Double Asymmetric Hydrogenation of Conjugated Dienes Catalysed by Ruthenium binap† Complexes

Hitoshi Muramatsu, Hiroyuki Kawano, Youichi Ishii, Masahiko Saburi,* and Yasuzo Uchida

Department of Industrial Chemistry, Faculty of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan

Buta-1,3-diene-2,3-dicarboxylic acid is smoothly hydrogenated in the presence of a ruthenium–(*R*)-binap complex as a catalyst *via* two consecutive 1,2-hydrogen additions, giving rise to (*S*,*S*)-2,3-dimethylsuccinic acid with 98% diastereoisomeric excess and 96% enantiomeric excess.

Although a number of reports concerned with asymmetric reduction have been published, only a few examples of double asymmetric hydrogenation have appeared so far.[1,2] However, double asymmetric hydrogenation of dienes is expected to be of much synthetic value, since by such a reaction two chiral centres may be introduced into one molecule in a single procedure. From this standpoint, the asymmetric hydrogenation of buta-1,3-diene-2,3-dicarboxylic acid (**2a**)[3] and 2,3-dibenzylidenesuccinic acid (**2b**)[4] was examined. In a previous communication, we reported that a binap[5] complex, $Ru_2Cl_4\{(R)$- or (*S*)-binap$\}_2NEt_3$, (*R*)-(**1**) or (*S*)-(**1**),[6] exhibits excellent catalytic activity and high stereoselectivity for the hydrogenation of itaconic acid and benzylidenesuccinic acid.[7] The diacids (**2a**) and (**2b**) contain two itaconic acid or benzylidenesuccinic acid moieties, respectively.

The acid (**2a**) was smoothly hydrogenated with complex (*R*)-(**1**) to give 2,3-dimethylsuccinic acid (**3a**) in 77% yield.‡ Chiral h.p.l.c. analysis of the dianilide from the resulting diacid (**3a**)§ indicated the ratio of the three isomers, (*S*,*S*)-, (*R*,*S*)-, and (*R*,*R*)-(**3a**), to be 97.0 : 1.2 : 1.8 [98% diastereoisomeric excess (d.e.), 96% enantiomeric excess (e.e.)] (entry 1 of Table 1).

As Scheme 1 shows, two reaction paths are possible for the hydrogenation of (**2a**). One proceeds *via* two consecutive 1,2-hydrogen addition steps, (**2a**) → (**4a**) → (**3a**), and the other proceeds *via* an initial 1,4-hydrogen addition, followed by hydrogenation of the remaining double bond, (**2a**) → (**5a**) or (**6a**) → (**3a**). The latter possibility was, however, ruled out since neither (**5a**) nor (**6a**) was appreciably hydrogenated under the conditions employed for (**2a**) [the conversions of (**5a**) and (**6a**) after 24 h were 20 and 0%, respectively]. Conversely the racemic (**4a**)[8] was easily hydrogenated to give (**3a**) as an isomeric mixture. We further observed by ^{1}H n.m.r. spectroscopy that the diacid (**4a**) was formed during the hydrogenation of (**2a**). These results support the conversion of (**2a**) to (**3a**) proceeding *via* the two consecutive 1,2-hydrogen addition processes.

† binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

‡ Diacid (**2a**) was hydrogenated at 35 °C under an initial pressure of hydrogen of 3 atm for 24 h. The mixture was evaporated, and the residue dissolved in 1 M NaOH and filtered. The filtrate was washed with chloroform (× 3), acidified with concentrated HCl to pH 1, and then extracted repeatedly with tetrahydrofuran–chloroform (1 : 9). The organic layer was dried over $MgSO_4$ and evaporated to give (**3a**) in 77% isolated yield.

