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ISOLATION AND RELATIVE REACTIVITIES IN CHROMIUM(VI) OXIDE OXIDATION OF THE ROTAMERS OF 9-(2-FORMYL-1-NAPHTHYL)FLUORENE AND RELATED ALCOHOLS[1)]

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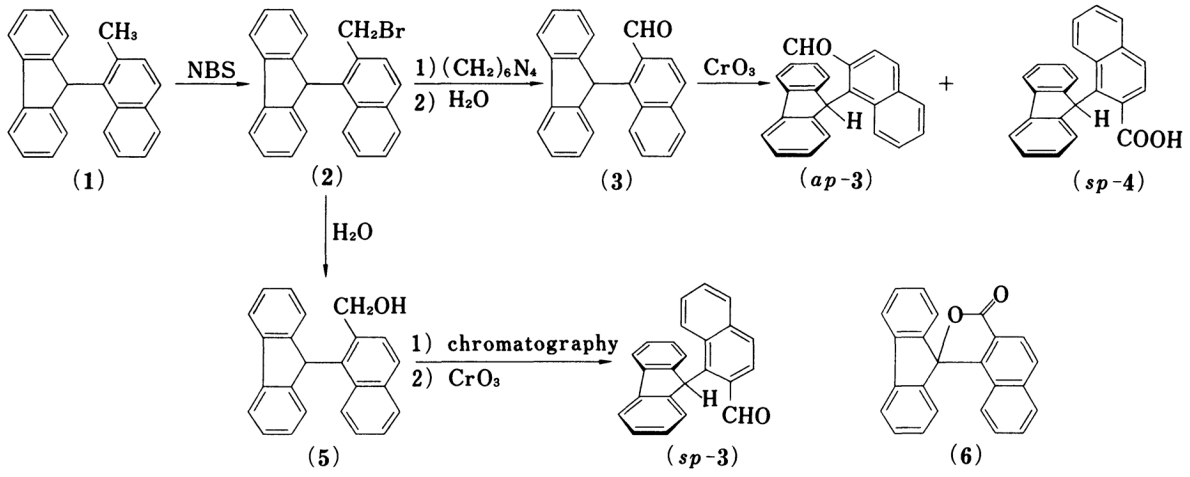
Rotational isomers (sp and ap) of 9-(2-formyl-1-naphthyl)fluorene were isolated. $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for rotation (sp → ap) were 24.0 kcal mol^{-1} and -7.9 e. u., respectively. Oxidation of the sp form afforded the corresponding carboxylic acid smoothly, whereas the ap form reacted very slowly to give a lactone. Oxidations of 9-(2-hydroxymethyl-1-naphthyl)fluorene and 9-[2-(α-hydroxybenzyl)-1-naphthyl]fluorene showed that the relative reactivities of the rotamers of the former were almost the same, while those of the latter differed to a great extent. The results suggest that the steric hindrance to the approach of a base to a proton in E2 elimination is the cause of poor reactivities of the ap forms of the aldehyde and the benzylic alcohol.

Reactivities of sp and ap isomers of 9-arylfluorene derivatives give sometimes surprising differences.[2)] Since the reactions investigated so far were confined to deprotonation and substitution reactions, we wished to extend the examination to other types of reactions. When we examined some reactivities of a formyl group in 9-(2-formyl-1-naphthyl)fluorene (3) rotamers, we found striking differences between the reactivities in an E2-type reaction of the rotamers.

Synthesis of the compound was carried out as follows. A rotameric mixture of 9-(2-methyl-1-naphthyl)fluorene (1) was brominated with N-bromosuccinimide in boil-



ing chlorobenzene to give 9-(2-bromomethyl-1-naphthyl)fluorene (2) which was treated under the Sommelet reaction conditions.[3] Oxidation of the aldehyde (3) mixture with chromium(VI) oxide was found to afford sp-carboxylic acid (4), leaving the ap-aldehyde intact. Thus the ap-aldehyde, mp 127-128°C, was obtained in a pure form. Hydrolysis of the bromide (2) gave 9-(2-hydroxymethyl-1-naphthyl)fluorene (5) rotamers which were separated by chromatography. Oxidation of the sp-alcohol (5) with chromium(VI) oxide yielded the pure sp-aldehyde, mp 102-104°C. Assignment of sp and ap conformations relies on the ring current effect in ^{1}H NMR spectra: ap-conformations give signals due to protons in the 2-substituent of the naphthyl group at a higher field than sp-conformations.

Barriers to rotation about the C_9-C_{naph} bond and the equilibrium constants were obtained by heating a solution of ap-3 or sp-3 in hexachlorobutadiene in an appropriate solvent bath. The data were treated as a reversible first order reaction to give the rate constants shwon in Table 1. Putting these data into the Eyring equation, we obtained $\Delta H^{\ddagger}$ 24.0 ± 0.7 kcal mol^{-1} (1 cal = 4.18 J) and $\Delta S^{\ddagger}$ -7.9 ± 2.0 e. u. (1 e. u. = 4.18 J K^{-1} mol^{-1}). The results assure that we can examine the reactivities of the respective rotamers if we run reactions at ambient temperatures.

