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Stereoconvergent approach to each of the stereoisomeric hydroxydiquinanes based on the anionic [1,3] rearrangement of bicyclo[3.2.1]oct-6-en-2-ols

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Abstract

The anionic [1,3] rearrangement of both stereoisomeric bicyclo[3.2.1]oct-6-en-2-ols by treatment with $KN(TMS)_2$ in toluene or in diglyme took place as a stereoconvergent route giving each of the stereoisomeric hydroxydiquinanes. © 1998 Elsevier Science Ltd. All rights reserved.

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Alkoxide accelerated [1,3] sigmatropic rearrangements have rarely been investigated from either the mechanistic or the synthetic point of view.[1,2] Very recently, we have reported the anionic [1,3] rearrangement leading to [5-5] fused-ring compounds, the so-called diquinanes, from the corresponding oxy-Cope systems including an etheno-bridge such as compounds **3a** and **4a**.[3] We wish to report herein the selective reaction conditions in the preparation of hydroxydiquinanes **5** and **6** and the two-carbon enlargement ketone **7a** and the mechanistic aspects of the transformations.

We first examined the reactions of the substrates lacking a vinyl group at the 2-position in which we need not consider the further migration of the [1,3] rearrangement products. Treatment of a bisphenyl derivative **3b** with $KN(TMS)_2$ in toluene at 50°C for 15 min gave **5b** mainly (run 1 of Table 1).[2] When THF was employed as the solvent instead of toluene, the ratio of **5b** to **6b** somewhat decreased (run 2). A similar reaction of **3b** in *diglyme* at -78 °C gave **6b** as the major product (run 3).

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[2] Reaction was monitored by VPC until the substrate was consumed. All new compounds reported here exhibit satisfactory spectral characteristics including HRMS.

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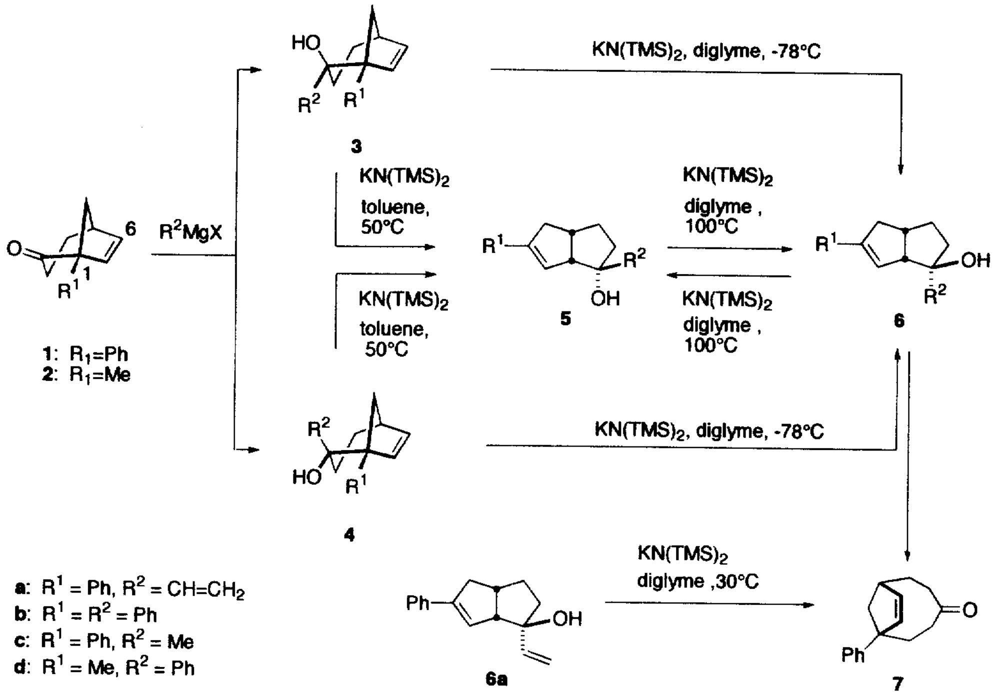

The stereoisomeric substrate **4b** behaved in a similar manner (runs 4—6). Thus, we can obtain each of the diquinanes **5b** and **6b** selectively from the ketone **1** through **3b** and/or **4b**.

