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Thermal Rearrangements of 1,5-Dimethyl- and 1,3,5-Trimethyl-8-vinyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ol and Their Alkoxides

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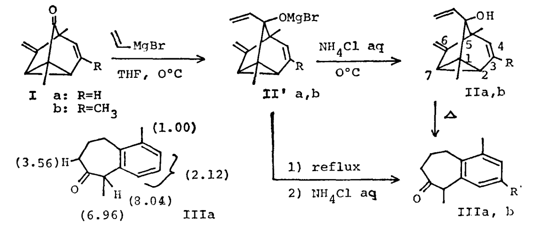
Synopsis. The reactions of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one with vinylmagnesium bromide at 0 °C afforded 1,5-dimethyl- and 1,3,5-trimethyl-8-vinyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ol, respectively. The thermal rearrangements of IIa,b and their alkoxybromomagnesium afforded 1,5-dimethyl or 1,3,5-trimethylbenzocyclohepten-6-one. It is suggested that the pathways involve an oxy-Cope rearrangement and the subsequent hydrogen migrations.



Scheme 1.

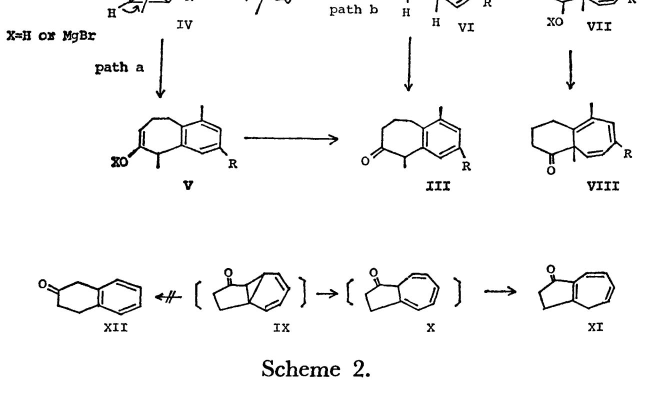
Recently, various anionic oxy-Cope rearrangements and their related sigmatropic rearrangements have been investigated, and the rate enhancements of metal alkoxides have been precisely demonstrated from the synthetic and mechanistic points of view.1—5) In relation to the synthesis and chemistry of polycyclic compounds containing cyclopropane ring,6,7) we ourselves tried to prepare the skeleton of bicyclo[5.4.0]undeca-1,3,5,8,10-pentaene,8) which has a methyl group on a bridgehead. However, benzocyclohepten-6-one derivatives were obtained by the reactions of 1,5-dimethyl- and 1,3,5-trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one (Ia and Ib) with vinylmagnesium bromide and the subsequent thermal rearrangements. Therefore, we will describe here a facile synthesis of benzocyclohepten-6-one derivatives.

The reactions of Ia and Ib with vinylmagnesium bromide in anhydrous tetrahydrofuran (THF) at 0 °C afforded 1,5-dimethyl- and 1,3,5-trimethyl-8-vinyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-ol (IIa and IIb) respectively in fairly good yields. The structures of IIa, b were assigned on the basis of their spectral properties (see Experimental). The stereochemical assignment of IIa was derived from the pseudo-contact NMR spectra obtained using Eu(fod)$_3$. The chemical shifts of the hydrogens at C-3 and C-4 were much shifted downfield compared to those of the exomethylene group and hydrogen at C-7. The attacking site of vinylmagnesium bromide on Ia is similar to the case of Ia,b with lithium aluminum hydride.9,10) Therefore, the orientation of the hydroxyl group of IIb should be the same as in the case of IIa. On the other hand, after Ia or Ib had been reacted with vinylmagnesium bromide at 0 °C, the reaction mixtures were allowed to reflux for 5 h under a nitrogen atmosphere. The benzocyclohepten-6-one derivatives, IIIa and IIIb, were thus obtained in fairly good yields. The structures of IIIa, b were determined on the basis of the spectral properties (see Experimental). The assignment of structures was also supported by the pseudo-contact NMR spectra of IIIa obtained using Eu(fod)$_3$. The relative downfield shifts (ppm/mol) of the δ's of characteristic hydrogens are given in parentheses in the structural formula IIIa in Scheme 1. When IIa or IIb was refluxed in benzene for 5 h, however, no thermal rearrangement into IIIa or IIIb occured, but IIa or IIb was recovered in a quantitative yield. It is known that the metal alkoxides enhance the rates of oxy-Cope rearrangements.1—5) Therefore, IIIa, b probably originate from the anionic oxy-Cope rearrangements of the alkoxybromomagnesium derivatives, II'a and II'b.

