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The Isomeric Friedelanes

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As mentioned in the preceding paper there was observed a discrepancy between the rotation measured by us for friedelane, $[\alpha]_D$ +21°, and the one recorded in literature, $[\alpha]_D$ +42° [1], compare [2]. Furthermore, it had been impossible to prepare solutions for rotation measurements of concentrations above 1 % at 20° (compare [1]). Such attempts invariably led to precipitation of crystals, either at once on cooling to room temperature, or (in cases of the concentration only slightly exceeding 1 %) in the tube. The discrepancy seemed so serious that it was deemed worth while to investigate it more closely, and the more so since the structure of friedelane is unknown.

It has been shown that friedelin should be classified as a pentacyclic triterpenoid ketone, with the formula $C_{30}H_{50}O$ [3-5] and this view has been accepted by Ruzicka *et al.*[1]. Friedelin may be represented by the partially resolved formula —CH—CH—CO—CH_2—CH_2—$C_{25}H_{44}$ [1]. The ketonic function is present in a ring, which must be at least six-membered, since friedelin dicarboxylic acid, represented by —CH—CH—COOH HOOC—CH_2—$C_{25}H_{44}$ on pyrolysis furnished a ketone, represented by —CH—CH—CO—CH_2—$C_{25}H_{44}$ [1], compare also [6] and I.R. evidence of a ketone in a six-membered ring reported in the preceding paper. The partial formula of friedelin may be extended further to —CH—CH—CO—CH_2—CH_2—$C_{24}H_{44}$, since friedelonic (friedonic) acid is a keto-acid [1,7]. Friedelin, therefore, has an enolisable tertiary centre adjacent to the carbonyl group. For this reason there might exist two isomers of friedelin, which could give rise to two isomeric friedelanes. The other isomer of friedelin, however, can be present only in minute amounts, since it has been claimed by Drake and Jacobsen [3] that friedelin is easily obtained in a state of high purity when purified through its enol benzoate, and this statement, that friedelin is regenerated from its enol benzoate, has not been disputed by Ruzicka *et al.* [1]. Nevertheless, such isomer might be predominant under the reduction conditions recorded in literature. It, therefore, was undertaken to repeat as exactly as possible all the reported procedures,

except the reduction of cerin to friedelane by the Clemmensen method. In all cases the main product showed m.p. and rotation values close to those reported in the preceding paper. In the cases of reduction of friedelin and cerin according to Huang-Minlon [2], the mother liquors were successively concentrated and the rotation and m.p. as well as mixed m.p. with a reference specimen were determined (for details see the experimental part). No deviations from the values of the physical constants of the reference specimen could be observed, until 10—20 mg of substance were left. This material consisted almost exclusively of a very much more soluble component, which crystallised in fine needles from chloroform/acetone or from chloroform/methanol.

It should be emphasised that when cerin was reduced, the precautions recommended by Huang-Minlon [2] for alkali-sensitive substances were strictly maintained, whilst they were ignored when friedelin was reduced, in order to obtain as large amount as possible of a second isomer. Apparently there was no difference between the relative amounts of the second isomer in the two cases.

The possibility existed that this new hydrocarbon originated from an impurity in friedelin. To establish whether this were so, friedelin was purified *via* its semicarbazone, which was prepared in analogy with the oxime [4]. Since it melted very unsharply at about 340° (vac.), the m.p. could not be used as a criterion of purity. It, therefore, was crystallised to constant rotation, $[\alpha]_D$ +1.7°. The determination was carried out in 8 % solution and 2 dm tube, *i. e.* with a reading accuracy of ±0.02° $[\alpha]_D$ should be accurate within *ca.* ± 0.1°.

One part of this semicarbazone was reduced according to Huang-Minlon [2], but the yield of hydrocarbon was quite low, 0.1 g from 0.8 g of semicarbazone. When crystallised as above, there were finally left 3—4 mg, which were crystallised from chloroform/methanol to give less than 2 mg of material of m.r. 155—215°. Concentration of the chloroform/methanol mother liquor furnished more material, of m.r. 105—125°.

The other part of the semicarbazone was treated with aqueous oxalic acid [8]. The regenerated friedelin showed m.p. 262—263° (vac.), $[\alpha]_D$—22° after crystallisation from chloroform/methanol, and was reduced according to Huang-Minlon [2]. After crystallisation etc. of the reduction product as above there finally resulted about 20 mg of material from which friedelane was removed as far as possible by treatment with petroleum. Finally there resulted a substance, supposedly the isomer friedelane II, of m.p. 207—208°, $[\alpha]_D$ +2°.

EXPERIMENTAL

M.p.'s are uncorrected. All rotations were measured in chloroform solution in a 1 dm tube at room temperature (20—25°), unless specified to the contrary; the values recorded have been approximated to the nearest degree. Petroleum refers to the fraction of b. r. 40/70°. In all cases of mixed m. p. determination the m. p. of the two compared substances and their admixture were taken all three at the same time.

