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Asymmetric Induction in 1,3-Dipolar Cycloaddition of Diazofluorene with Menthyl or 8-Phenylmenthyl Acrylate and Fumarate Derivatives

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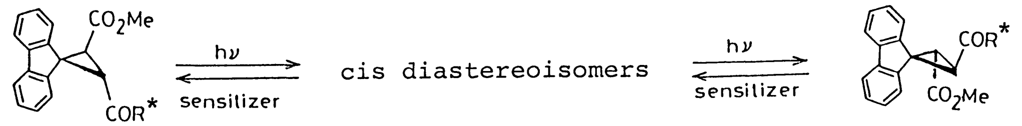
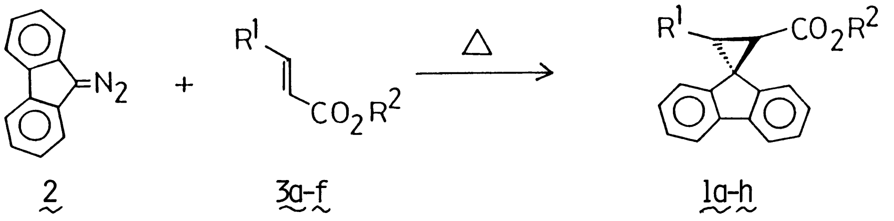
Optical yields in the 1,3-dipolar cycloaddition of diazofluorene with chiral acrylate or fumarate derivatives were found to be considerably improved by use of Corey's 8-phenylmenthyl group as a chiral O-alkyl group in these esters. The absolute stereochemistry of resulting cyclopropanes is different from the one expected from the "diazo-exchange" mechanism proposed by Walborsky et al.

We have recently reported that photochemically induced asymmetric transformation between diastereomers of trans-2,3-disubstituted spirocyclopropanefluorenes **1** is highly diastereoselective when suitable chiral auxiliaries (R*) and sensitizers are used (Scheme 1).[1)] The absolute stereochemistry of **1** and related compounds has been determined by the CD and chemical transformation methods.[2)] In connection with these studies, we have also examined direct methods to prepare optically active **1** from diazofluorene. A classical work of asymmetric induction in the 1,3-dipolar cycloaddition of diphenyldiazomethane with menthyl acrylate has been reported by Walborsky and his co-workers to give "anti-Prelog" type optical active 2,2-diphenylcyclopropanecarboxylic acid in poor optical yield (2% enantiomeric excess (ee) after saponification).[3a)] After Walborsky's study, asymmetric induction in the 1,3-dipolar cycloaddition with diazo compounds has been little explored.[4)] This may be due to poor optical yields in 1,3-dipolar cycloadditions. However, in view of recently developed asymmetric induction in Lewis acid-catalyzed Diels-Alder reactions,[5,6)] it is expected that the use of 8-phenylmenthyl group as a chiral auxiliary, found by Corey and his co-workers,[5)] may improve the diastereoselectivity in the 1,3-dipolar cycloadditions with diazo compounds. We report here asymmetric induction in the 1,3-dipolar cycloaddition of diazofluorene with menthyl or 8-phenylmenthyl acrylate and fumarate derivatives.



1 Scheme 1. **1'**

All the reactions were carried out in benzene solution at 60 °C. The cyclopropanes were produced in high yields in all cases. Table 1 summarizes the results of the 1,3-dipolar cycloaddition (Eq. 1). The absolute stereochemistry of the



(1)

a: R^1=H,R^2=(-)-menthyl; b: R^1=H,R^2=(-)-8-phenylmenthyl; c: R^1=CO_2Me,R^2=(-)-menthyl d: R^1=CO_2Me,R^2=(-)-8-phenylmenthyl; e: R^1=CO_2R^3,R^2=R^3=(-)-menthyl; f: R^1=CO_2R^3, R^2=R^3=(-)-8-phenylmenthyl; g: R^1=H,R^2=Me; h: R^1=CO_2Me,R^2=Me

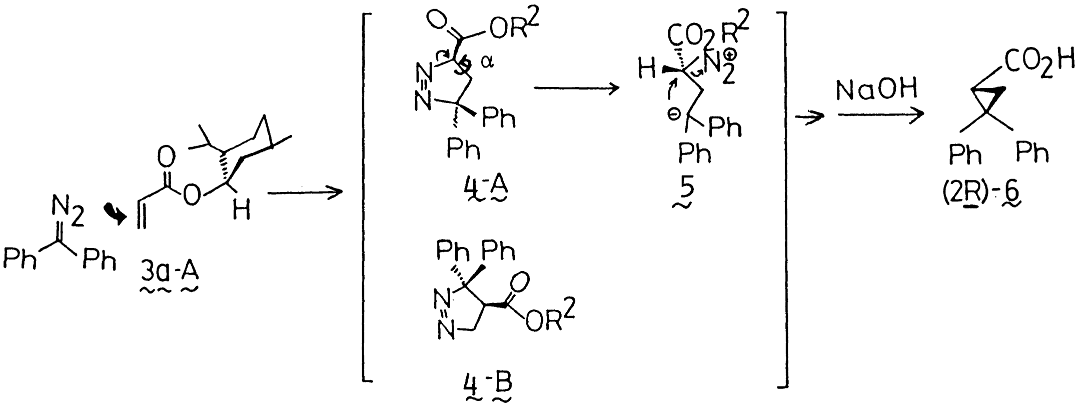
Table 1. The 1,3-dipolar cycloadditions of diazofluorene with optically active acrylates and fumarates