The ratios of **5b** to **6b** were not reproducible when the reactions were carried out in diglyme at about 30 °C. This seemed to suggest the possibility of equilibrium between them. An equilibrium mixture was derived from both **5b** and **6b** by heating at 100 °C for 30 min (runs 7 and 8).

Runs 9—14 indicate that a series of derivatives (**c**-series) behaves in a similar manner to that of the **b**-series under the corresponding reaction conditions. A compound of the **c**-series was slightly less reactive than the corresponding one of the **b**-series. The selectivity of the rearrangement in diglyme at -78 °C was lower than that of the **b**-series.

The reactivities of the bridgehead methyl derivatives (**d**-series) were different from those of the two foregoing series. The bridged compounds **3d** and **4d** were consumed by heating under reflux in xylene. However, the ratios of **5d** to **6d** were reversed (runs 15 and 17). In diglyme, the bridged compounds were recovered even at 50 °C. Mixtures of **5d** and **6d** were derived at higher temperature in diglyme, while their total yields were low. Thus, the bridge-head substituent controls mainly the easiness of the anionic [1,3] rearrangement.[3]

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[3] The activation by the 2-furyl group at the C-1 position was very similar to that by the phenyl group.

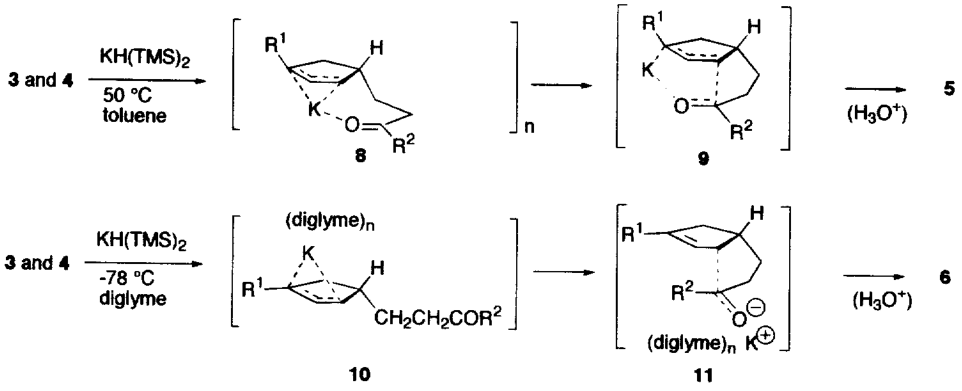
Table 1. Anionic [1,3] rearrangement of bicyclo[3.2.1]oct-6-en-2-ols.^{a}

