

C₃ News



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Newsletter of College Chemistry Canada/La Chimie Collégiale au Canada



NOTES FROM THE EDITOR

I must begin this issue of C₃ news by apologizing to all C₃ members for the lack of issues published in

the past year. Had I known my workload and personal matters would be taking so much time during this second year as editor, I doubt I would have volunteered to take the job on. I will not be seeking another term as editor and I encourage you to give all the support you can to the new editor who will be voted in at the AGM in Calgary at this year's C₃ conference. I still believe this newsletter can be a great forum for chemical education and I urge you to get involved. I would like to thank Lamine Diop for her excellent contribution of an article to this issue: an undergraduate experiment dealing with the resolution of enantiomers. Also included in this issue are two ideas for articles I am suggesting others can contribute to C₃ News: (a) Chemistry People Profiles and (b) Chemistry Department Activities. I start things off with some news from UCC. Good health and good chemistry to all. Ed.

2004 C₃ CONFERENCE AT OKANAGAN UNIVERSITY COLLEGE

The 2004 C₃ conference is being planned for mid June next year at OUC in Kelowna BC. Pat Baird (pbair@ouc.bc.ca) is the Conference Coordinator and Stephen McNeil (smcneil@ouc.bc.ca) will be the Program Coordinator. Hope to see all there!. Ed.

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CHEMISTRY PEOPLE PROFILES: DR. JIM DAVIES - UNIVERSITY COLLEGE OF THE CARIBOO

After a long, varied and successful career Dr. Jim Davies is retiring from his position teaching physical chemistry at UCC in Kamloops BC. Jim is well known locally for his activities in the annual UCC Wonder of Chemistry show and his trademark demonstration, a model of a dust explosion can be found on page 4. Jim spent the last 13 years of his career at UCC teaching in the UCC chemistry degree programs at all levels from first year through to advanced physical chemistry at the third and fourth year levels. Jim started out with a Ph.D. in thermochemistry at Manchester. He noted to me that grad students were allowed to try sitting in John Dalton's chair, something that is not possible now that the chair is in a museum, rather than in a chemistry lecture hall. Part of his Ph.D. work was also done at the University of Lund in Sweden. Jim then moved on to a post doc in thermochemistry at the University of Colorado and from there to the University of Western Ontario where he studied the reaction kinetics of ammonium perchlorate. Jim likes to study fast reactions, as evidenced by the pictures from his retirement party, also on page 4. From Western Jim moved back to the UK where he taught P Chem at the University of Kingston in London for three years. Next, Jim moved back to Canada and was a project scientist at York University in Toronto. Jim notes that besides his research in thermochemistry at York, he also taught a course in the science of flight. In fact for many years flying was Jim's recreational passion, having obtained both a glider licence and a commercial single engine aircraft licence. Following his time at York Jim moved to Montreal where he taught first and second year chemistry at Vanier College for seventeen years. In 1989 Jim joined the faculty at UCC where, in collaboration with Yoshi Koga of UBC, Jim has been researching the thermochemistry of aqueous solutions. Jim has been publishing data on the thermal expansivity and partial molar (**cont'd on page 4**)

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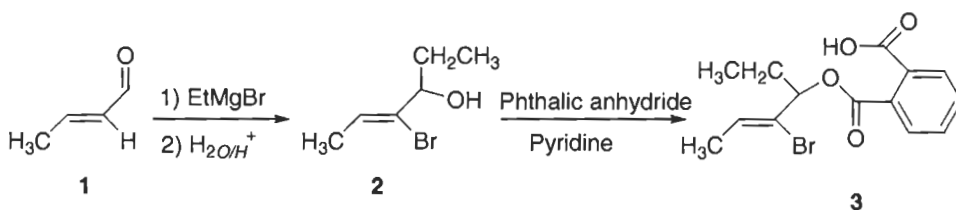
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The Resolution of (E)-4-Bromo-4-hexen-3-ol via Diastereomeric Separation by Fractional Crystallization

