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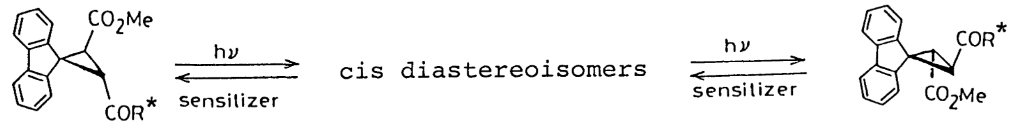
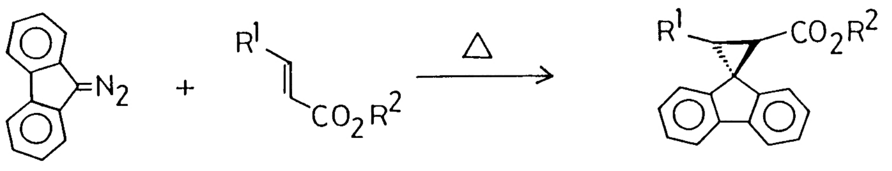
Optical yields in the 1,3-dipolar cycloaddition of diazofluorene with chiral acrylate or fumarate derivatives were found to be considerably improved by use of Corey's 8-phenylmenthyl group as a chiral O-alkyl group in these esters. The absolute stereochemistry of resulting cyclopropanes is different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



2 3a-f 1a-h (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

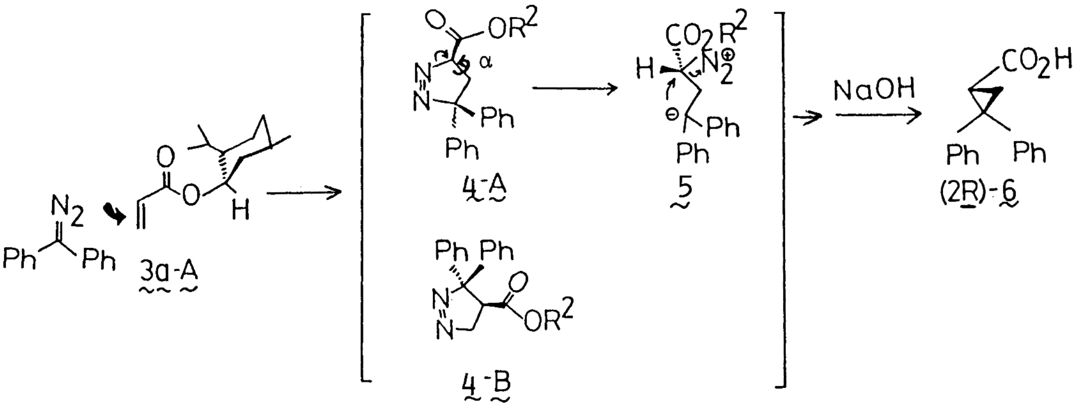
Table 1. The 1,3-dipolar cycloadditions of diazofluorene with optically active acrylates and fumarates

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

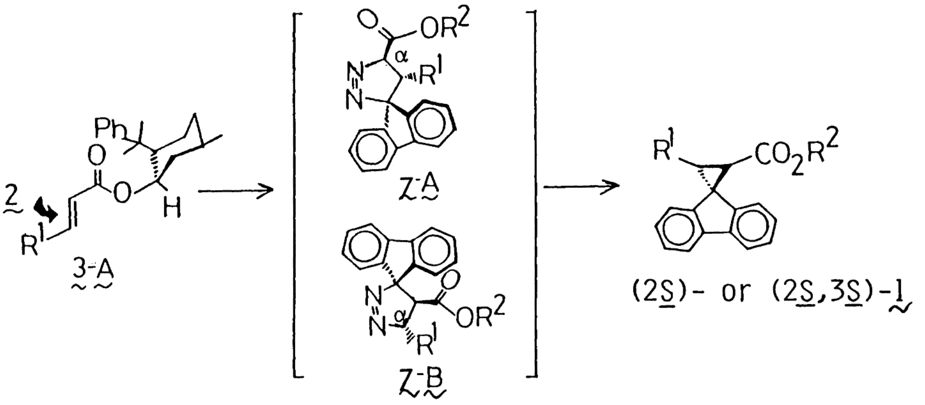
a) (2S)/(2R) or (2S,3S)/(2R,3R), determined by HPLC.
b) After alkaline hydrolysis and subsequent methylation with diazomethane.

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.

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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.
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