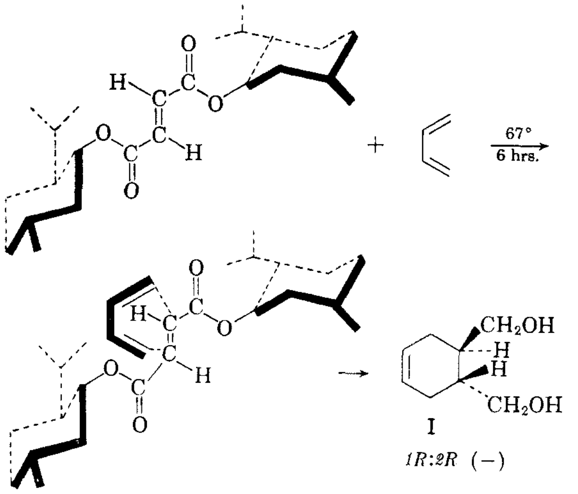
Partial Asymmetric Syntheses: The Diels-Alder Reaction[1]

Sir:

Asymmetric syntheses by the addition of various reagents to an olefinic moiety in both catalytic[2] and noncatalytic[3] reactions have previously been observed. We wish to report that the addition of butadiene to (−)-dimethyl fumarate results in a partial asymmetric synthesis, and that furthermore when $AlCl_3$ is used to catalyze the Diels-Alder reaction,[4] the same product is obtained but of *opposite sign and configuration.*



I

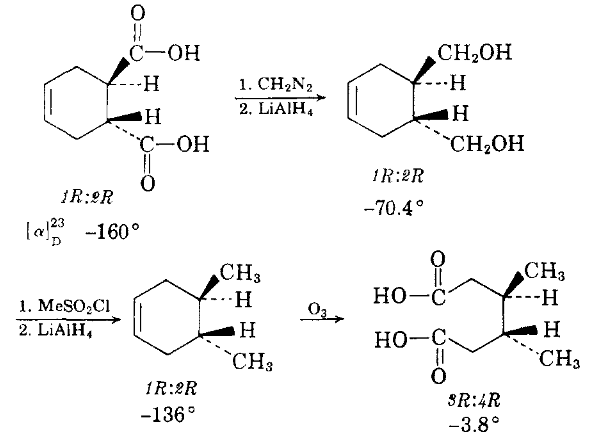
1R:2R (−)

(−)-Dimethyl fumarate (10 g., 0.025 mole), butadiene (10 g., 0.186 mole), and hydroquinone (0.1 g.) were dissolved in 20 cc. of benzene and heated in a sealed tube at 67° for six hours. To avoid possible resolution the solvent was stripped from the reaction mixture, and the residue was reduced by lithium aluminum hydride to yield 4-cyclohexene-*trans*-1,2-dimethanol(I) (2.7 g., 72%), b.p. 100–101° at 0.2 mm., $[\alpha]^{23}_{\mathrm{D}}$ − 0.8 ± 0.2° (*c* 10.9, chloroform,[5] the infrared spectrum was identical in all respects with that of an authentic sample. The rotation corresponds to 1.1% asymmetric synthesis. Repetition of the above experiment at a temperature of 160° for six hours produced the glycol in 42% yield, $[\alpha]^{23}_{\mathrm{D}}$ − 1.7 ± 0.2° (*c* 9.6, chloroform), 2.4% asymmetric synthesis.

To a mixture of aluminum chloride (0.025 mole) and benzene (75 cc.) cooled to −80° was rapidly added a precooled (−80°) solution of 10 g. of (−)-dimethyl fumarate and 10 g. of butadiene dissolved in 50 cc. of benzene. The reaction mixture was stirred at −80° for one hour,[6] and filtered; the solvent was removed and the residue reduced by lithium aluminum hydride as described above. The glycol was isolated in 71% yield, $[\alpha]^{22}_{\mathrm{D}}$ + 40.4 ± 0.5° (*c* 7.0, chloroform), *57% asymmetric synthesis.*

