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Steric Hindrance in Alkyl-Substituted Atropic Acids

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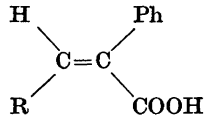
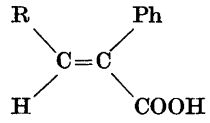
The ultraviolet spectra of the methyl- and ethyl-atropic acids and unsubstituted atropic acid (α-phenyl-acrylic acid) have been recorded. On the basis of these spectra the *cis*-structure is assigned to the low-melting isomers and the *trans*-structure to the high-melting isomers of the alkyl-substituted atropic acids.

The two isomers of methylatropic acid (2-phenyl-2-butenoic acid) are known, one melting at 99° and the other at 137°.[1] Carpino [2] has prepared both by treatment of 3-methyl-4-phenyl-4-chloro-2-pyrazolin-5-one with aqueous sodium hydroxide. He suggests that the low-melting isomer has the *cis*-structure and consequently that the high-melting has the *trans*-structure.



cis



trans

R = Me, Et

The supports for these tentative structures are (1) the fact that the low-melting isomer is formed in a higher yield than the high-melting (the method as a rule gives a mixture in which the more labile isomer predominates), (2) the greater acidity of the low-melting isomer and (3) its lesser rate of esterification. The present work supports this assignation by ultraviolet spectra (Table 1) recorded for the methyl-atropic acids as well as for the ethyl-atropic acids and the unsubstituted atropic acid. Spectra of the low-melting isomers of methyl- and ethyl-atropic acids are very similar and so are the spectra of their high-melting isomers. However, if the spectra of the low-melting and high-melting forms are compared, there are striking differences.

The low-melting isomers have a marked maximum of absorption just below 2500 Å as for the unsubstituted atropic acid. Contrary to this their high-melting isomers show only a sloping curve with a faint inflexion instead of a maximum. (The spectrum of the high-melting methyl-atropic acid is

Table 1. Ultraviolet spectra of atropic acids determined in ethanol solution.

$RHC=C\begin{matrix}Ph\\COOH\end{matrix}$ R	λ Å	log ε	λ Å	log ε
H	2460	3.77		
CH_3 (*cis*)	2470	3.99	2910[a]	2.46
CH_3 (*trans*)	2340[a]	3.74		
C_2H_5 (*cis*)	2490	4.04	2910[a]	2.57
C_2H_5 (*trans*)	2350[a]	3.74		

[a] shoulder.

reported earlier. Campbell *et al.*[3] give two inflexion points: $\lambda = 2280$ Å, $\varepsilon = 5840$ and $\lambda = 2540$ Å, $\varepsilon = 2505$, while Morton and Grovenstein [4] report only that the absorption curve has no maximum).

The explanation of this must be that in the high-melting isomers the conjugation between the benzene nucleus and the rest of the molecule is hindered for sterical reasons. This is easily demonstrated by Stuart-Briegleb models and is also shown in Fig. 1 which demonstrates a plane-projection of

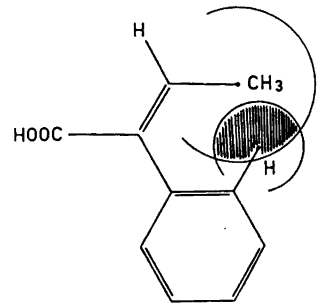


Fig. 1. Steric interference in *trans*-methyl-atropic acid. As reasonable values for the radii of interaction 0.85 of the van der Waals radii have been chosen (for H 1.0 Å, for CH_3 1.7 Å). The bond lengths used are Ph–H 1.1 Å, Ph–C 1.44 Å, C=C 1.34 Å, C–CH_3 1.54 Å and the benzene bonds 1.39 Å.[10] All angles are 120°.

trans-methyl-atropic acid. The methyl (and the ethyl) group occupies a portion of space which is sufficient to hinder the coplanar arrangement of the phenyl group and the double bond in the *trans*-structure, *i.e.*, the isomer where the alkyl and phenyl groups are on the same side of the double bond. In the *cis*-structure the coplanar arrangement of the phenyl group and the double bond is not hindered by the alkyl group. Thus, the *cis*-acid can be expected to have a spectrum reminiscent of that of the unsubstituted atropic acid. The spectra of the high-melting isomers show both a hypsochromic and a hypochromic shift compared to the spectra of the low-melting ones. This is a well-known effect in spectra of crowded molecules.[5] These facts clearly show that the *trans*-structure must be assigned to the high-melting and the *cis*-structure to the low-melting isomers.

Table 2. Infrared spectra of atropic acids.

Atropic acid 3100 b (64), 3058 (66), 3020 (66), 2923 b (64), 2895 b (64), 2850 b (61), 2720 b (52), 2610 b (53), 2520 (44), 2203 (23), 2050 (22), 1960 (23), 1930 (30), 1893 (24), 1750 (31), 1680 (84), 1649 sh (64), 1608 (64), 1482 (45), 1419 (78), 1400 (39), 1323 (50), 1310 (65), 1280 (51), 1220 (84), 1090 (53), 1070 (45), 1023 (34), 999 (26), 965 (69), 898 (67), 812 (34), 770 (66), 755 (44), 695 (78), 678 (40).

