relativ schwacher PMT-Fleck, ein deut-licher Quatrimycin- und ein starker Tetra-cyclinfleck erhalten. Beim Chromatogra-phieren mit einer grossen Anzahl anderer Lösungsmittelssysteme wurde stets Über-einstimmung zwischen den Zersetzungs-produkten des PMT und Tetracyclin samt Quatrimycin erhalten.

Als ein weiterer Beweis für die Zerset-zung des PMT zu Tetracyclin kann folgen-der Versuch dienen.

Eine Lösung von 0.2 g PMT in 4 ml Wasser und 6 ml 0.1 N HCl (pH = 2.0) wurde 4 Tage bei Zimmertemperatur auf-bewahrt. Während dieser Zeit zeigten wie-derholte papierchromatographische Analy-sen der herausgenommenen Proben, dass in der Lösung die oben erwähnte Umwand-lung geschah. Sodann wurde die Lösung mit NaOH bis pH = 6.2 versetzt und aus-gefällte Substanz durch wiederholtes Zen-trifugieren isoliert — nach Trocknen im Vakuum insgesamt etwa 93 mg. Die er-haltene Substanz wurde durch Bestimmen des IR-Spektrums (KBr-Platte) als Tetra-cyclin identifiziert.

Weitere Versuche, das Einwirken ver-schiedener Lösungsmittel auf PMT zu ver-gleichen, zeigten, dass keine Zersetzungs-produkte wiedergefunden werden konnten, wenn es auf dem Papier in frisch zuberei-teter Lösung in Wasser oder Dioxan abge-setzt wurde, während Lösungen in Alko-holen, wie Methanol, Äthanol und Butanol — selbst bei schnellem Arbeiten — Chro-matogramme gaben, die starke Zersetzung aufwiesen.

Ein Chromatographierungsverfahren von Kelly und Buyske[4] mit Butanol als Hauptkomponent der Entwicklungsflüssig-keit gab demzufolge ein Chromatogramm, das auf eine Umwandlung des grössten Teils des PMT in Tetracyclin hindeutete, auch wenn die Absetzungen mit wässriger Lösung gemacht waren.

Wir haben somit die Erfahrung gemacht, dass die Stabilität der PMT-Lösungen sehr stark von der Natur des Lösungsmittels abhängig ist. Da die Zersetzung ausser-ordentlich schnell einsetzen kann, muss dieser Umstand ebenfalls dann beachtet werden, wenn es sich um eine Behandlung von so kurzer Dauer wie die papierchro-matographische Prüfung handelt. Unse-ren Erfahrungen nach kann Selzer und Wright's Methode für die papierchroma-tographische Identifizierung und Quali-tätsbeurteilung des PMT verwendet wer-den, wenn die Probe als frisch zubereitete wässrige Lösung abgesetzt wird.

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New Synthesis of Bicyclo[3.2.1] octane-2-ol

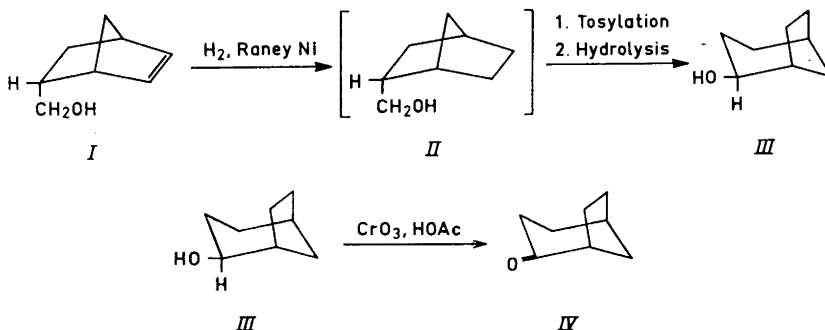POUL NEDENSKOV, HENNING HEIDE and NIELS CLAUSON-KAAS

Centrallaboratoriet, Sadolin & Holmblad A/S, Copenhagen, Denmark

Hydrogenation of commercial bicyclo[2.2.1]hept-5-ene-2-methanol (I) to bicyclo[2.2.1]heptane-2-methanol (II), tosylation of this compound with toluene-sulfonyl chloride in pyridine, and hydrolysis of the resulting tosylester with aqueous acetic acid gives bicyclo[3.2.1]octane-2-ol (III). The synthesis may be carried out without isolating the intermediate com-pounds pure. The overall yield in the three reactions is 91 %, and the purity of the resulting bicyclooctanol (III) 93 %. If the purities of starting material and reaction product are considered, the overall yield of pure bicyclooctanol based upon pure starting material is 88 %, which is the figure to be used when the yield of the reaction is considered from a theoretical point of view.

The identity of the bicyclooctanol was established by oxidation to the correspond-ing ketone (IV) (yield 74 %, yield based upon pure materials 80 %), and by pre-paration of the *p*-nitrobenzoate.

The steric configuration of the hydroxyl group may be inferred from the infrared absorption spectrum to be predominantly *cis* (*cf.* Ref.[1]) to the ethylene bridge.