In order to confirm this point, the thermal rearrangements of IIa and IIb were carried out at high temperatures. When IIa was heated in refluxing xylene for 30 min, a clean conversion of IIa to IIIa occured. Similarly, IIb was rearranged to IIIb in 1,2-dichlorobenzene during 15 min at the refluxing temperature.

For the facile rearrangements of IIa,b, or II'a,b, two mechanistic interpretations can be considered. In both reaction pathways, the oxy-Cope rearrangement affording IV might be the first step of the present thermal reaction, as is shown in Scheme 2. One of the possible pathways involves, perhaps, a simple stepwise aromatization of IV to III *via* V (Path a). The other possible pathway is the thermally allowed concerted [1,5]-sigmatropic rearrangement (Berson-Willcott rearrangement)11) of IV to VI, which can give III by the cleavage of the cyclopropane ring and a concurrent hydrogen-shift.

It is known that compound IX, which has a skeleton



Scheme 2.

homologous with VI, affords bicyclo[5.3.0]decatrienone, XI, and does not afford XII.[12,13] Therefore, if the intermediate of norcaradiene, VI, is involved in the present thermal rearrangement, it should be possible for VI to equelibrate with cycloheptatriene, VII. However, VIII could not be obtained, hence, VI could not be involved in the present thermal rearrangement. Therefore, the present thermal rearrangement affording IIIa,b must proceed through Path a.

The much strained IV, which has a bridgehead double bond, could not undergo Berson-Willcott rearrangement. Since compounds Ia,b are synthesized very easily by the thermal reactions of 2,6-dimethylphenyl and 2,4,6-trimethylphenyl propargyl ether[14] respectively, the present reactions should be very useful for the preparation of benzocycloheptenone derivatives.

Experimental

Reactions of 1,5-Dimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one (Ia) with Vinylmagnesium Bromide. To a stirred solution of vinylmagnesium bromide, which was prepared by a usual procedure[15] using 0.730 g (30 mg-atom) of magnesium turnings, 3.50 g (32.7 mmol) of vinyl bromide, and 50 ml of anhydrous tetrahydrofuran (THF), was added 1.60 g (10 mmol) of Ia in 10 ml of THF at 0 °C. This reaction mixture was stirred another 3 h at 0 °C and then treated with aqueous ammonium chloride, followed by ether extraction. The evaporation *in vacuo* of the dried (Na_2SO_4) organic portion gave a clean oil of IIa (1.84 g, 98%): bp 66—70 °C/7 mmHg (1 mmHg=133.32 Pa); IR (neat) 3600—3400, 1600 cm^{-1}; NMR (CCl_4) δ 1.00 (s, 3H), 1.10 (s, 3H), 1.55 (s, 1H), 1.68—1.85 (m, 2H), 4.51 (s, 1H), 4.53 (s, 1H), 4.90—5.22 (m, 4H), 6.05 (m, 1H); MS *m/e* 188 (M^+). Found: C, 82.71; H, 8.64%. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57%.

Reaction of Ia with Vinylmagnesium Bromide and Subsequent Thermal Rearrangement. To a stirred solution of vinylmagnesium bromide, which had been prepared using 1.75 g (16.0 mmol) of vinyl bromide, 0.356 g (15.0 mg-atom) of magnesium turnings, and 25 ml of THF, was added 800 mg (5 mmol) of Ia in 5 ml of THF at an ambient temperature. This reaction mixture was allowed to reflux for another 4 h, and then it was treated with aqueous ammonium chloride, followed by ether extraction (30 ml × 3). The evaporation *in vacuo* of the dried (Na_2SO_4) organic portion gave an oil of IIIa (888 mg, 95%): bp 100 °C/4 mmHg; IR (neat) 1710 cm^{-1}; NMR (CCl_4) δ 1.36 (d, J=7.0 Hz, 3H), 1.82—2.18 (m, 2H), 2.31 (s, 3H), 2.15—2.60 (m, 2H), 2.68—2.90 (m, 2H), 3.55 (q, J=7.0 Hz, 1H), 7.00 (s, 3H); MS *m/e* 188 (M^+). Found: C, 82.87; H, 8.49%. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57%.