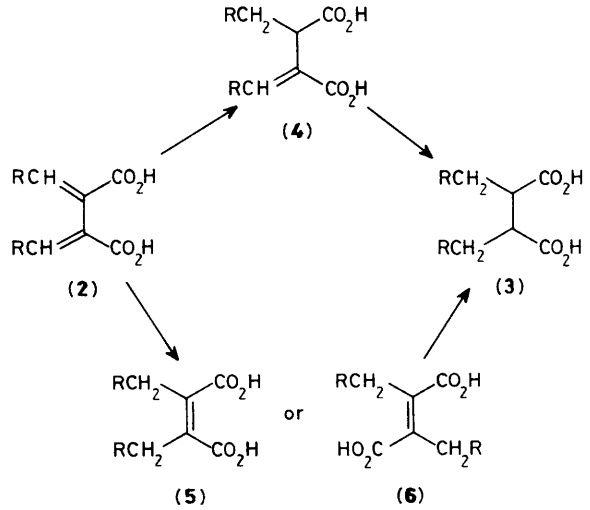
§ To (**3a**) in anhydrous tetrahydrofuran were added dicyclohexylcarbodiimide, 4-dimethylaminopyridine, and aniline, and the mixture was stirred at room temperature for 24 h. After removal of the solvent, the residue was dissolved in ethyl acetate and washed with 5% HCl. Column chromatography on silica gel with ethyl acetate as eluant afforded 2,3-dimethylsuccinanilide. It was analysed by chiral h.p.l.c. on DAICEL CHIRALCEL OD with n-hexane–propan-2-ol (9 : 1) as eluant.

As mentioned above, the hydrogenation of racemic (**4a**) catalysed by complex (*R*)-(**1**) afforded (**3a**) as an isomeric mixture. Chiral h.p.l.c. analysis revealed that the ratio of (*S*,*S*)-, (*R*,*S*)-, and (*R*,*R*)-(**3a**) was 49.9 : 31.6 : 19.2 (entry 2). Based on this result, the ratios of the pseudo-first-order rate constants, k_3/k_4 and k_5/k_6, are estimated to be 62 and 1.6, respectively. The configuration of the newly formed chiral centre of (**3a**) is controlled by two factors. The first is the contribution from the catalyst (*R*)-(**1**), leading to selectivity for the (*S*)-configuration (catalyst control). The second is the effect of the neighbouring chiral centre, which shows a preference for the formation of the same chirality as that of the existing chiral centre (substrate control). As a result of the co-operation of these factors, (*S*)-(**4a**) gave almost exclusively (*S*,*S*)-(**3a**) (k_3/k_4 62). In the case of (*R*)-(**4a**), however, the two effects contributed in opposition so that (*R*,*S*)- and (*R*,*R*)-(**3a**) were obtained with low selectivity (k_5/k_6 1.6). Taking the k_3/k_4 ratio and the product ratio in entry 1 into consideration, k_1/k_2 is calculated to be 70.

Table 1. The product ratio in asymmetric hydrogenation.

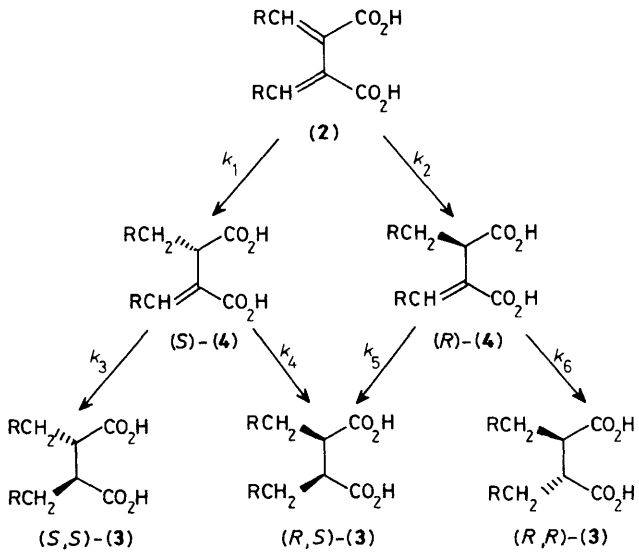
Entry	Substrate	Product ratio (*S*,*S*)-(**3**) : (*R*,*S*)-(**3**) : (*R*,*R*)-(**3**)
1[a]	(**2a**)	97.0 : 1.2 : 1.8
2[a]	(*RS*)-(**4a**)	49.2 : 31.6 : 19.2
3[b]	(**2b**)	12.9 : 13.3 : 73.8
4[b]	(*RS*)-(**4b**)	27.6 : 22.5 : 49.9

[a] Using complex (*R*)-(**1**). [b] Using complex (*S*)-(**1**).



a; R = H **b**; R = Ph

Scheme 1. Possible paths of the double asymmetric hydrogenation.



a; R = H **b**; R = Ph

Scheme 2. The courses of double asymmetric hydrogenation.

