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ESTABLISHMENT OF THE STRUCTURES OF AZATROPOLONES AND THEIR REARRANGEMENT PRODUCTS BY *X*-RAY ANALYSIS[1]

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The structure of the azatropolone methyl ether [7-(4'-bromophenyl)-4-ethoxycarbonyl-3-methoxy-6-phenyl-2H-azepin-2-one] was determined by *X*-ray analysis using the heavy atom method. The result indicated that the azatropolone nucleus is not planar and has a chirality. The structures of solvolytic rearrangement products of azatropolones were also established by *X*-ray analyses as pyridine-2-carboxylates.

Previously we reported syntheses of the azatropolones, **5** and **9**, and showed that they readily undergo rearrangement on merely keeping in protic solvents to yield the compounds supposed to be pyridine-2-carboxylates, **11** and **13**[2]. In spite of the expected aromaticity like α-tropolone, such high reactivity of the azatropolones still left some ambiguities on their structures and requires rigid structure proof not only of the azatropolones but also of their rearrangement products.

Therefore we planned *X*-ray analyses of these compounds. The compounds for *X*-ray analyses were synthesized according to the route[2] shown in Sheme I.

The 4'-bromo derivatives newly synthesized had following properties.

The cyclobutene (**4**): pale yellow plate, mp 171-176°. ν_{max}^{Nujol} 1775, 1740, 1700 cm^{-1}. $\lambda_{max}^{Dioxane}$ 258(18,300), 382(700), 402 nm (600). δ 6.47(s, C_6-H).

The azatropolone (**6**): mp 153-154°. ν_{max}^{Nujol} 3290, 1720, 1695, 1615, 1590 cm^{-1}. $\lambda_{max}^{Dioxane}$ 235(20,500), 282(10,000), 375 nm (9,400).

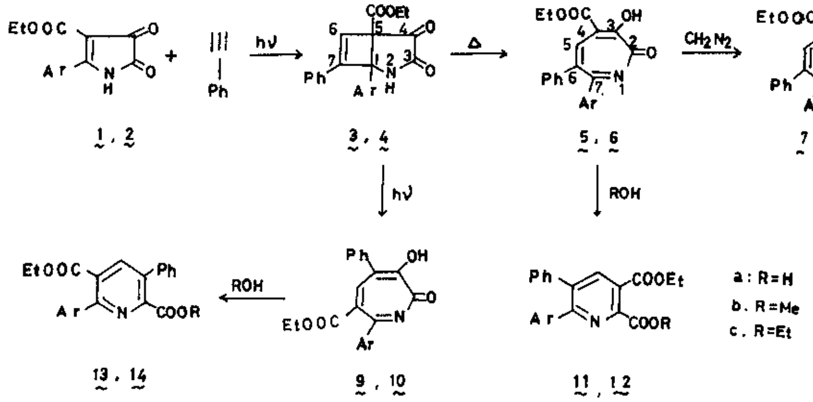
The methyl ether (**8**): mp 133-136°. ν_{max}^{Nujol} 1735, 1700, 1610, 1590 cm^{-1}.

$\lambda_{max}^{Dioxane}$ 263(18,600), 280(18,600), 360 sh (6,200). δ 7.80(s, C_5-H).

The methyl ester (12b): mp 118-121°. ν_{max}^{Nujol} 1745, 1730, 1595 cm^{-1}. λ_{max}^{EtOH} 235(18,600), 305 sh nm (11,900). δ 4.00(s, COOMe), 8.23(s, C_4-H).

The methyl ester (14b): mp 127-129°. ν_{max}^{Nujol} 1750, 1730, 1595 cm^{-1}. λ_{max}^{EtOH} 273 nm (20,300). δ 3.75(s, COOMe), 8.13(s, C_4-H).

The azatropolone (10) was not isolated in pure form and the crystals of 5, 6, and 9 were not suitable for *X*-ray analyses. The *X*-ray analysis was performed for 8.



Ar=Ph for odd-numbered compounds
Ar=p-Br-C_6H_4 for even-numbered compounds

Scheme I

The crystals of 8 are monoclinic, space group $P2_1$, with a=10.926, b=9.642, c=10.736 Å, β=118.47°, and Z=2. The intensity data were collected on a Philips PW-1100 diffractometer using graphite-monochromated Cu-*K*α radiation. The structure was solved by the heavy atom method. Block-diagonal least-squares refinement of positional and thermal parameters based on 1997 observed reflections reduced *R* to 0.057. At this stage, anomalous scattering factors of the bromine atom were introduced and refinement was continued to result in *R* of 0.055 for the configuration shown in Fig. 1. For its mirror image *R* was 0.058, suggesting that the compound is chiral. This was confirmed by an amomalous dispersion method. The intensities of 555 reflections of 2θ angle within 130° including 475 Friedel pairs were re-measured and those of crystallographical equivalence were averaged. The ratios $Rc=|Fc^+|/|Fc^-|$ were calculated for 158 pairs of $||Fo^+|-|Fo^-||\geq 2\sigma(Fo)$ by adopting the values $\Delta f'=-0.767$ and $\Delta f''=1.283$ as anomalous dispersion terms of a bromine atom. Comparisons of Rc with the observed ratios $Ro=|Fo^+|/|Fo^-|$ for

100 Friedel pairs which had Rc of differing more than 5% from the unity clearly indicated that the both had the same deviations. The absolute configuration was therefore established as that in Fig. 1.

