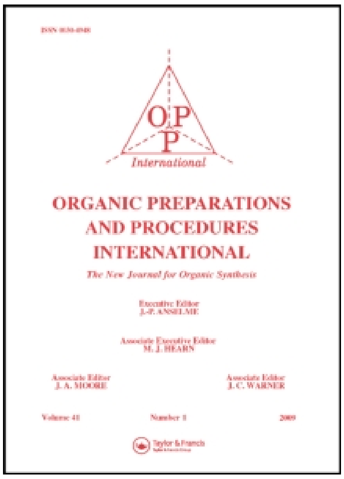


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

THE (±)-*p*-MENTHANE-2,5-DIONES AND THE (±)-2-t-BUTYL-5-METHYL-1,4-CYCLOHEXANEDIONES

Robert D. Stolow[a]; Robert R. Krikorian[a]
[a] Department of Chemistry, Tufts University, Medford, Massachusetts

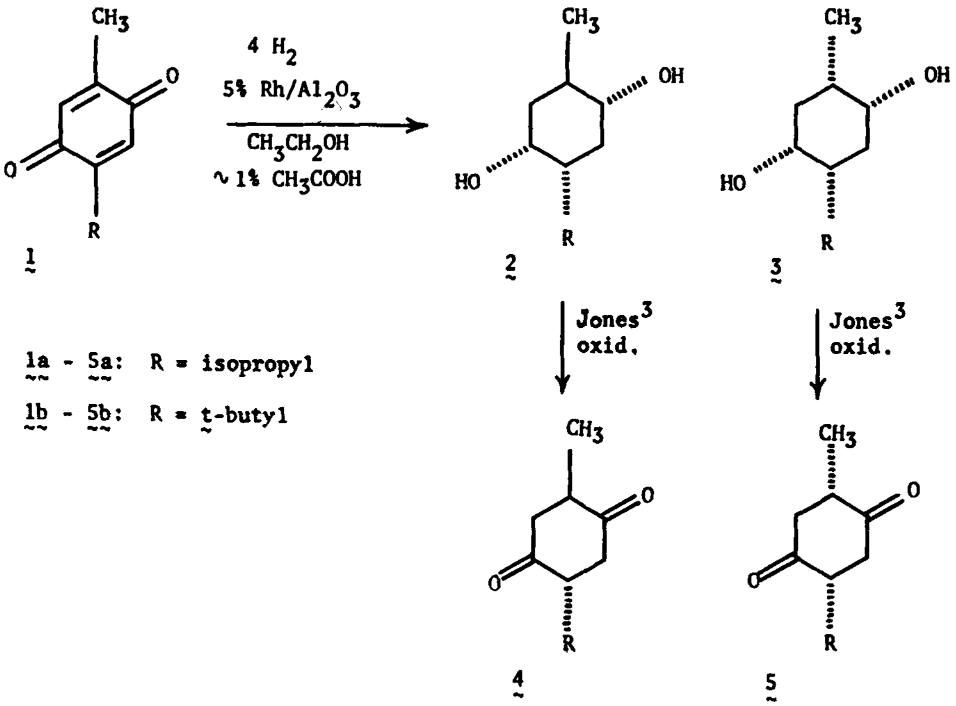
To cite this Article Stolow, Robert D. and Krikorian, Robert R.(1971) 'THE (±)-*p*-MENTHANE-2,5-DIONES AND THE (±)-2-t-BUTYL-5-METHYL-1,4-CYCLOHEXANEDIONES', Organic Preparations and Procedures International, 3: 1, 39 — 44
To link to this Article: DOI: 10.1080/00304947109356030
URL: http://dx.doi.org/10.1080/00304947109356030

ORGANIC PREPARATIONS AND PROCEDURES INT. 3(1), 39-44 (1971)

THE (±)-*p*-MENTHANE-2,5-DIONES AND THE (±)-2-*t*-BUTYL-5-METHYL-1,4-CYCLOHEXANEDIONES.[1]

Robert D. Stolow and Robert R. Krikorian

Department of Chemistry, Tufts University
Medford, Massachusetts 02155



1a - **5a**: R = isopropyl

1b - **5b**: R = *t*-butyl

(±)-*trans*-*p*-Menthane-2,5-dione (**4a**), mp 43 - 43.5°, containing less than 0.5% of its (±)-*cis*-isomer (**5a**),[2] has been prepared by Jones oxidation[3] of the (±)-*p*-menthane-2,5-diol (**2a**), mp 143.5 - 144°, which has the configuration pictured above with its alkyl groups *trans* to one another.[4] (±)-Diol **2a** was isolated along with the known[2] (±)-*cis,cis,cis*-*p*-menthane-

2,5-diol (3a) from among the products of hydrogenation of thymoquinone (1a) catalyzed by rhodium on alumina. This route to 3a is preferable to that described previously.[2]

Similarly, (±)-*trans*-2-*t*-butyl-5-methyl-1,4-cyclohexanedione (4b), mp 49.5 - 50°, was prepared from the (±)-2-*t*-butyl-5-methyl-1,4-cyclohexanediol (2b), mp 156 - 156.5°.[5] (±)-Diol 2b was isolated along with its known[2] (±)-*cis,cis,cis*-isomer (3b) from among the products of hydrogenation of 2-*t*-butyl-5-methylbenzoquinone (1b).