Reaction of 1,3,5-Trimethyl-6-methylenetricyclo[3.2.1.$0^{2,7}$]oct-3-en-8-one (Ib) with Vinylmagnesium Bromide. To a stirred solution of vinylmagnesium bromide, which had been prepared using 1.75 g (16.4 mmol) of vinyl bromide, 0.365 g (15 mg-atom) of magnesium turnings, and 25 ml of THF, was added 870 mg (5 mmol) of Ib in 10 ml of THF at 0 °C. This reaction mixture was stirred for another 4 h at 0 °C, treated with aqueous ammonium chloride, and then extracted with ether (30 ml × 3). The evaporation *in vacuo* of the dried (Na_2SO_4) organic portion gave an oil of IIb (997 mg, 99%): bp 40—46 °C/4 mmHg; IR 3400, 1650 cm^{-1}; NMR (CCl_4) δ 0.95 (s, 3H), 1.22 (s, 3H), 1.95 (d, J=1.5 Hz, 3H), 1.50 (s, 1H), 1.66 (d×d, J=7.0 Hz, 3.5 Hz, 1H), 1.90 (d, J=7.0 Hz, 1H), 4.62 (s, 1H), 4.66 (s, 1H), 5.38 (m, 1H), 5.0—5.2 (m, 2H), 5.40 (m, 1H); MS *m/e* 202 (M^+). Found: C, 82.96; H, 8.67%. Calcd for $C_{14}H_{18}O$: C, 83.12, H, 8.97%.

Reaction of Ib with Vinylmagnesium Bromide and Subsequent Thermal Rearrangement. To a stirred solution of vinylmagnesium bromide, which had been prepared using 1.75 g (16.4 mmol) of vinyl bromide, 0.365 g (15.0 mg-atom) of magnesium turnings, and 25 ml of THF, was added 870 mg (5 mmol) of Ib in 10 ml of THF at an ambient temperature. After the reaction mixture had been refluxed for 4 h, it was treated with aqueous ammonium chloride and extracted with ether (30 ml × 3). The evaporation *in vacuo* of the dried (Na_2SO_4) organic portion gave an oil of IIIb (950 mg, 95%); mp 60—61 °C (from hexane); IR (nujol) 1720 cm^{-1}; NMR (CCl_4) δ 1.40 (d, J=7.0 Hz, 3H), 2.30 (s, 6H), 1.75—2.10 (m, 2H), 2.10—2.60 (m, 2H), 2.80 (m, 2H), 3.55 (q, J=7.0 Hz, 1H), 6.80—7.0 (m, 2H); MS *m/e* 202 (M^+). Found: C, 83.50; H, 8.67%. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

Thermal Reaction of Ia in Benzene. 30 mg of Ia in 1 ml of benzene was refluxed for 5 h. No rearrangement occured and Ia was recovered in a 95% yield.

Thermal Rearrangement of IIa to IIIa. 188 mg (1 mmol) of IIa in 1 ml of xylene were refluxed for 30 min in a nitrogen atmosphere. Subsequent VPC analysis (5% SE-30, column temp 120—160 °C) indicated a single component which was identified with the product derived *via* the Grignard-reagent procedure. This reaction mixture was chromatographed on alumina (2.5 g). Elution with hexane–benzene (4/1) gave 170 mg (90%) of IIIa.

Thermal Rearrangement of IIb to IIIb. 202 mg (1 mmol) of IIb in 1 ml of 1,2-dichlorobenzene were refluxed for 15 min in a nitrogen atmosphere. The subsequent evaporation *in vacuo* of the 1,2-dichlorobenzene gave an oil. This oil was chromatographed on alumina (10 g), using hexane as the eluent, to give 182 mg (90%) of IIIb.

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