Cis-methyl-atropic acid 3073 (46), 3055 (48), 3018 (49), 2755 (38), 2615 (39), 2558 (39), 1945 (33), 1875 b (34), 1685 sh (61), 1660 (83), 1618 (50), 1592 (39), 1480 (37), 1425 (53), 1408 sh (36), 1373 (29), 1340 (39), 1290 (56), 1267 (43), 1230 (64), 1193 sh (31), 1155 (27), 1108 (26), 1068 (28), 1025 (25), 995 (25), 932 (49), 850 (36), 790 (25), 777 (33), 750 (54), 690 (68), 648 (30).

Trans-methyl-atropic acid 3080 (54), 3055 (57), 3020 (55), 2978 (56), 2946 (55), 2850 (55), 2800 sh (52), 2620 b (51), 2530 (49), 2350 b (32), 2020 b (24), 1940 (25), 1870 (26), 1660 (88), 1625 (70), 1595 (48), 1488 (43), 1420 (66), 1375 (37), 1350 (30), 1295 (84), 1195 (58), 1158 (29), 1110 (25), 1065 (30), 1015 (30), 930 (67), 870 (40), 770 (53), 743 (53), 689 (80, 668 (53).

Cis-ethyl-atropic acid 3050 b (61), 3020 (60), 2963, (62) 2930, (56) 2870 (52), 2610 vb (36), 1953 (25), 1685 (73), 1640 (63), 1590 sh (46), 1483 (39), 1433 sh (39), 1415 (43), 1395 (46), 1372 sh (38), 1340 (32), 1305 (37), 1268 (42), 1243 (50), 1210 (72), 1180 (64), 1130 (44), 1063 (33), 1013 (29), 885 (47), 808 (32), 772 (38), 742 (39), 692 (67), 647 (32).

Trans-ethyl-atropic acid 3075 (54), 3053 (56), 3020 (56), 2972 sh (63), 2963 (66), 2928 (61), 2868 (59), 2635 b (49), 2600 b (49), 2545 b (46), 2350 b (35), 1943 (27), 1870 (27), 1800 (29), 1670 (86), 1620 (59), 1593 (46), 1488 (39), 1445 (40), 1435 (32), 1415 (61), 1368 (38), 1285 (78), 1249 (56), 1195 (57), 1128 (33), 1065 (30), 1025 (35), 963 (42), 923 (44), 910 (48), 800 (37), 780 (50), 745 (49), 690 (74), 669 (46).

The spectra were recorded with the KBr disc technique (*ca.* 1 mg of the sample in 300 mg of KBr). Percentage absorption is indicated in brackets after the wave number in cm^{-1}.

b broad, vb very broad, sh shoulder.

The infrared spectra of all five acids have been recorded (Table 2) to examine whether there are differences, which may be used for assignment of *cis*- and *trans*-structure. The differences are not very significant. The *trans*-acids have a medium to strong band at 668 cm^{-1} (methyl acid) and 669 cm^{-1} (ethyl acid) which is missing in the *cis*-acids. Instead these have a medium to strong band at 648 cm^{-1} (methyl acid) and 647 cm^{-1} (ethyl acid). Besides the *trans*-acids have a strong band at 1195 cm^{-1}, which is missing in the *cis*-acids (however, *cis*-ethyl-atropic acid has two strong bands at 1180 and 1210 cm^{-1}).

Of the two ethyl-atropic acids only the *trans*-isomer has been earlier reported.[6] Both the methyl- and ethyl-substituted acids have in the present work been prepared mainly according to methods, which Jönsson [1] has described for the preparation of the methyl acids. *Via* the cyanohydrins of propiophenone and butyrophenone, ethyl-phenyl-glycolic acid and propyl-phenyl-glycolic acid are prepared,[7] which then are dehydrated to the unsaturated acids. The *cis*-acids are formed when the elimination of water is accomplished by cold concentrated sulphuric acid and the *trans*-acids when the water-eliminating agent is boiling hydrochloric acid.

Just as is the case with the *cis*-methyl-atropic acid,[1] the *cis*-ethyl-atropic acid can be converted to the *trans*-structure by boiling hydrochloric acid.

EXPERIMENTAL

Cis-*methyl-atropic acid.* This acid was prepared according to the method described by Jönsson.[1] Dissolution of the crude product in alcohol and precipitation with water gave 58 % of a product melting at 94—95°. Recrystallization from water gave pure *cis*-methyl-atropic acid melting at 97—98° (lit. values: 98.5—98.9°[1], 98.5—100°[2]). Absence of absorption bands at 668 cm^{-1} (strong) and 870 cm^{-1} (medium), which appear in the spectrum of *trans*-methyl atropic acid, showed that the product was free from this isomer (Table 2).

p *Bromo-phenacylic ester of cis-methyl-atropic acid.* The ester was prepared (like all the other *p*-bromo-phenacylic esters in this work) according to the general procedure recommended by Shriner, Fuson and Curtin.[8] M.p. 65.0—65.5°, recrystallized from alcohol.

