2,2′-Anhydro-1-(5′-*O*-trityl-β-D-arabinofuranosyl)uracil (III). **A.**[1]—A solution of 3.25 g. (6.7 mmoles) of 5′-*O*-trityluridine and 1.34 g. (7.4 mmoles) of bis(imidazol-1-yl)thione in 30 ml. of toluene was heated at reflux for 0.5 hr. After cooling, the solid product was collected and recrystallized from ethanol. The yield of III, was 2.7 g. (86%), m.p. 217–219°, $[\alpha]^{24}\text{D}$ −20.5° (*c* 1, CH_3OH).

B.—A solution of 100 mg. of 5′-*O*-trityluridine 2′,3′-thionocarbonate (II) and 25 mg. of imidazole in 4 ml. of toluene was heated at reflux for 0.5 hr. After a work-up as in part A, a nearly quantitative yield of III was obtained. Similar results were obtained when 200 mg. of II was heated at reflux with 30 mg. of potassium *t*-butoxide in 4 ml. of ethanol for 5 min.

2′,3′-Didehydro-2′,3′-dideoxy-5′-*O*-trityluridine (IVa).—Raney nickel (1.5 g.) was boiled with a mixture of 75 ml. of acetone, 15 ml. of ethanol, and 1 ml. of ethyl acetate for 2 hr. After the addition of 1.6 g. of the thionocarbonate II, refluxing was continued for 6 hr. After removal of the catalyst and solvent, the residual syrup was triturated with ether to obtain 400 mg. of the crystalline cyclonucleoside III. The ethereal filtrate was chromatographed on silica gel (40 g.). Elution with methanol–methylene chloride, 1.5:98.5, furnished 250 mg. of the unsaturated nucleoside IVa, m.p. 193°, t.l.c. R_f 0.62. The melting point, mixture melting point, t.l.c. running rate, and infrared spectrum were identical with those of a sample of IVa prepared by the method of Horwitz.[4]

3-*N*-Methyl-5′-*O*-trityl-2′,3′-didehydro-2′,3′-dideoxyuridine (IVb).—A mixture of 3.4 g. of the thionocarbonate II and 15 ml. of trimethyl phosphite was heated at reflux under a nitrogen atmosphere for 65 hr. Most of the trimethyl phosphite was removed *in vacuo*, and the residue was stirred with 300 ml. of 0.5 *N* sodium hydroxide for 0.5 hr. The product was extracted into ether and dried over magnesium sulfate, and the solvent was pumped off. The crude product was obtained as a glass, 2.76 g. (89%). Thin layer chromatography showed a large spot with R_f 0.92 and a much smaller spot with R_f 0.60. A sample of the crude product was extracted repeatedly with hot petroleum ether (b.p. 30–60°). Upon cooling the extracts, an amorphous solid separated, m.p. 60–80°, which now showed one spot, R_f 0.92. The n.m.r. spectrum in deuteriochloroform showed a signal at τ 6.68 for 3-NCH_3, and no signal corresponding to 3-NH: $\lambda_{\max}^{\text{EtOH}}$ 260 mμ (ϵ 7370), $\lambda_{\max}^{\text{EtOH}}$ 244 mμ (ϵ 5120). The spectrum was essentially unchanged in alkaline solutions.

Anal. Calcd. for $C_{29}H_{26}N_2O_4$: C, 74.66; H, 5.62; N, 6.01. Found: C, 74.03; H, 5.80; N, 6.16.

Acid Hydrolysis of IVb.—A solution of 1.7 g. of IVb in 80% acetic acid was heated on the steam bath for 10 min. After dilution with water, trityl alcohol was separated by extraction with ether. Evaporation of the aqueous layer yielded 0.95 g. of oil, which was chromatographed on silica gel. Elution with methanol–methylene chloride, 1:24, yielded crystals of 3-methyluracil: m.p. 179–181°[8]; $\lambda_{\max}^{\text{pH 7}}$ 259 mμ; $\lambda_{\min}^{\text{pH 7}}$ 230 mμ; $\lambda_{\max}^{\text{pH 12}}$ 283, 223 mμ; $\lambda_{\min}^{\text{pH 12}}$ 243 mμ.[9]

Anal. Calcd. for $C_5H_6N_2O_2$: C, 47.62; H, 4.80; N, 22.22. Found: C, 47.69; H, 4.87; N, 22.15.