Equilibrium mixtures of epimeric diones 4a plus 5a or 4b plus 5b are easily prepared.[2] The (±)-*cis*-dione (5a or 5b) is less soluble and higher melting than the (±)-*trans*-dione (4a or 4b). Although the (±)-*cis*-dione (5a or 5b) can be separated from the equilibrium mixture by fractional recrystallization, previous attempts to isolate the (±)-*trans*-dione (4a or 4b) from the same mixture have not been successful.[2]

Jones oxidation[3] can be carried out with negligible epimerization at the positions α to the carbonyl group. With care, (±)-diol 2a or 2b gives the corresponding (±)-*trans*-dione (4a or 4b) in high yield, and after recrystallization, essentially free of the epimeric (±)-*cis*-dione (5a or 5b). Similarly, the (±)-*cis,cis,cis*-diol (3a or 3b) gives the corresponding (±)-*cis*-dione (5a or 5b).

EXPERIMENTAL

Isolation of the (±)-*p*-Menthane-2,5-diol (2a), mp 143.5 - 144°, and (±)-*cis,cis,cis*-*p*-Menthane-2,5-diol (3a), from Hydrogenation of Thymoquinone (1a). — To a solution of 10.0 g (0.061 mole) of thymoquinone (1a)[6] dissolved in 150 ml of absolute ethanol containing 1 ml of glacial acetic acid in a 500 ml Parr hydrogenation bottle was added 5.0 g of 5% rhodium on alumina catalyst. The mixture, under 3 atm hydrogen pressure, was shaken for 24 hr, by which time the required pressure drop for reaction of 0.24 mole of hydrogen had occurred. The catalyst was removed by filtration and 3 x 25 ml of ethanol was used to wash the bottle and catalyst. The resulting ethanol filtrate was evaporated under reduced pressure. The residual oil, 9.95 g, was dissolved in 20 ml of 1:1 hexane-benzene. The crystals which formed in the solution after one week at 3° were collected and recrystallized twice from benzene to give 1.75 g of (±)-*cis,cis,cis*-diol (**3a**), mp 102.5 - 103.5°, identified by comparison of its infrared spectrum and gas chromatographic retention time with an authentic sample,[2] mp 105 - 105.5°.

The above hexane-benzene filtrate was concentrated and the residual oil, dissolved in 10 ml of 1:1 benzene-anhydrous ether, was chromatographed on a 30 mm O.D. column packed with 250 g of alumina (Fisher A-540). Elution with 1:1 benzene-anhydrous ether, then anhydrous ether, and finally 9:1 anhydrous ether-methanol, gave an additional 1.03 g of the (±)-*cis,cis,cis*-diol (**3a**), mp 102 - 103° (eluted with ether) followed by 0.68 g of **2a** (eluted with 9:1 ether-methanol). Three recrystallizations from benzene gave (±)-*p*-menthane-2,5-diol (**2a**), mp 142.5 - 143°. Gas chromatography showed no detectable amount of **3a** in the sample of **2a**. A final recrystallization gave **2a**, mp 143.5 - 144°.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70.

Found: C, 69.83; H, 11.58.

(±)-*trans*-*p*-Menthane-2,5-dione (**4a**). — To a solution of 0.81 g (4.7 mmoles) of (±)-*p*-menthane-2,5-diol (**2a**), mp 142.5 - 143°, in 75 ml of acetone (distilled from $KMnO_4$) at 0°, was added dropwise with vigorous stirring 5.61 ml (100% excess) of 2.48 *M* chromium oxide solution[3] during 13 min. The temperature was maintained at 0 - 5° during the addition and for 12 min of further stirring following the addition. Then 1.02 g of $NaHSO_3$ in 10 ml of water at 0° was added. The resulting green solution was immediately extracted with 3 x 50 ml of ether. The combined ether extracts were washed[7] with 2 x 25 ml of 10% ammonium chloride solution, followed by 2 x 25 ml of 10% sodium bicarbonate solution, and finally 2 x 25 ml of water. The ether solution was dried over anhydrous sodium sulfate (1 hr) and the ether was removed under reduced pressure to give 0.68 g (86%) of **4a**, mp 40-42°. Three recrystallizations from hexane gave (±)-*trans*-*p*-menthane-2,5-dione (**4a**), mp 43 - 43.5°, containing only a trace (<0.5%) of the *cis* epimer (**5a**) detected by gas chromatography.[2]

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58.