Table 1. Rate Constants for Rotation and Equilibrium Constants of the Aldehyde Rotamers

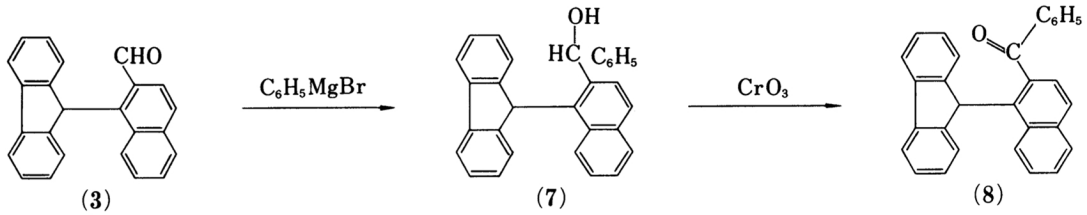
Temperature / °C	k(ap → sp) / s^{-1}	K([sp]/[ap])
55.6	1.28 x 10^{-5}	1.48
64.0	3.66 x 10^{-5}	1.49
73.2	9.58 x 10^{-5}	1.46
78.2	1.41 x 10^{-4}	1.49

The difference in reactivities of sp-3 and ap-3 during the oxidation was striking: although alkylbenzaldehydes are known to be less reactive than other benzaldehyde in chromium(VI) oxide oxidation,[4] the electronic effect of the substituent must be, at least, almost the same in rotational isomers. Oxidation of ap-3 with chromium(VI) oxide in aqueous acetone reconfirmed its very low reactivities under the conditions. Prolonged oxidation under the conditions afforded a lactone (6) which was apparently formed by oxidation at the 9-position to form a hydroxy-compound which then was oxidized at the aldehydic group to lactonize.

The oxidation with chromium(VI) oxide under neutral conditions is known to proceed via addition of water followed by E2 type elimination.[5] Steric hindrance to the reaction may be strong in either of these two steps in addition to the coordination step of the chromium(VI). Our experience of the preparation of the aldehyde (3) by oxidation of the corresponding alcohol (5) suggests, however, that the coordination of chromium(VI) to oxygen in 5 is facile since both forms of 2 are oxidized very fast to give 3. Since the space-filling molecular models show that the aldehyde-oxygen in 3 are as much exposed as that in the alcohol (5), it is hardly believable that the coordination of chromium(VI) is slow to retard the

reaction of ap-3. To diagnose the cause for the retardation of oxidation in ap-3, we ran competitive oxidations of alcohols.

Equal amounts of sp-5, mp 103-105°C, and ap-5, mp 134-135.5°C, were dissolved in aqueous acetone and oxidized with insufficient amount of chromium(VI) oxide at room temperature. The reaction proceeded almost instantaneously. ^{1}H NMR spectra of the product indicated that the reactivity ratio k_{ap}/k_{sp} was 1.4. Since the rotational barrier of 9-(2-methyl-1-naphthyl)fluorene is known to be ca. 29 kcal mol^{-1},[6] the results can be taken to indicate the real reactivities of the rotamers. If the difference is taken significant, then probably steric acceleration in the ap-form may be responsible.



(3) (7) (8)

sp-9-[2-(α-Hydroxybenzyl)-1-naphthyl]fluorene (7), mp 175-177°C, and the ap-isomer, mp 176-177°C, were prepared by the addition of phenylmagnesium bromide to 3 rotamers. Preliminary examination of barriers to rotation about the C_9-C_{naph} bonds of these rotamers showed that they were, at least, higher than the aldehyde (3). Thus the reaction at room temperature should show the reactivities of sp- and ap-7. Independent oxidation of the respective rotamer indicated that, whereas the sp-form was oxidized almost instantaneously to give sp-9-(2-benzoyl-1-naphthyl)fluorene (8), mp 162.5-164°C, the ap-form required a few minutes to give the sign of oxidation to produce ap-8, mp 123-124°C. Competitive reactions were carried out and k_{sp}/k_{ap} was obtained as ca. 30.

