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THE STEREOCHEMISTRY OF NUCLEOPHILIC ADDITION OF THIOPHENOLS TO PROPIOLIC ACID AND ETHYL PROPIOLATE

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β-ARYL-mercapto-acrylic acids, cis (I) and trans (II), were previously prepared by Montanari and Negrini:[1] (I) by base-catalyzed addition of thiophenols to propiolic acid and by nucleophilic substitution of halogen with thiols in cis-β-chloro-acrylic acid, (II) by similar nucleophilic substitution in trans-β-chloro-acrylic acid, by thermal inversion of (I) and by reduction of trans acids (III). The sulphones, sulphoxides, esters and chlorides of acids (I) also undergo thermal inversion in the same sense.

In a recent paper[2] W.E. Truce assigned the opposite configuration to (I) and (II), on the basis of I.R. spectra, dipole moments, and the rate of cyclization of (I) and (II) to thia-chromones. Truce obtained his "trans" acid (I) by addition of p-toluenethiol to propiolic acid,

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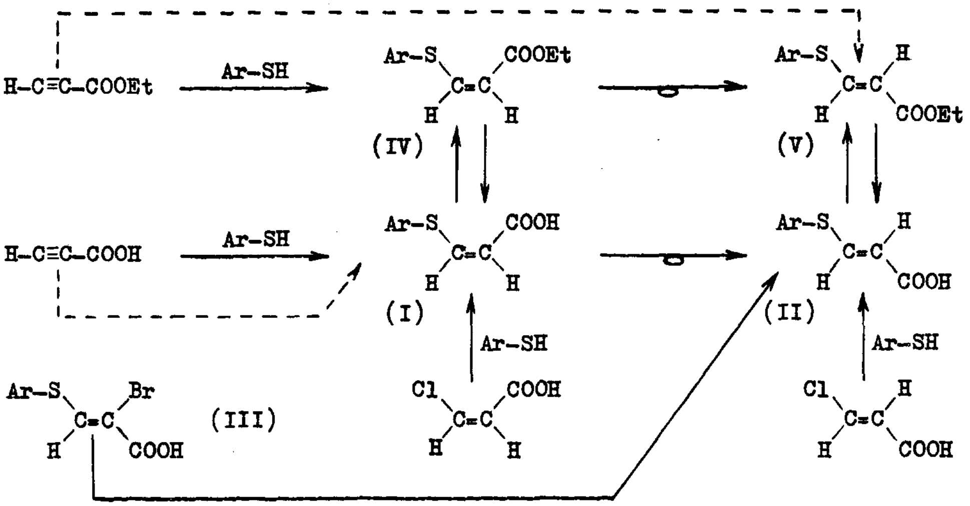
[1] F. Montanari and A. Negrini, Gazz. chim. ital. **87**, 1073, 1102 (1957).

[2] W.E. Truce et al., J.Am.Chem.Soc. **81**, 4931 (1959); see also: ibid. **79**, 5311 (1957).

and his "cis" acid (II) by analogous addition of p-toluenethiol to ethyl propiolate, followed by saponification. (— reactions by Montanari, — reactions by Truce).



Ar = C_6H_5 (I) m.p. 106° (II) m.p. 127-8°

Ar = p-CH_3-C_6H_4- (I) m.p. 143-4° (II) m.p. 137-8°

Thus two opposite mechanisms, of respectively cis and trans addition, would occur in the two cases, with violation of the rule of trans-nucleophilic addition of thiols to triple bond in propiolic acid.

Truce's paper made necessary a complete re-examination of the problem, and we wish to report our principal conclusions.

i) The addition of p-toluenethiol to ethyl propiolate at room temperature for 24 hr, with a catalitic amount of morpholine in ethanol, yields 96%

ester (IV) [m.p. 47-8°, hexane; Found: S, 14.32. $C_{12}H_{14}O_2S$ requires S, 14.42] ; saponification gives acid (I) which may be esterified again to (IV).