Chiral olefin	Diastereomer ratio[a]	Major stereoisomer ($[\alpha]^{25}$D)[b]	Enantiomeric excess[b]/%	Product yield[b]/%
3a	49:51	(2R)-1g (-2.6°)	1	82
3b	60:40	(2S)-1g (+56.4°)	21	96
3c	54:46	(2S,3S)-1h (+34.0°)	10	80
3d	71:29	(2S,3S)-1h (+136°)	40	91
3e	75:25	(2S,3S)-1h (+171°)	50	76
3f	95:5	(2S,3S)-1h (+285°)	85	79

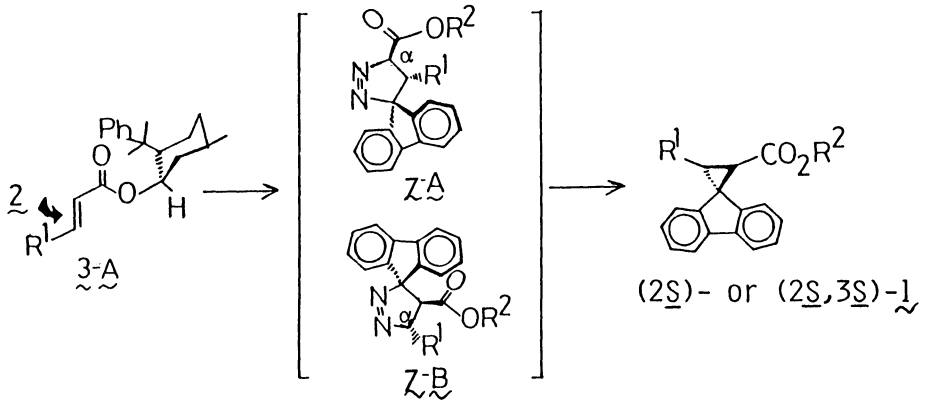
a) (2S)/(2R) or (2S,3S)/(2R,3R), determined by HPLC.
b) After alkaline hydrolysis and subsequent methylation with diazomethane.

predominant enantiomer (obtained after alkaline hydrolysis and methylation), 2-carbomethoxy spirocyclopropane-1,9'-fluorene (1g) ($[\alpha]^{25}$D +265° (*c* 0.4, EtOH) for (2S)-(+)-1g) or trans 2,3-dicarbomethoxy spirocyclopropane-1,9'-fluorene (1h) ($[\alpha]^{25}$D +340° (*c* 0.5, EtOH) for (2S,3S)-(+)-1h), is also listed in the table. No detectable amount of cis 2,3-dicarbomethoxy compound was formed. Several points are apparent from Table 1. First, 8-phenylmenthyl group considerably improves the selectivity in all cases. Second, the fumarates derivatives 3c-f show higher selectivity than the acrylate derivatives 3a and 3b. Especially, the highest selectivity (90% de) was observed, when di-8-phenylmenthyl fumarate (3f) was used. A small difference in the values between diastereomeric excess and enantiomeric excess is probably due to the reluctant reactivity of 8-phenylmenthyl ester towards alkaline hydrolysis [6.6 M aqueous NaOH:MeOH:THF = 1:2.3:1.7 (v/v), reflux 15-50 h]. Third, 3b-f gave 1g or 1h with preferable formation of (2S) or (2S,3S)-isomer, whereas 3a gave 1g with a slight excess of (2R)-isomer.

It should be noted that the selectivity in the reactions of 3b-f, where higher optical yields compared with that of 3a were obtained, is opposite to that reported by Walborsky et al. for the 1,3-dipolar cycloadditions of diphenyldiazomethane with menthyl acrylates.[3)] They obtained, after saponification, anti-Prelog-type product (2R)-6 as a slightly predominant isomer with 2% ee (10% ee for menthyl methacrylate) and rationalized the selectivity in terms of the "diazo-exchange" mechanism[3b)] (Scheme 2). This mechanism proceeds through the predominant formation of the pyrazoline 4-A by the preferential attack of diphenyldiazomethane from the



Scheme 2.