The synthesis is at present the simplest and cheapest way of preparing the bi-cyclooctanol (III) in a reasonably pure state. The high yield in the new rearrange-ment reaction as well as the purity of the reaction product agrees well with the fact, that the original bicycloheptene-

methanol (I) consists mainly of the *endo* isomer [2] (only this isomer is shown in the drawing of the structural formulas).

Experimental. Bicyclo[2.2.1]heptane-2-methanol (II) (cf. Refs.[3],[4]). Bicyclo[2.2.1] hept-5-ene-2-methanol (I)* (50.0 g, 0.388 mole of pure product) was shaken (6 h) with Raney nickel (5 g) under hydrogen (25 atm.) at 120°. The nickel was removed by filtration and washed with pyridine (30 ml).

Tosylester of II. The above solution of bicycloheptanemethanol (49.0 g of pure product, 0.388 mole) in pyridine (about 25 ml) was added in one portion to a solution of *p*-toluenesulfonyl chloride (85.0 g, 0.446 mole) in pyridine (100 ml) and the mixture stirred (24 h) at 20° (precipitation of pyridine hydrochloride begins after a few min). The reaction mixture is poured on cracked ice (250 g). Ether (200 ml) is added, and the resulting emulsion brought to pH 3.5 by dropwise addition of concentrated hydrochloric acid (about 85 ml) with cooling and vigorous stirring. The etheral layer is separated, washed with water (2 × 60 ml) (final pH of wash water must be 5 or above), dried over magnesium sulfate, and evaporated from a water bath (75°), at last under 10 mm. The tosylester remains as an oil (104 g), which crystallizes partially on standing.

Bicyclo[3.2.1]octane-2-ol (III). The above tosylester (104 g) is heated with acetic acid (120 ml), *p* toluenesulfonic acid (1.0 g) and

water (550 ml) with stirring under reflux (24 h). The heterogeneous reaction mixture is cooled somewhat, 40 % aqueous sodium hydroxide solution (265 g) added, and the mixture heated further under reflux (3 h) to saponify any acetates formed in the rearrangement reaction. The mixture is steam distilled and the crystals formed in the distillate recovered by saturation of the aqueous layer with sodium chloride and extraction three times with ether (400 ml in all). The etheral solution is dried with magnesium sulfate and the ether removed by distillation from a water bath (50°), at last under 15 mm. 46.0 g (91 %) of bicyclooctanol is hereby obtained [m.p. 140—166° (Hershberg app., corr.)]. Considering the purity of the starting material (96 %) and of the reaction product (93 %, see below), the overall yield of pure bicyclooctanol is 88 %.

The product melts at 140—166° (Hershberg app., corr.). Goering *et al.*[1] report 176—177° for *cis*-bicyclooctanol and 194—196° for the *trans* compound. Elementary analyses gave: C 77.1; H 11.1; O 12.0. Calc. for $C_8H_{14}O$ (126.2): C 76.2; H 11.2; O 12.6. The product was chromatographed in the gaseous phase under the conditions recommended by Walborsky *et al.*[5] The product was acetylated in the usual way, and the acetate chromatographed on a 2 m column of 20 % diisooctylphthalate on 60—80 mesh chromosorb at 175° (investigation for bicycloheptanemethanol). Finally the infrared absorption of the product was measured and the spectrum in particular inspected around 965 and around 1040 cm⁻¹, the two regions best suited for an estimation of the *cis-trans* ratio (cf. Refs.[1],[6]).

The product was oxidized with chromium trioxide in acetic acid as described by Youseff *et al.*[7], using, however, 12 % more chromium trioxide and only one third of the amount of acetic acid recommended by these authors. The reaction mixture was extracted with

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* Commercial product from Interchemical Cooperation, U.S.A., n_D^{25} 1.4972, composition minimally 76 % of *endo*, 19 % of *exo* isomer. The product was found by us by acetylation analysis to have an equivalent weight of 129 (calc. 124). If one assumes that the product contains no alcoholic impurities, this figure corresponds to a purity of 96 %.

benzene and the benzene solution found by oxime titration [8] to contain 74 % of the theoretical amount of bicyclo[3.2.1]octane-2-one (IV). The yield is 80 % based upon the content of pure bicyclooctanol in the starting material. From the benzene solution the semicarbazone of bicyclooctanone was prepared in the way recommended for the preparation of camphor semicarbazone [9]. The yield was 73 % of recrystallized, analytically pure material, m.p. 173—174° (previously [1,7] found 171—172°). [Found: C 59.4; H 8.2; N 23.2. Calc. for $C_9H_{15}N_3O$ (181.2): C 59.6; H 8.3; N 23.2].

The product was transformed into the *p*-nitrobenzoate in the usual way. After two crystallizations from pentane the yield of *p*-nitrobenzoate was 60 % and the melting point 78—79°. Further crystallization did not change the melting point (previously [1] found for the *cis* compound 80°).

It was inferred from the above experiments that bicyclooctanol, obtained after the new synthesis as described, contains about 93 % of a 1:20 mixture of *trans*- and *cis*-bicyclo [3.2.1]octane-2-ol, the main impurities (7 % in all) being bicyclic hydrocarbons.

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