5′-*O*-Trityluridine 2′,3′-dimethylorthocarbonate (V).—A solution of 528 mg. of the thionocarbonate II in 20 ml. of dry methanol was stirred overnight with 2.5 g. of silver carbonate at room temperature. After filtration, the solvent was removed *in vacuo*. The crude product was taken up in ether and filtered, and the solution was evaporated. Recrystallization from ethanol yielded 320 mg. of V: m.p. 198–200°, t.l.c. R_f 0.60, $\lambda_{\max}^{\text{EtOH}}$ 258 mμ (ϵ 9730), $\lambda_{\min}$ 242 mμ. The n.m.r. spectrum in deuteriochloroform showed signals at τ 6.55 (doublet, H-5′), 6.52, and 6.60 (–OCH_3). The integrated curve indicated eight protons for this group of signals. In pyridine solution the signals occurred at τ 6.30 (multiplet, H-5′), 6.44, and 6.54 (–OCH_3). The remainder of the spectrum is consistent with the nucleoside structure.

Anal. Calcd. for $C_{31}H_{30}N_2O_8$: C, 66.90; H, 5.07; N, 5.03, methoxyl, 11.4. Found: C, 66.70; H, 5.52; N, 5.26; methoxyl, 10.3.

Uridine 2′,3′-Carbonate (VI).—A solution of 100 mg. of V in 2 ml. of 80% glacial acetic acid was heated on the steam bath for 15 min. After removal of trityl alcohol, the nucleoside was recrystallized from ethanol. The substance forms a viscous melt at 95° and liquifies at 140°: $\lambda_{\max}^{\text{Nujol}}$ 5.55 (cyclic carbonate), 2.9 (OH), 5.9–6.0 (pyrimidinone) μ; t.l.c. R_f 0.16.

Anal. Calcd. for $C_{10}H_{10}N_2O_7$: C, 44.45; H, 3.73; N, 10.37. Found: C, 44.38; H, 4.00; N, 10.24.

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The Reaction of β-Chloro-α,β-alkenoic Esters with Nucleophiles

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It has been reported[2] that displacement of the halogen atom of ethyl β-chloro-*cis*- and -*trans*-crotonates by sodium benzenethiolate gave products with partial inversion of configuration. Jones, *et al.*,[2] state that the *cis*-chloro isomer gave 12% of the *trans* product and the *trans* isomer gave 36% of the *cis* product. We found that the reaction of the sodium benzene- and mesitylenethiolates with the isomeric chlorocrotonates gave products of essentially retained configuration (<5% inversion), Table I. In addition, the reaction of ethyl 3-chloro-4-methyl-2-pentenoate with sodium benzenethiolate gave only one replacement product, ethyl 3-phenylthio-4-methyl-2-pentenoate. From infrared and n.m.r. spectra and stability considerations we believe that both reactant and product have the *cis* configuration.[3] We found no evidence for the existence of the *trans* isomer.

TABLE I

THE REACTION OF ETHYL β-CHLORO-*cis*- AND -*trans*-CROTONATES WITH CERTAIN NUCLEOPHILES

Chlorocrotonate	Nucleophile	Product, % *cis*	Product, % *trans*	Product yield, %
cis	PhS^-	97	3	80
trans	PhS^-	5	95	95
cis	$MesS^-$ [a]	100	0	95
trans	$MesS^-$ [a]	5	95	55

[a] $MesS^-$ refers to the mesitylthio anion.

The discrepancy between our work and that reported earlier[2] appears to be owing to the method of estimation of the *cis–trans* isomer ratio. It is known[2] that the *trans* isomer undergoes thermal isomerization, and thus any method depending upon distillation or gas chromatographic techniques is questionable. We determined the isomer ratio by using the areas of the vinylic proton peaks in the n.m.r. spectra of the crude esters as a quantitative measure of the amount of each isomer present. The reaction mixture was kept at 3° and the crude esters were isolated at room temperature, thus keeping thermal isomerization to a

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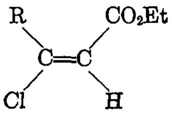
[3] J. S. Pizey and W. E. Truce, *ibid.*, 865 (1964).

minimum. We feel that the method gives a more accurate picture of the isomer ratio of the products of the reaction than previous procedures. We obtained similar results to those of Jones[2] when the products of the reaction were isolated by distillation and the ratio was determined from the amounts of isolated *cis* and *trans* isomers.