The isolation of friedelin and cerin as well as the preparation of the reference specimen of friedelane are described in the preceding paper.

Friedelane

a) A specimen of friedelane provided by Dr. J. F. McGhie, through the good offices of Professor D. H. R. Barton and Mr. P. de Mayo, showed m. p. 242—244°, $[\alpha]_D$ +10° (*c*, 0.60). It was crystallised from chloroform, m. p. 247—248°, $[\alpha]_D$ +18° (*c*, 0.50). It gave no depression on admixture with the reference specimen.

b) Friedelane according to Ruzicka *et al.*[1]

The amounts of friedelin and reagents given by these authors were heated to 215° during 2 hours and kept at this temperature for 6 hours. The obtained hydrocarbon, isolated with ether and filtered through alumina in petroleum, was crystallised once from chloroform, m.p. 245—246°, $[\alpha]_D$ +20° (*c*, 0.69), undepressed on admixture with the reference specimen.

c) Friedelane according to Drake and Jacobsen[3]

Friedelin (100 mg) was refluxed in acetic acid (50 ml) with zinc amalgam (prepared from zinc (4 g) and mercuric chloride (4 g) in 50 % ethanol (50 ml)) for three hours. During this time hydrochloric acid (20 ml, *d*, 1.19) was added in portions of 2.5 ml, the last portion 1/2 hour before the reaction was interrupted. The reaction product was isolated and purified as above, and crystallised from chloroform, m.p. 245—246°, $[\alpha]_D$ +19° (*c*, 0.68), undepressed on admixture with the reference specimen.

d) Friedelane according to Huang-Minlon[2]

1. Cerin (0.6 g) was heated for 1/2 hour with diethylene glycol (10 ml) and hydrazine hydrate (1 ml). Then potassium hydroxide (1 g) in conc. aqueous solution was added, and the heating continued for further 20 min., when water was distilled off until the temperature had reached 200° in the vapours at the top of the flask. The reaction mixture was refluxed for 2 hours. The reaction product was isolated and purified in the usual way and crystallised once from chloroform, m.p. 245—246°, $[\alpha]_D$ +22° (*c*, 0.69), undepressed on admixture with the reference specimen.

The mother liquor from this crystallisation was concentrated to about 1/2 of its original volume. The substance which crystallised on cooling, showed m.p. 240—242°, undepressed on admixture with the reference specimen, $[\alpha]_D$ +23° (*c*, 0.70).

The mother liquor was concentrated once more, to a very small volume. The obtained crystals were no longer completely colourless, m.p. 241—244°, $[\alpha]_D$ +26° (*c*, 0.47), undepressed on admixture with the reference specimen.

Finally the mother liquor was evaporated to dryness, and the residue dissolved in a small amount of petroleum. The precipitated, minute amount of crystals was somewhat miscoloured, m.p. 242—244°, no colour with tetranitromethane. The residue melted at 170—190°, $[\alpha]_D$ +17° (*c*, 0.53).

This petroleum mother liquor was concentrated to a small volume, when a substance crystallised on cooling as fine, somewhat felted needles, m.p. 192—195°; a mixture with friedelane melted at 195—235°. The substance was recrystallised from chloroform/methanol, m.p. 193—194°, $[\alpha]_D$ +2° (*c*, 0.65); no colour with tetranitromethane.

2. Friedelin (1 g) was heated for 1/2 hour with diethylene glycol (30 ml), potassium hydroxide (3 g) and hydrazine hydrate (1 ml). Water was distilled off until about 200° in the vapours, and then the heating was continued for 2 hours. The reaction product was isolated and purified as above and crystallised from chloroform, m.p. 245—246°, undepressed on admixture with the reference specimen, $[\alpha]_D$ +22° (*c*, 0.83).

The mother liquor was concentrated. The crystals which separated, melted at 246—247°, undepressed on admixture with the reference specimen, $[\alpha]_D$ +22° (*c*, 0.59).

Again the mother liquor was concentrated. The precipitated substance showed m.p. 242—244°, undepressed on admixture with the reference specimen, $[\alpha]_D$ +23° (*c*, 0.53).

This mother liquor was evaporated to dryness, and the residue dissolved in a little petroleum. On standing a small amount of somewhat miscoloured crystals was obtained, m.p. 241—243°, undepressed on admixture with the reference specimen. The filtrate was concentrated further and another small crop of crystals was obtained, m.p. 240—242°, also undepressed on admixture with the reference specimen.

Concentration of the mother liquor to a very small volume furnished fine, colourless needles, which were crystallised from chloroform/methanol, m.p. 195—196°, $[\alpha]_D$ +14° (*c*, 1.05), recrystallised from chloroform/acetone, m.p. 195—202°, $[\alpha]_D$ +14° (*c*, 0.87).

At this stage of the investigations the rotation of the reference specimen was checked: $[\alpha]_D$ +20° (*c*, 0.64).