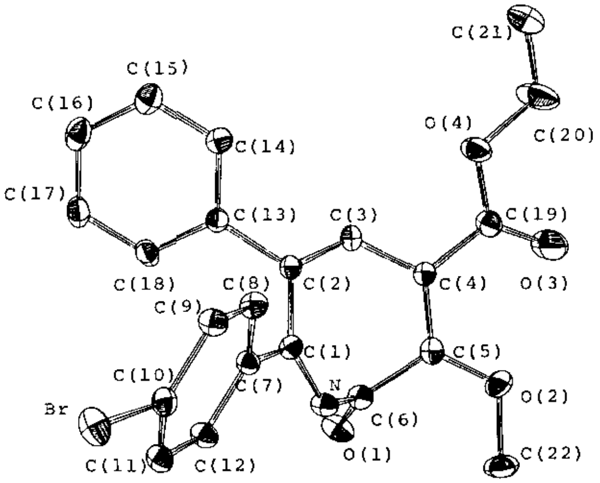


Fig.1. A computer generated perspective drawing of the molecule 8, which implies *S*-configuration.

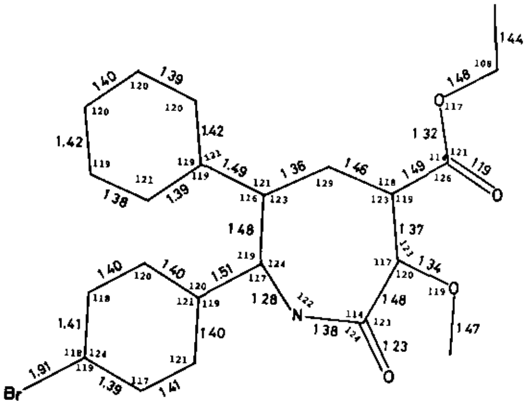


Fig. 2 Bond distances and angles.

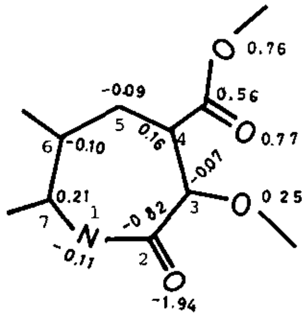


Fig. 3 Deviation (Å) from the average plane formed by C_3-C_7 and N.

The result rigidly established not only our assigned structure of the azatropolone (6) but also the position of methyl ether group (two enolated forms are possible for 6). Interestingly and unexpectedly, the seven-membered nucleus of this heterocycle is not planar, the carbonyl carbon being deviated 0.8 Å from the best plane formed by C_3, C_4, C_5, C_6, C_7, and N (Fig. 3). Moreover, the space group $P2_1$ of this molecule and the above result indicate that all the molecules in the crystal analysed have the same chirality with the absolute configuration shown in Fig. 1, thus suggesting that the compound is a conglomerate of crystals of *d*- and *l*-forms. Whether the above non-planarity of azatropolone nucleus came from its inherent nature or from the steric hindrance due to ortho-substituted two benzene rings which, in fact, are almost perpendiculary arranged, is not clear at this stage. However, we suppose that the former will be the real reason and that the unexpected reactivity of azatropolones is attributable to this character, although it should be clarified yet.

The *X*-ray analyses of the rearrangement products were carried out for **11c** and **14b**. The crystals of **11c** are monoclinic, space group $P2_1/n$ with a=19.873, b=10.797, c=9.647 Å, β=103.95°, Z=4, and the crystals of **14b** are triclinic, space group $P\bar{1}$, with a=13.988, b=8.951, c=8.416 Å, α=79.07, β=78.52, γ=96.10°, Z=2. The intensity data were collected as above. The structure of **11c** was solved by direct methods with the MULTAN program[3] and that of **14b** by the heavy atom method. Block-diagonal least-squares refinements of positional and thermal parameters based on 2329 and 3132 observed reflections reduced R values to 0.096 for **11c** and to 0.063 for **14b**, respectively. The resulting structures are shown in Figures 4 and 5, respectively. **14b** provides good proof of the structures of the azatropolone **10** and hence of **9**.

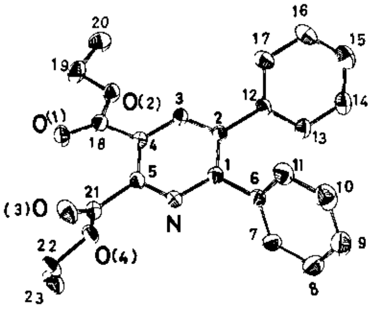


Fig. 4 (**11c**)

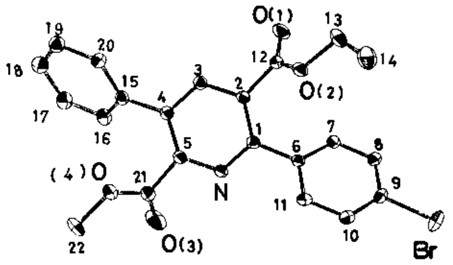


Fig. 5 (**14b**)

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