Run	Subst	Solvent	Temp,°C	Time, min	Products (ratio, %)^{b}			Isolated yield (%)^{c}		
1	**3b**	toluene	50	15	**5b** (93),	**6b** (7)		**5b** (75),	**6b** (7)	
2	**3b**	THF	30	15	**5b** (81),	**6b** (19)		**5b** (51),	**6b** (11)	
3	**3b**	diglyme	-78	15	**5b** (8),	**6b** (92)		**5b** (12),	**6b** (80)	
4	**4b**	toluene	50	15	**5b** (91),	**6b** (9)		**5b** (70),	**6b** (11)	
5	**4b**	THF	30	15	**5b** (65),	**6b** (25)		**5b** (49),	**6b** (11)	
6	**4b**	diglyme	-78	15	**5b** (3),	**6b** (97)		**5b** (6),	**6b** (79)	
7	**5b**	diglyme	100	30	**5b** (45),	**6b** (55)		**5b** (47),	**6b** (50)	
8	**6b**	diglyme	100	30	**5b** (45),	**6b** (55)		**5b** (43),	**6b** (48)	
9	**3c**	toluene	50	60	**5c** (99),	**6c**^{d}			**5c** (93)	
10	**3c**	diglyme	-78	120	**5c** (16),	**6c** (84)		**5c** (23),	**6c** (70)	
11	**4c**	toluene	50	60	**5c** (99),	**6c**^{d}			**5c** (90)	
12	**4c**	diglyme	-78	120	**5c** (31),	**6c** (69)		**5c** (24),	**6c** (60)	
13	**5c**	diglyme	50	150	**5c** (42),	**6c** (58)		**5c** (24),	**6c** (41)	
14	**6c**	diglyme	50	90	**5c** (42),	**6c** (58)		**5c** (19),	**6c** (45)	
15	**3d**	xylene	145	120	**5d** (41),	**6d** (59)		**5d** (35),	**6d** (54)	
16	**3d**	diglyme	50	120	**3d** (99)^{e}				**3d** (93)^{e}	
17	**4d**	xylene	145	300	**5d** (13),	**6d** (87)		**5d** (11),	**6d** (73)	
18	**4d**	diglyme	50	120	**4d** (99)^{e}				**4d** (92)^{e}	
19	**3a**	toluene	50	5	**5a** (84),	**6a**,	**7**(2)		**5a** (79)	
20	**3a**	diglyme	-78	15	**5a** (3),	**6a** (47),	**7** (40)		**6a** (50),	**7** (36)
21	**3a**	diglyme	30	10	**5a** (33),	**6a** (33),	**7** (34)		**6a** (38),	**7** (26)^{f}
22	**3a**	diglyme	100	60			**7** (81)			**7** (67)
23	**4a**	toluene	50	30	**5a** (96),	**6a**		**5a** (91)		
24	**4a**	diglyme	-78	15	**5a** (7),	**6a** (73),	**7** (12)		**6a** (68),	**7** (10)
25	**4a**	diglyme	30	15	**5a** (58),	**6a**,	**7** (37)	**5a** (55),		**7** (14)
26	**4a**	diglyme	100	60			**7** (90)			**7** (76)
27	**5a**	diglyme	100	60			**7** (77)			**7** (73)
28	**6a**	diglyme	30	15			**7** (96)			**7** (81)

a) Reaction was carried out in a 0.03M solution using 3 molar amounts of potassium bis(trimethylsilyl)amide under argon. b) Determined by VPC. c) Purified by silica-gel chromatography. d) Less than 1%. e) Recovered. f) With 16% of **5a**.

According to the results of these three series, we set up reaction conditions for the oxy-Cope system (**a**-series). The reactions in toluene at 50 °C gave the diquinane **5a** including a *trans*-Cope system. The diquinane **6a** containing a *cis*-Cope system was derived in diglyme at -78 °C along with the tandem oxy-Cope product **7**. The anionic oxy-Cope rearrangement of **6a** to **7** apparently competes with the isomerization between **6a** and **5a** in diglyme at about 30°C. Some reactions (run 22 and runs 26—28) supported this presumption and gave the two-carbon enlargement product of **1**, that is, **7**.

These [1,3] rearrangements are not stereospecific reactions. Thus, we should rule out a concerted sigmatropic process for the anionic [1,3] rearrangement.[4] If the C_1-C_2 bond of **3** or **4** was cleaved heterogeneously in toluene, one of the most likely products seems to be an allylpotassium compound **8**.[5] The potassium atom of **8** may not be solvated well by toluene, while it should be coordinated strongly by the carbonyl group. If the distance between the potassium and oxygen atoms becomes sufficiently short, the resulting model **9** should reflect the cyclic transition state for intramolecular allylation leading to **5**. In contrast to the hydrocarbon solvent, diglyme strongly solvated to potassium cation,[6] and the C_1-C_2 bond of **3** or **4** was cleaved even at -78 °C. The plausible intermediate seems to be a solvated



allylpotassium compound like **10**. The allylpotassium part and the carbonyl group seem to be arranged like **11** in the transition state leading to **6**, according to the dipole-dipole interactions.

In conclusion, stereo-convergent preparation of each stereoisomer of hydroxy-diquinanes was accomplished by anionic [1,3] rearrangement of the alcohols derived from 1-phenylbicyclo[3.2.1]oct-6-en-2-one. The stereochemical courses were controlled by the selection of the solvents. Further mechanistic investigation and synthetic application of the rearrangement are currently underway in this laboratory.

Acknowledgments

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