The molecular model of ap-7 (Fig. 1) suggests that the coordination of chromium(VI) to oxygen of the alcohol is not sterically hindered. Therfore, the

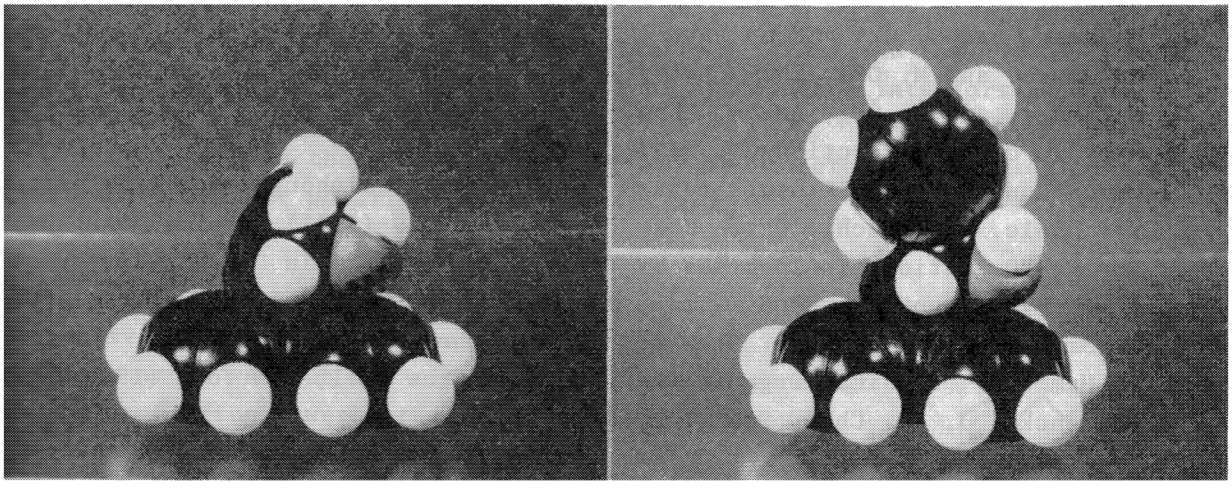


Fig. 1 CPK models of ap-9-(2-hydroxymethyl-1-naphthyl)fluorene (2) (left) and ap-9-[2-(α-hydroxybenzyl)-1-naphthyl]-fluorene (7) (right)

retardation of the oxidation of ap-7 must be attributed to the E2 elimination step. Although, at a glimpse, the easy oxidation of ap-5 and the slow oxidation of ap-7 are contrasting, inspection of the molecular models in Fig. 1 suggests the reasons. As can be seen in the figure, the proton to be attacked by a base in E2 elimination of the chromate of ap-7 is burried deeply in a pocket made by the fluorene, the phenyl, and the substituted naphthalene. In the transition state of the reaction, the proton must be exposed to the attack at the expense of stable conformations. In contrast, one of the protons to be removed in ap-5 (Fig. 1) is exposed to suggest that the E2 elimination of the chromate should suffer no difficulty.

As to the oxidation of the aldehyde (3), either addition or the elimination step can be slow. However, we wish to attribute the slow oxidation to the slow elimination for the following two reasons. Firstly, oximation of the aldehyde (3) in the presence of acetic acid proceeded smoothly to afford ap-oxime, mp 171.5-172.5°C, and ap-oxime, mp 170.5-171.5°C. This indicates taht the addition of hydroxylamine to the carbonyl proceeds smoothly because the rate determining step in the oxime formation is the nucleophilic attack to the protonated carbonly group by hydroxylamine under acidic conditions.[7] In the addition reaction, a small group, hydrogen in this case, directs toward the fluorene ring to minimize the steric hindrance, of which conformation must be similar with ap-7 (Fig. 1). Secondly the ap conformation of the adduct made from the aldehyde and water is highly congested as is in ap-7: this will make the E2 elimination very slow.

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References and Notes

1) Reactivities of Stable Rotamers. Part 7. For Part 6, see S. Seki, T. Morinaga, H. Kikuchi, T. Mitsuhashi, G. Yamamoto, and M. Ōki, Bull. Chem. Soc. Jpn., in press.
2) M. Nakamura and M. Ōki, Chem. Lett., 1975, 671; H. Kikuchi, t. Mitsuhashi, N. Nakamura, and M. Ōki, Chem. Lett., 1980, 209; S. Murata, S. Kanno, Y. Tanabe, M. Nakamura, and M. Ōki, Angew. Chem., in press.
3) S. Angyal, Organic Reactions, 8, 197 (1954).
4) Electron-donating substituents retard the oxidation, although steric effects are questionable. E. Lucchi, Gazz. Chim. Ital., 71, 729 (1941) and following papers.
5) J. Rocek, "Oxidation of Aldehydes by Transition Metals", in "The Cheimstry of the Carbonyl Group" ed. by S. Patai, John-Wiley, New York (1966), pp. 462-478.
6) T. H. Siddall, III, and W. E. Stewart, J. Org. Chem., 34, 233 (1969).
7) L. P. Hammett, "Physical Organic Chemistry", McGraw Hill, New York (1940), p.333; W. P. Jencks, J. Am. Chem. Soc., 81, 475 (1959).

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