Trans-*methyl-atropic acid.* The acid was prepared according to Jönsson [1] but instead of concentrated hydrochloric acid a 20 % hydrochloric acid was used to avoid the evolution of hydrogen chloride. Dissolution of the crude product in glacial acetic acid and precipitation with water gave 64 % of acid melting at 136.5—137.5°. Recrystallization from water raised the melting point to 137.5—138.0° (lit. values: 136.6—137.0°,[1] 134—136.5°[2]). Absence of absorption bands at 648 cm^{-1} (medium) and 1230 cm^{-1} (strong), which appear in the spectrum of *cis*-methyl-atropic acid, showed that the product was free from this isomer. (Table 2).

p-*Bromo-phenacylic ester of trans-methyl-atropic acid.* The ester, recrystallized from alcohol, melted at 81.5—82.5° (lit. values: two modifications melting at 78° and 86.6—87.8°.[4] These two modifications were not observed).

Cis-*ethyl-atropic acid.* 75.0 g of propyl-phenyl-glycolic acid were dissolved in 375 ml of concentrated sulphuric acid with stirring at room temperature. After 5 min the dark-coloured solution was poured into 3 liters of ice-water. *Cis*-ethyl-atropic acid precipitated as an oil, which soon solidified. The precipitate was filtered and washed with water and was then dissolved in 500 ml of light petroleum (b.p. 40—60°). The solution was washed with water to remove remaining sulphuric acid and then dried over anhydrous magnesium sulphate. The solvent was evaporated until approximately 70—80 ml remained. (In small-scale preparation it is better to proceed in the following way: the crude acid is dissolved in ether, washed with water, dried, evaporated to dryness and then recrystallized from light petroleum). The yield was 44.4 g (65 %) with m.p. 43.5—46.0°. After further recrystallizations from light petroleum and water the pure *cis*-ethyl-atropic acid melted at 46.5—47.5°. (Found: C 74.8; H 6.75. Required: C 75.0; H 6.86). Absence of absorption bands at 669 cm^{-1} (medium) and 1285 cm^{-1} (strong), which appear in the spectrum of *trans*-ethyl-atropic acid, showed that the product was free from this isomer. (Table 2).

p-*Bromo-phenacylic ester of* cis-*ethyl-atropic acid.* The ester, recrystallized from alcohol, melted at 68.0—68.5°.

Trans-*ethyl-atropic acid* (from propyl-phenyl-glycolic acid). 30.0 g of propyl-phenyl-glycolic acid were refluxed with 600 ml of 20 % hydrochloric acid for 24 h. On cooling the *trans*-ethyl-atropic acid slowly crystallized. The solid was filtered and thoroughly washed with water. The dried crystals were recrystallized from petroleum (b.p. 80—110°). The yield was 16.9 g (62 %) melting at 63.5—65.5°. On further recrystallizations from petroleum and water pure *trans*-ethyl-atropic acid was obtained with m.p. 65.5—66.0° (lit. values: 67.5—68.5°[6]). (Found: C 75.0; H 6.94. Required: C 75.0; H 6.86). Absence of absorption bands at 647 cm^{-1} (medium) and 1210 cm^{-1} (strong), which appear in the spectrum of *cis*-ethyl-atropic acid, showed that the product was free from this isomer. (Table 2).

Trans-*ethyl-atropic acid* (from *cis*-ethyl-atropic acid). 1.00 g of *cis*-ethyl-atropic acid was refluxed with 20 % hydrochloric acid for 24 h. On cooling the *trans*-ethyl-atropic acid solidified, was filtered, washed with water and dried. The yield was 0.75 g, which recrystallized from water gave 0.43 g (43 %) of *trans*-acid melting at 64.5—65.0°.

p-*Bromo-phenacylic ester of* trans-*ethyl-atropic acid.* The ester, recrystallized from alcohol, melted at 76—77°.

Atropic acid. The atropic acid used was kindly placed at the author's disposal by Mr. L.-E. Nilsson, which hereby is gratefully acknowledged. It was prepared according to Bougault [9] and melted at 107—108°. Infrared spectrum in Table 2.

p-*Bromo-phenacylic ester of atropic acid.* The ester, recrystallized from alcohol, melted at 82.0—82.5°.

The ultraviolet spectra were recorded with a Beckman DU spectrophotometer and the infrared spectra with a Perkin-Elmer Model 221 prism-grating instrument at the Infrared Laboratory, Chemical Institute, Lund. Determinations of the melting points were made with a Kofler micro hot stage. The analyses were carried out at the Department of Analytical Chemistry, Chemical Institute, Lund.

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