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The achievement of optically pure compounds by resolution of racemic mixtures remains a big challenge in organic chemistry, particularly in the pharmaceutical industry, because of the differing biological activities of the enantiomers. There are well-documented cases in which one enantiomer can have therapeutic properties while the other one has toxic effects (1,2). The procedure of the resolution is based on the reaction of an enantiomerically pure compound with a racemic mixture. This transforms the racemate into a mixture of diastereomers. Because of the different physical properties of the diastereomers the second mixture is separable by conventional means (e. g. crystallization, distillation and chromatography). This paper reports the resolution of the racemic mixture of (E)-4-bromo-4-hexen-3-ol **2** by diastereomeric separation using fractional crystallization. This classical method was chosen, after attempting, in vain, to use the elegant kinetic resolution method of Sharpless (3).

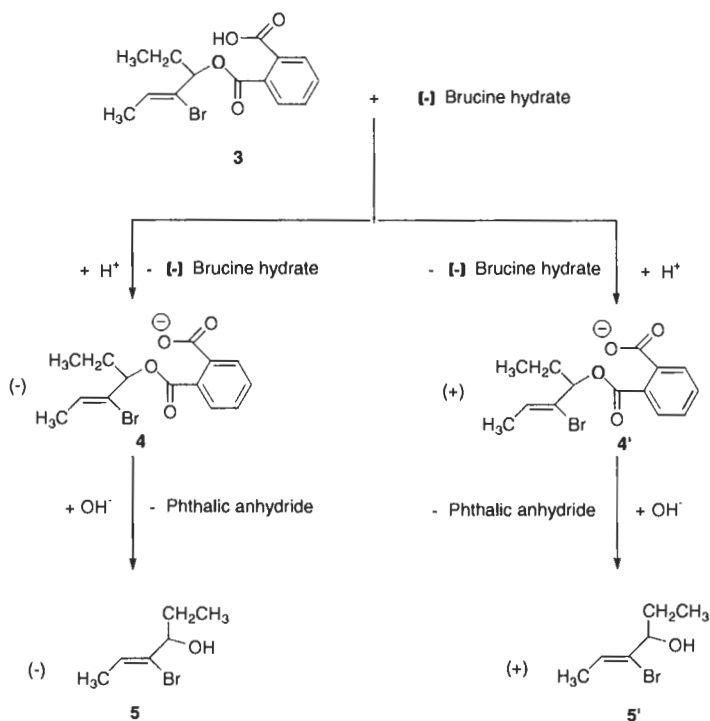
The (E)-2-bromo-2-butenal **1** is readily available via a regioselective trans-addition of bromine to trans-crotonaldehyde followed by a stereoselective trans-addition as described by Chow (4). The aldehyde **1** was added drop wise, at 15 °C, to the Grignard reagent prepared from ethyl bromide to give, after the addition of aqueous ammonium chloride, the alcohol **2** in 86% yield. Compound **2** added to an equal amount of phthalic anhydride and pyridine, in diethyl ether, was refluxed for 5 h, in order to increase the acidity of the hydroxyl group. After quenching at 0 °C, with 2N hydrochloric acid, the recrystallisation of the obtained residue, from petroleum ether, gave 62% of (E)-4-bromo-4-hexen-3-hydrogenphthalate **3** as colourless crystals (Scheme I).



(-)-Brucine dihydrate was dissolved in a solution of **3** in hot acetone and the resulting diastereomeric mixture was separated by fractional crystallization from acetone. The separated diastereomers were acidified with 4 N hydrochloric acid and then hydrolysed with 12.5 N sodium hydroxyde to liberate [(-)-(E)-4-bromo-4-hexen-3-ol **5** and [(+)-(E)-4-bromo-4-hexen-3-ol **5'** with an enantiomeric excess, respectively, of 95% and 63% (Scheme II). The enantiomeric excess were determined by 1H NMR analysis in the presence of [Eu(tcf)₃].