Friedelin semicarbazone. Friedelin (3.6 g) and semicarbazide hydrochloride (2.3 g) were heated with benzene (72 ml) and ethanol (18 ml). Sodium acetate (2.1 g) in ethanol (18 ml) was added and the mixture was refluxed for 1 1/2 hours [4]. The reaction mixture was poured into water and the reaction product isolated with benzene. The benzene solution was evaporated until incipient crystallisation. The precipitated substance was filtered after standing for a considerable time, m.p. 342—345° (vac., dec.), $[\alpha]_D$ +2.7° (*c*, 8.09, 2 dm tube), crystallised from chloroform/methanol, m.p. 341—345° (vac., dec.), $[\alpha]_D$ +1.7° (*c*, 8.09, 2 dm tube), recrystallised, $[\alpha]_D$ +1.6° (*c*, 8.05, 2 dm tube); yield 0.9 g. (Found C 75.6, 75.4; H 10.65, 10.7. $(C_{31}H_{53}N_3O)_3 \cdot CH_3OH$ (999.56) requires C 75.7, H 11.09.) The mother liquor from the recrystallisation was evaporated to dryness and the residue, together with some crystallised material, was used for the reduction of the semicarbazone (see below). The remaining mother liquors were combined and evaporated and crystallised to give further 0.3 g of the semicarbazone with $[\alpha]_D$ +1.8° (*c*, 8.49, 2 dm tube).

Friedelane from the semicarbazone. Friedelin semicarbazone (0.8 g, compare above) was heated with diethylene glycol (10 ml) and potassium hydroxide (1 g) until the temperature was 200° in the vapour at the top of the flask. The mixture was refluxed for 2 hours and the reaction product isolated and filtered through alumina as above. 0.1 g was eluted and crystallised from chloroform, m.p. 245—246°, no depression with the reference specimen, $[\alpha]_D$ +17° (*c*, 0.65). Two subsequent concentrations of the mother liquors furnished material of m.p. 244—245° and 240—241°, respectively, no depression with the reference specimen.

The final mother liquor was evaporated to dryness and the residue (3—4 mg) crystallised from chloroform/methanol to give less than 2 mg of m.r. 155—215°. Concentration of the mother liquor afforded material with m.r. 105—125°.

Regenerated friedelin. Friedelin semicarbazone (0.7 g) was heated overnight in a boiling water-bath with oxalic acid (1.5 g) and water (1.1 ml) [8]. The reaction product was isolated with ether and crystallised from chloroform/methanol, m.p. 262—263° (vac.), $[\alpha]_D$ −22° (*c*, 1.16, 2 dm tube).

Friedelane and friedelane II from regenerated friedelin

The regenerated friedelin (0.6 g) was treated with diethylene glycol (50 ml), potassium hydroxide (5 g) and hydrazine hydrate (1 ml) and the reaction product isolated and filtered through alumina (0.5 g) and crystallised as above. The first crystallisate melted at 245—246°, $[\alpha]_D$ +27° (*c*, 0.66), the second at 244—245° $[\alpha]_D$ +28° (*c*, 0.58) and the third at 244—245°, $[\alpha]_D$ +26° (*c*, 0.93). The material in the mother liquor from the last crystallisation was repeatedly crystallised from chloroform/methanol. The product melted constantly at 197—204°, but the rotation steadily decreased. The material, therefore, was repeatedly treated with small amounts of petroleum to remove as far as possible any friedelane present. The success of this procedure depended on the fact that friedelane was much less soluble in petroleum than friedelane II. Finally the material was crystallised three times from chloroform/methanol m.p. 207—208°, $[\alpha]_D$ +2° (*c*, 1.47); +3°, (*c*, 1.09). (Found * C 87.05; H 12.75. $C_{30}H_{52}$ (412.72) requires C 87.3; H 12.7).

SUMMARY

The isomeric friedelanes, friedelane, m.p. 244—245°, $[\alpha]_D$ +22° and, in a state of high purity, friedelane II, m.p. 207—208°, $[\alpha]_D$ +2°, have been prepared.

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REFERENCES

1. Ruzicka, L., Jeger, O., and Ringnes, P. *Helv. Chim. Acta* **27** (1944) 972.
2. Huang-Minlon, *J. Am. Chem. Soc.* **71** (1949) 3301.
3. Drake, N. L., and Jacobsen, R. P. *J. Am. Chem. Soc.* **57** (1935) 1570.
4. Drake, N. L., and Shrader, S. A., *J. Am. Chem. Soc.* **57** (1935) 1854.
5. Drake, N. L., and Haskins, W. T. *J. Am. Chem. Soc.* **58** (1936) 1684.
6. Drake, N. L., and Wolfe, J. K. *J. Am. Chem. Soc.* **61** (1939) 3074.
7. Drake, N. L., and Campbell, W. P. *J. Am. Chem. Soc.* **58** (1936) 1861.
8. Ruzicka, L., Plattner, Pl. A., and Wild, H. *Helv. Chim. Acta* **26** (1943) 1637.

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