The above procedure was repeated at 22° and for a twenty-minute reaction time to yield the glycol in 45% yield, $[\alpha]^{26}_{\mathrm{D}}$ + 19.25 ± 0.42° (*c* 9.9, chloroform), 26% asymmetric synthesis.[7]

The (−) glycol I was shown to have the *1R:2R* absolute configuration by relating (−)-4-cyclohexene-*trans*-1,2-dimethanol to (−)-*threo*-3,4-dimethyladipic acid whose absolute configuration has been established as *3R:4R* by Carnmalm.[8] The relationship is as follows:[9]



The role of the catalyst and the general scope

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(1) This work was supported by research grant CY 4065, National Institutes of Health, Public Health Service.

(2) M. G. Vavon and B. Jakubowicz, *Bull. Soc. Chim.*, **53**, 111 (1953); D. Lipkin and T. D. Stewart, *J. Am. Chem. Soc.*, 61, 3295 (1939); Y. Nakamura, *J. Chem. Soc. Japan*, **61**, 1048 (1940); C. L. Arcus and D. G. Smyth, *J. Chem. Soc.*, 35 (1955); A. Pedrazzoli, *Helv. Chim. Acta*, **40**, 80 (1957); S. Akabori, S. Sakurai, Y. Izum, and Y. Fujii, *Biokhimiya*, 22, 154 (1957).

(3) M. P. Balfe, J. Kenyon, and D. Y. Wadden, *J. Chem. Soc.*, 1367 (1954); F. J. Impastato, L. Barash, and H. M. Walborsky, *J. Am. Chem. Soc.*, **81**, 1514 (1959); H. M. Walborsky, T. Sugita, M. Ohno, and Y. Inouye, *J. Am. Chem. Soc.*, **82**, 5255 (1960); H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 486 (1961).

(4) P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960); G. I. Fray and R. Robinson, *J. Am. Chem. Soc.*, **83**, 249 (1961).

(5) The product was shown, by gas chromatography, not to be contaminated by (−)- menthol. The residue from the distillation had a zero rotation and showed the absence of carbonyl absorption in the infrared.

(6) Longer reaction time caused extensive polymerization.

(7) At our present state of knowledge we cannot assess the role that the aluminum chloride is playing in the asymmetric synthesis. Indeed, the observation that the glycol of opposite configuration is obtained may not be due to the catalyst at all but to a temperature effect [see H. Pracejus, *Ann.*, **624**, 9 (1960)]. Another possibility is that the product from the thermal reaction is the thermodynamically controlled product whereas the $AlCl_3$ catalyzed reaction gives rise to the kinetically controlled product.

(8) B. Carnmalm, *Arkiv för Khim.*, **15**, 215 (1960).

(9) All new compounds gave satisfactory elemental analyses. All rotations were taken in chloroform with the exception of 4-cyclohexene-*trans*-1,2-dicarboxylic acid which was taken in ethanol.

of this reaction, as it pertains to asymmetric synthesis, is currently being investigated.[10]

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[10] We gratefully acknowledge the technical assistance of Mr. D. M. Borgnaes.

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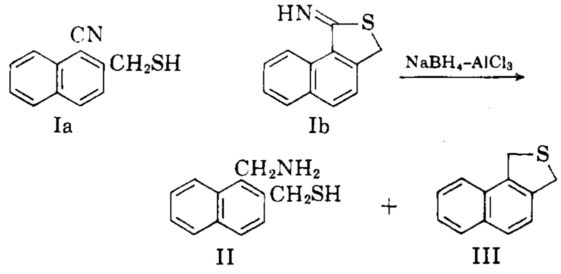
A Tautomeric Nitrile–Thiol Iminothiolactone System

Sir:

In working with an intermediate, thought to be a 2-mercaptomethyl-1-naphthonitrile (Ia),[1] an interesting type of ring-chain tautomerism has been observed. When (Ia,b)[2] was reduced with sodium borohydride–aluminum chloride (3:1), its tautomeric character became apparent in that products corresponding to both chain (II, 17%) and ring (III, 48%) forms resulted. 2,5-Naphtho(1,2-*c*)-thiophene (III) was separated from the reaction mixture after it had been poured into ice water and recrystallized from ethanol, m.p. 111–112°. *Anal.* Calcd. for $C_{12}H_{10}S$: C, 77.38; H, 5.41; S, 17.21. Found: C, 77.50; H, 5.23; S, 17.12. After the separation of III, a tacky solid remained which was treated with concentrated hydrochloric acid; crystallization of the resulting material from methanol-ether gave 1-aminomethyl-2-mercaptomethylnaphthalene hydrochloride (II), m.p. 219–220.5° dec. *Anal.* Calcd. for $C_{12}H_{14}ClNS$: C, 60.11; H, 5.89; N, 5.84. Found: C, 59.91; H, 5.90; N, 5.87.



It was found that when the proportion of sodium borohydride to aluminum chloride was increased from 3:1 to 4:1, II was obtained as the sole product (90%). The formation of III under the alternate conditions constitutes a new sulfide synthesis. The structure of III was readily confirmed by desulfurization with Raney nickel to 1,2-dimethylnaphthalene.

In the solid state, the structure of Ia,b appears to be Ib as there is no band for the $C\equiv N$ at 2225 cm.$^{-1}$ or for SH at 2555 cm.$^{-1}$, as in the case for the corresponding 4-mercaptomethyl-1-naphthonitrile, m.p. 97–98°. *Anal.* Calcd. for $C_{12}H_9NS$: C, 72.31; H, 4.55; S, 16.09. Found: C, 72.19; H, 4.93; S, 15.91. Further, Ia,b forms a hydrochloride and acetyl derivative, and the latter derivative can be degraded with Raney nickel to yield the anticipated product.

Under basic conditions, it was possible to demonstrate the acyclic tautomeric structure by other reactions. With alkaline hydrogen peroxide, Ib oxidized smoothly to a disulfide (86%), m.p. 192.5–193°. *Anal.* Calcd. for $C_{24}H_{16}N_2S_2$: C, 72.70; H, 4.07; S, 16.17. Found: C, 72.62; H, 4.15; S, 16.35. Also Ib reacted with benzyl chloride in ethanolic sodium hydroxide to give the anticipated sulfide, 2-benzylmercaptomethyl-1-naphthonitrile, m.p. 53.5–54.5°. *Anal.* Calcd. for $C_{19}H_{15}NS$: C, 78.86; H, 5.23; S, 11.08. Found: C, 78.75; H, 5.32; S, 11.23.

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[1] Compound Ia,b was prepared from 2-(1-methylisothiuronium)-1-naphthonitrile bromide in 81% yield. The isothiouronium salt in turn was obtained from 2-bromomethyl-1-naphthonitrile (78%) while the latter substance was prepared by the action of *N*-bromosuccinimide on 2-methyl-1-naphthonitrile in a 71% yield.

[2] The form Ib may also be represented as an amino tautomer, *cf.*, A. J. Boulton and A. R. Katritzky, *Tetrahedron*, 12, 51 (1961).

Titanium-Catalyzed Isomerization and Olefin-Exchange Reactions of Alkylmagnesium Halides: A Novel Method for Preparation of the Grignard Reagent

Sir:

George and Ladd[1] found that when isopropylmagnesium bromide reacts with chlorosilanes in the presence of titanium tetrachloride the coupled product contains both isopropyl and *n*-propyl groups.

$$(CH_3)_2CHMgBr + \equiv SiCl \xrightarrow{TiCl_4} (CH_3)_2CHSi\equiv + CH_3CH_2CH_2Si\equiv \quad (1)$$

This discovery prompted us to undertake a further investigation of the effect of small amounts of titanium tetrachloride on the reactions of Grignard reagents. It has been found that the formation of rearranged products from isopropylmagnesium bromide is not peculiar to reactions of chlorosilanes, but is a general reaction, presumably due to isom-

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[1] P. D. George and J. R. Ladd, Abstracts of Papers presented at the 140th Meeting of the American Chemical Society, Chicago, Ill., September, 1961.