Experimental Procedure

Melting points were taken on a IA 6304 Electrothermal apparatus and are not corrected. Infrared spectra were determined on a Shimadzu IR-400 spectrophotometer. Nuclear magnetic resonance spectra were determined on Varian EM-360 spectrometer. Chemical Shifts are given in δ relative to internal Me₄Si with the following abbreviations for multiplicity: s = singlet, d = doublet, t = triplet, q = quartet. Mass spectra were taken on Varian MAT 8222 spectrometer. Solvents used were of p. a. quality, or they were purchased from Merck and Jansen and used as received.



Scheme II. Resolution

Preparation of [(±)-(E)]-4-bromo-4-hexen-3-ol 2

To a stirred solution of Grignard reagent, prepared from magnesium (1.85 g, 75 mmol) and ethyl bromide (8.17 g, 75 mmol), was added slowly a solution of (E)-2-bromo-2-butenal **1** (10.45 g, 65 mmol) in an equal volume of anhydrous diethyl ether at 15 °C. The mixture was then allowed to warm up to room temperature and was poured into a solution of ice-cooled 10% aqueous hydrochloric acid and extracted with diethyl ether. The organic layer was separated, washed with water, dried over anhydrous magnesium sulphate, and filtered. The diethyl ether was removed by rotary evaporation under reduced pressure and fractional distillation of the residue yielded 10.05 g (86%) of a colourless oil.

bp: 35 - 37 °C at 9 mbar

IR (liquid film): 3350 cm⁻¹ (-OH); 2950 - 2850 cm⁻¹ (-CH); 1660 cm⁻¹ (-C=C-); 1060 cm⁻¹ (-C-O-).

¹H NMR (CDCl₃, 360 MHz): 6.05 ppm (q, 1H, CH₃-CH=C(Br)-, J = 7 Hz); 3.90 ppm (t, 1H, -CH(CH₂-CH₃)-OH, J = 6 Hz); 3.45 ppm (s, 1H, -CH(CH₂-CH₃)-OH); 1.80 ppm (d, 3H, -CH₂-CH₃, J = 7 Hz); 1.70 ppm (m, 2H, -CH₂-CH₃, J = 7 Hz); 0.85 ppm (t, 3H, CH₃-CH=C(Br), J = 7 Hz).

¹³C NMR (CDCl₃, 360 MHz): 10 ppm (1C, -CH₂-CH₃), 16 ppm (1C, CH₃-CH=C(Br)); 28 ppm (1C, -CH₂-CH₃); 78 ppm (1C, -CH(CH₂-CH₃)-OH); 125 ppm (1C, CH₃-CH=C(Br)); 132 ppm (1C, CH₃-CH=C(Br)).

Preparation of [(±)-(E)]-4-bromo-4-hexenyl hydrogen phthalate **3**.

A mixture of **2** (9.20 g, 51 mmol), pyridine (4.11 mL, 67 mmol), phthalic anhydride (7.80 g, 51 mmol) and 25 mL diethyl ether was refluxed for 5 h. The mixture was

allowed to go to room temperature, then poured into a solution (60 mL) of 2N aqueous hydrochloric acid at 0 °C and extracted with diethyl ether.

The combined diethyl ether phases were dried over anhydrous magnesium sulphate. After the evaporation of the solvent under reduced pressure, the obtained residue crystallized after one week of storage in the refrigerator. Recrystallization from petroleum ether (40 - 65 °C) gave 10.07 g (62% yield) of **3** as colourless crystals.

mp: 98 °C.

IR (KBr): 1730 cm⁻¹ (-O-C=O); 1700 cm⁻¹ (HO-C=O); 1600 - 1580 cm⁻¹ (-C=C-); 1300 - 1060 cm⁻¹ (-C-O-); 740 - 690 cm⁻¹ (C-H of benzene group).