Ester (IV) is partially inverted to its isomer (V) by thiolate ion in ethanol at room temperature or by vacuum distillation, i.e. under Truce's conditions. Since ester (V) [b.p. 149.5-150.5° (4 mm), n_D^{20} 1.5752; Found: S, 14.32. $C_{12}H_{14}O_2S$ requires S, 14.42] is identical to the product obtained by Truce [b.p. 134-8° (1.3-1.5 mm), n_D^{20} 1.5748] we may conclude that Truce's conditions are not correct, and the nucleophilic addition of thiols to propiolic acid and ethyl propiolate follows a single steric course.

ii) The I.R. spectrum in Nujol of acid (II) (Ar = C_6H_5) exhibits a strong absorption band at 960 cm^{-1}, absent in (I), which is typical of trans disubstituted ethylenes.[3,4] The same band was recorded by Truce, but it was unaccounted for.

iii) Truce claims to have measured the rate of cyclization to thia-chromones of acids (I) and (II), but under the conditions followed he actual=

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[3] The Author wishes to express his gratitude to Professor San-ichiro Mizushima of the University of Tokyo, for discussion and interpretation of the infrared spectra. He is also indebted to Prof. A. Foffani of the University of Padua for infrared measurements.

[4] L.J. Bellamy, The Infra-red Spectra of Complex Molecules p. 40. John Wiley, New York (1954); F.A. Miller, in H. Gilman, Organic Chemistry Vol. III, p. 154. John Wiley, New York (1953); W.J. Potts and R.A. Nyquist, Spectrochimica Acta 679 (1959).

ly measured the total rate of chlorination and successive cyclization.

iv) The dipole moments of sulphones related to (I) and (II) may hardly be used as a proof of *cis-trans* configuration, the true conformation of Ar-SO_2-group in both isomers being unknown.

v) Retention of configuration and no deuteration was found by C.A. Vernon[5] in the reaction products of *cis*- and *trans*-β-chloro-ethyl-crotonate and $EtS^{(-)}$, when run in CH_3OD. This is a definitive proof of direct nucleophilic attack on the halogenated carbon, in agreement with the mechanism we proposed for the synthesis of (I) and (II) from *cis*- and *trans*-β-chloroacrylic acids.[1,6]

vi) P-tolyl-mercapto-propiolic acid (VI) Me-C_6H_4-S-C≡C-COOH [m.p. 92-3°, benzene/pet. ether; Found: S, 16.57. $C_{10}H_8O_2S$ requires S, 16.68] is catalitically hydrogenated (Pd-charcoal or Ni-Raney W-5, excess) to give 15% of isomer (I), m.p. 143-4° (all of the remaining product is absorbed by the catalyst and no other compound is isolated). Hydrogenation of (VI) with $NaBH_4$ in diglyme at 0° furnishes quantitatively (II), m.p. 137-8°.[7]

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[5] Private communication of C.A.Vernon (University College, London) to G.Modena, of this Department; D.E. Jones and C.A. Vernon, *Nature* **176**, 791 (1957).

[6] F. Montanari et al., *Boll.sci.Fac.chim.ind.,Bologna* **16**, 31, 140 (1958); *Gazz.chim.ital.* **89**, 1543 (1959); see also: G.Modena et al., *Ricerca sci.* **28**, 341 (1958); *Gazz.chim.ital.* **89**, 854, 866, 878 (1959).

[7] These conditions are similar to those for trans-hydrogenation of triple bond with $LiAlH_4$ [R.A.Raphael, *Acetylenic Compounds in Organic Synthesis* Butterworths Scient. Publ., London (1955), p. 29, 202] but differ from cis hydrogenation with $NaBH_4$ and boron trifluoride etherate [H.C. Brown and G.Zweifel, *J.Am.Chem.Soc.* **81**, 1512 (1959)].

vii) In the Diels-Alder reaction with cyclopentadiene, cis acid $C_6H_5-SO_2-CH=CH-COOH$ gives 91% endo adduct (carboxyl), m.p. 198-9°, and 9% exo, m.p. 233-5°, while trans gives 39% endo, m.p. 183°, and 61% exo, m.p. 179-81°,[8] in agreement with the Alder rule.[9]

All these results are consistent with a cis configuration for acids (I) and a trans configuration for acids (II).

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[8] D. Albera and F. Montanari, research in progress.

[9] K. Alder and G. Stein, Angew. chem. **50**, 510 (1937).