Scheme 3.

sterically less hindered *re*-face of the transoid **3a-A** (Prelog-type attack),$^{6)}$ ring opening to the zwitterionic species **5** ("diazo-exchange"), and then ring closure with inversion of the configuration at C_α. According to this mechanism, one would expect higher selectivity for anti-Prelog-type products by replacement of menthyl group to more efficient$^{5)}$ 8-phenylmenthyl group. This is, however, not observed in the reactions of diazofluorene (**2**) with the acrylate and fumarate derivatives **3a-f**.

The observed selectivity for (2*S*)-**1g** and (2*S*,3*S*)-**1h** is rationalized in Scheme 3. Preferential Prelog-type attack of **2** to the transoid **3-A** gives the pyrazoline **7-A** or **7-B**. Subsequent extrusion of nitrogen and ring closure with retention of the configuration at C_α afford the (2*S*)- or (2*S*,3*S*)-cyclopropane.$^{7)}$ The absence of the corresponding *cis*-isomer in the reactions with the fumarate derivatives **3c-f** accords with the retention of configuration in the formation of **1h**. Inversion at C_α may occur in part in the case of reactions with less crowded acrylate derivatives **3a** and **3b**.$^{8)}$ This can be a reason for the low optical yield with **3a** and **3b**; however, a major reason will be poor stereo-differentiation in the sterically favorable transition state leading to **7-A** (R^1=H), where the fluorenyl group poorly overlaps with the chiral auxiliaries. The reason for inverted stereochemistry in the reaction with **3a** is not certain. The poor optical yield (1%) would hardly justify any discussions on the mechanism.

In conclusion, the use of 8-phenylmenthyl group as a chiral auxiliary in acrylate and fumarate esters appreciably improves the optical yield of 1,3-dipolar cycloaddition of diazofluorene, and in addition the stereochemical outcome casts a question to the Walborsky's "diazo-exchange" mechanism proposed for a similar 1,3-dipolar cycloaddition.

References

1) K. Okada, F. Samizo, and M. Oda, J. Chem. Soc., Chem. Commun., 1986, 1044.
2) K. Okada, F. Samizo, M. Oda, N. Harada, and H. Uda, Tetrahedron Lett., 27, 4493 (1986).
3) a) H. M. Walborsky and F. M. Hornyak, J. Am. Chem. Soc., 81, 1514 (1959); H. M. Walborsky, L. Barash, A. E. Young, anf F. J. Impastato, ibid., 83, 2517 (1961); b) H. M. Walborsky and C. G. Pitt, ibid., 84, 4831 (1962).
4) H. M. Walborsky, T. Sugita, M. Ohno, and Y. Inoue, J. Am. Chem. Soc., 82, 5255 (1960); R. D. Gareev, G. M. Loginova, and A. N. Pudovik, Zh. Obshch. Khim., 49, 493 (1979), C. A., 91, 4894w (1979); H. Abdallah, R. Gree, and R. Carrie, Tetrahedron Lett., 23, 503 (1982); Metal catalyzed cyclopropanation has been well studied, see L. A. Paquett, "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, New York (1984), Vol. 3, pp. 494-496; H. Brunner and W. Miehling, Monatsh. Chem., 115, 1237 (1984), and references cited therein.
5) E. J. Corey and H. E. Ensley, J. Am. Chem. Soc., 97, 6908 (1975); H. E. Ensley and R. V. C. Carr, Tetrahedron Lett., 1977, 513; H. E. Ensley, C. A. Parnell, and E. J. Corey, J. Org. Chem., 43, 1610 (1978).
6) This model is different from that proposed by Oppolzer et al. in the Lewis acid-catalyzed Diels-Alder reactions with 8-phenylmenthyl acrylate: W. Oppolzer, M. Kurth, D. Reichlin, and C. Chapuis, M. Mohnhaupt, and F. Moffatt, Helv. Chim. Acta, 64, 2802 (1981); The absolute stereochemistry of the Diels-Alder products can be altered in the absence of Lewis acid: H. M. Walborsky, L. Barash, and T. C. Davis, Tetrahedron, 19, 2333 (1963).
7) Although thermal decomposition of pyrazolines forming cyclopropanes has been usually considered to proceed via diradicals, the reaction of 3,4-dicaromethoxy-1-pyrazolines, to which 7 is related, has been reported to proceed stereospecifically.[9)]
8) Bond rotation in the possible diradical intermediate derived from 7-A or 7-B ($R^1=CO_2R^3$) will experience steric repulsion between the two ester groups. However, such repulsion is little expected in the diradical derived from the acrylate derivatives.
9) K. von Auwers and H. König, Justus Liebigs Ann. Chem. 496, 252 (1932); D. E. McGreer and W.-S. Wu, Can. J. Chem., 45, 461 (1967).

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