Found: C, 71.02; H, 9.34.

(±)-*cis*-*p*-Menthane-2,5-dione (**5a**). — By use of the procedure above, 0.99 g of (±)-diol **3a** gave 0.84 g (86%) of (±)-*cis*-dione (**5a**), mp 65.5 - 67°. Two recrystallizations from hexane gave 0.54 g of **5a**, mp 68.5 - 69.5°, containing less than 0.5% of the *trans*-epimer (**4a**) according to gas chromatographic analysis; reported[2] for (±)-*cis*-*p*-menthane-2,5-dione (**5a**), mp 72 - 73°.

Hydrogenation of 2-*t*-Butyl-5-methyl-*p*-benzoquinone (**1b**). Isolation of the (±)-2-*t*-Butyl-5-methyl-1,4-cyclohexanediol (**2b**), mp 156 - 156.5°, and (±)-*cis,cis,cis*-2-*t*-Butyl-5-methyl-1,4-cyclohexanediol (**3b**). — To a solution of 12.33 g (0.069 mole) of 2-*t*-butyl-5-methyl-*p*-benzoquinone (**1b**)[2] in 150 ml of absolute ethanol containing 1 ml of glacial acetic acid was added 4.03 g of 5% rhodium on alumina catalyst. Hydrogenation as above for **1a**, but for 71 hr, gave 12 g of residual oil. The oil, dissolved in 20 ml of benzene, gave after 24 hr at 3°, 0.48 g of solid. Three recrystallizations from benzene gave (±)-diol **2b**, mp 156 - 156.5°.[5]

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.91.

Found: C, 71.10; H, 11.88.

The recovered oil in 10 ml of benzene was placed on a 45 mm. O.D. column containing 700 g of alumina (Fisher A-540). Elution with benzene, benzene-ether mixtures, ether, and finally 9:1 ether-methanol gave from 1:1 benzene-ether and from ether, 3 g of the known (±)-*cis,cis,cis*-diol (**3b**), mp 99 - 100°, after crystallization once from hexane; reported[2] mp 99 - 100°. The ether-methanol fractions, after two recrystallizations from benzene, gave an additional 0.5 g of **2b**, mp 155.5 - 156°.

(±)-*trans*-2-*t*-Butyl-5-methyl-1,4-cyclohexanedione (**4b**). — As above for preparation of **4a**, Jones oxidation of (±)-diol **2b** (0.90 g) gave **4b** (0.81 g, 92%), mp 47 - 48.5°. Three recrystallizations from pentane gave (±)-*trans*-2-*t*-butyl-5-methyl-1,4-cyclohexanedione (**4b**), mp 49.5 - 50°.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95.

Found: C, 72.31; H, 9.78.

(±)-*cis*-2-t-Butyl-5-methyl-1,4-cyclohexanedione (**5b**). — As above, Jones oxidation of 1.00 g of (±)-*cis,cis,cis*-diol (**3b**) gave **5b** (0.94 g, 96%), mp 64 - 67.5°. Two recrystallizations from hexane gave (±)-*cis*-2-*t*-butyl-5-methyl-1,4-cyclohexanedione (**5b**), mp 67.5 - 68°, reported.[2] mp 69 - 70°.

REFERENCES

1. This work was supported in part by Public Health Service Research Grant GM-08813 from the National Institutes of Health, in part by the National Science Foundation, and in part by the Research Corporation.

2. R. D. Stolow, P. M. McDonagh, and M. M. Bonaventura, J. Am. Chem. Soc., *86*, 2165 (1964).

3. J. Meinwald, J. Crandall, and W. E. Hymans, Org. Syn., *45*, 77 (1965); R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, J. Chem. Soc., 457 (1953).

4. The configuration of (±)-diol **2a** (pictured above) has been established unequivocally by Krishna Sachdev, Doctoral Dissertation, Tufts University, 1966. (±)-Diol **2a** is the racemate of the (-)-*p*-menthane-2,5-diol, mp 157°, described by R. D. Stolow, J. Am. Chem. Soc., *86*, 2170 (1964).

5. The configuration of (±)-diol **2b** (pictured above) has been established as (±)-2α-*t*-butyl-2β-methyl-1α,4α-cyclohexanediol by James L. Marini, Doctoral Dissertation, Tufts University, 1969.

6. E. Kremers, N. Wakeman, and R. M. Hixon, Org. Syn. Coll. Vol. I, 511 (1941).

7. To reduce the amount of epimerization during the work-up of the Jones oxidation product mixture, the extractions and washings should be done rapidly. The wash solutions should be prepared in advance and kept cold (0 - 5°).

(Received July 28, 1970)