¹H NMR (360 MHz, CDCl₃): 12.75 ppm (s, 1H, -COOH); 7.80 ppm (m, 4H, CH_{aromat}.); 6.25 ppm (q, 1H, CH₃-CH=C(Br)-, J = 6 Hz); 5.45 ppm (t, 1H, -CH(CH₂-CH₃)-, J = 6 Hz); 1.90 ppm (m, 2H, -CH₂-CH₃); 1.80 ppm (d, 3H, CH₃-CH=C(Br), J = 7 Hz), 0.90 ppm (t, 3H, -CH₂-CH₃, J = 7 Hz).

MS (70 eV) m/z (relative intensity %): 247 (30); 167 (24); 149 (100); 122 (23); 104 (41).

Resolution of [(±)-(E)]-4-bromo-4-hexenyl hydrogen phthalate **3**

(-) Brucine dihydrate (19.30 g, 45 mmol) was added to a stirred solution of 10g, 30 mmol) of **3** in hot acetone (50 ml). After dissolution, half of the solvent was evaporated to give a crystalline residue. The residue was recrystallized from acetone until its mp was constant (163 - 165 °C). The crystals were then treated, at 0 °C, with 30 mL of 4N hydrochloric acid, and the free acid recrystallized from petroleum ether (40 - 65 °C). The obtained crystalline mass (2 g, 6.11 mmol) was hydrolysed with 1.17 mL of a solution of 12.5N NaOH and extracted with ethyl ether. The extract was dried over magnesium sulphate, concentrated under reduced pressure and purified by bulb to bulb distillation to yield pure compound **5** (0.74 g, 27%); [α]_D²¹ = -2.13 (c = 2.13, EtOH), 95% ee.

The remaining solvents (acetone) from the fractional crystallization were collected, concentrated under reduced pressure, and worked up as described above to give **5'** (0.85 g, 31%); [α]_D²¹ = +1.22 (c = 1.47, EtOH), 68% ee.

The IR-, NMR spectra and boiling point of **5** and **5'** are the same as those of compound **2**.

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DEPARTMENT ACTIVITIES: ANNUAL UCC CHEMISTRY COMPETITION FOR HIGH SCHOOL STUDENTS ENJOYS INCREASED PARTICIPATION

On Wednesday May 21st 2003 the University College of the Cariboo held its 6th annual Chemistry Contest for Grade 11 and Grade 12 students. The contest consists of a multiple choice exam for the Grade 11's and a 50/50 combination of multiple choice and written answers of the calculate, describe and explain type. Top students are given cash and book prizes. This year saw requests from area high school teachers for 400 grade 11 and 300 grade 12 contest exams. Schools as far away as Vancouver, Prince George and Grand Forks BC participated. A select group of forty Grade 11 students were given the opportunity to write the exam on campus at UCC and then spend the afternoon doing a lab experiment for the experience. The contest is part of UCC's Chemistry Outreach Program, which is in part funded by a grant from NSERC's PromoScience Program of funding. Ed.

CHEMISTRY PEOPLE PROFILES CONT'D,,,,,, (cont'd from page 1)

volumes of dilute aqueous solutions of organic compounds. This work attempts to relate the above physical parameters to intermolecular attractions and arrangements of molecules in solution. Jim has been a great asset to the Physical Sciences department at UCC and he will be greatly missed by all as he takes up a well deserved retirement. Rumor has it that Jim plans to stay active with some part time teaching at UCC when it is available.



Grade 11 students from British Columbia's southern interior enjoy an afternoon in the lab at UCC learning a spectroscopic method for the analytical determination of ASA in over the counter cold medications.

CONT'D FROM PAGE 1



Jim Davies performing his trademark dust explosion demonstration at the annual UCC wonder of chemistry show.



Even at his retirement party Jim could not resist demonstrating his fascination with rapid reactions. Here he demos the "don't do this at home with a hydrogen balloon" experiment!