It would therefore appear that the partial inversion of configuration observed by Jones[2] in the reaction of sodium benzenethiolate with the ethyl β-chlorocrotonates was due to thermal isomerization during the isolation of the product and is not inherent in the reaction. Our results show that there is no inversion of configuration of reactants during the reaction and also that the products are obtained with essentially retained configuration (>95%). It would thus seem that the mechanism advanced by Jones, *et al.*,[2] requires some modification. They suggest that inversion should take place when the grouping R is bulky. We synthesized the chloroalkenoate having



R = isopropyl, ethyl 3-chloro-4-methyl-2-pentenoate, and did not observe any inversion of configuration in the substitution reaction with sodium benzenethiolate. Thus, the reaction does not obey the simple steric hindrance factors they postulate. The mechanism advanced by Miller and Yonan,[4] in which they postulate inversion at a carbon atom adjacent to the reaction site to be faster than internal rotation, would agree with our facts. We assume the incoming nucleophile and the electron pair enter *trans* in the plane of the original π-orbital and the halide departs only when it is *trans* to the electron pair. It will thus be seen that, for retention to occur, the halide ion needs only to rotate through 30° and the steric hindrance factors advanced by Jones, *et al.*,[2] are relatively unimportant. This would agree with the observed retention figures given in Table I and also the retention of configuration in the reaction of sodium benzenethiolate with ethyl 3-chloro-4-methyl-2-pentenoate.

It must, however, be stated that the experimental evidence for the two assumptions given above is inadequate, and thus further work is necessary before any final conclusion may be made about the mechanism of the reaction.

Experimental Section

The configuration of the products was determined using infrared spectra[2] in the region of 800–1000 cm.$^{-1}$ and by determination of the vinylic proton and vinylic methyl chemical shifts with a Varian A-60 n.m.r. spectrometer[3] operating at a frequency of 60 Mc.p.s. Samples were run in carbon tetrachloride at approximately 10% concentration using tetramethylsilane as an internal standard.

The products were obtained by the reaction of the appropriate ethyl chloroalkenoate (*ca.* 10% excess) in alcohol with the sodium salt of the thiol in alcohol. The solutions were mixed at 3° and left to stand at 3° for 4 hr. The mixture was then poured into water and the product was either filtered off or extracted with peroxide-free ether.

The preparation and physical data of the compounds discussed in this paper have been described elsewhere.[5]

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Magnetic Nonequivalence of Methylene Group Protons in 1,2-Disubstituted Ferrocenes

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Diastereomeric[2] methylene protons adjacent to an element of dissymmetry such as an asymmetric atom[3,4] or a twisted biphenyl[2,5] have been reported to show magnetic nonequivalence in a variety of solvents and over a range of temperatures. Uncertainty has existed, however, as to the relative importance of conformational effects *vs.* the "intrinsic asymmetry" of the molecule. Somewhat opposing views have been presented recently by Roberts,[4] *et al.*, and Gutowsky, *et al.*[6]

A recent n.m.r. investigation[7] of a series of *ortho*- and *meta*-substituted N,N-dimethylbenzylamines has demonstrated that an asymmetric group in the *ortho* or *meta* side chain in every case was accompanied by magnetic nonequivalence of the methylene group protons in the amine side chain. Those benzylamines which did not bear an asymmetric group exhibited an apparent methylene singlet. These results are supported by n.m.r. spectra of two phthalans[8] related to the compounds previously studied. The present report concerns the n.m.r. spectra of the 1,2-disubstituted ferrocene analogs of five of the previously studied symmetrical *ortho*-substituted benzene derivatives, their formulas being I–V. As expected,[7,8] all five ferrocenes displayed magnetically nonequivalent methylene-group protons, providing a novel demonstration of the asymmetry of these ferrocenes.[9] The results reveal a difference in chemical shift for the expected[7,8] nonequivalent methylene-group protons as large as 1 order of magnitude greater than in the corresponding *ortho*-substituted benzene compounds. Conformational effects which are peculiar to ferrocenes[10] do not allow an unambiguous assignment of the origin of the observed nonequivalence.

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