The asymmetric hydrogenation of 2,3-dibenzylidenesuccinic acid (**2b**) was also examined by using complex (*S*)-(**1**) under more severe conditions than those employed for (**2a**) in order to force the reaction to completion.¶ G.c. and chiral h.p.l.c. analysis of the dimethyl ester from the resulting diacid (**3b**)‖ revealed that the ratio of three isomers, (*S*,*S*)-, (*R*,*S*)-, and (*R*,*R*)-(**3b**), was 12.9 : 13.3 : 73.8 (73% d.e., 70% e.e.) (entry 3). Racemic (**4b**)[9] was also hydrogenated under the same conditions, and the ratio of the products was similarly determined as 27.6 : 22.5 : 49.9 (entry 4). In this case, the difference as to whether the two effects (catalyst and substrate control) contributed in the same or opposite direction was more pronounced (k_2/k_1 2.8, k_4/k_3 0.81, k_6/k_5 500) than that in the hydrogenation of (**2a**). Although the severe conditions lowered the enantioselectivity for (*R*)-(**4b**) in the first step (48% e.e.), (*R*,*R*)-(**3b**) was obtained with high enantioselectivity (70% e.e.) because of the effective asymmetric induction in the second hydrogenation.

In conclusion, the asymmetric hydrogenation of diacids (**2a**) or (**2b**) to the optically active 2,3-dialkylsuccinic acid (**3a**) or (**3b**) was achieved by employing complex (**1**) as a catalyst. This provides a simple and versatile method of introducing two adjacent chiral centres into the succinic acid backbone by a single process with high diastereo- and enantio-selectivity. Its application to the syntheses of naturally occurring compounds is now in progress.

This study was supported by Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan (No. 63607510).

Received, 24th February 1989; Com. 9/00851I

¶ Diacid (**2b**) was hydrogenated at 50 °C under 10 atm of initial hydrogen pressure for 48 h.

‖ The diacid (**3b**) was converted into its dimethyl ester with diazomethane and chromatographed on silica gel with ether as eluant. The diastereoselectivity was determined by g.c. and the enantioselectivity by chiral h.p.l.c.

References

1 J.-C. Poulin and H. B. Kagan, *J. Chem. Soc., Chem. Commun.*, 1982, 1261.
2 H. Kawano, Y. Ishii, M. Saburi, and Y. Uchida, *J. Chem. Soc., Chem. Commun.*, 1988, 87.
3 W. J. Bailey and W. R. Srenson, *J. Am. Chem. Soc.*, 1956, **78**, 2287; U. Záhorszky and H. Musso, *Liebigs Ann. Chem.*, 1973, 1777.
4 J. Andersson and L. Eberson, *Nouv. J. Chim.*, 1977, **1**, 413.
5 A. Miyashita, H. Takaya, T. Souchi, and R. Noyori, *Tetrahedron*, 1984, **40**, 1245.
6 T. Ikariya, Y. Ishii, H. Kawano, T. Arai, M. Saburi, S. Yoshikawa, and S. Akutagawa, *J. Chem. Soc., Chem. Commun.*, 1985, 922.
7 H. Kawano, Y. Ishii, T. Ikariya, M. Saburi, Y. Uchida, and H. Kumobayashi, *Tetrahedron Lett.*, 1987, **17**, 1905.
8 P. Dowd, M. Shapiro, and J. Kang, *Tetrahedron*, 1987, **17**, 1905.
9 H. G. Heller and B. Swinney, *J. Chem. Soc.*, 1967, 2452.