HETEROCYCLES, Vol. 9, No. 6, 1978

THE SYNTHESES OF AZATROPOLONES[1]

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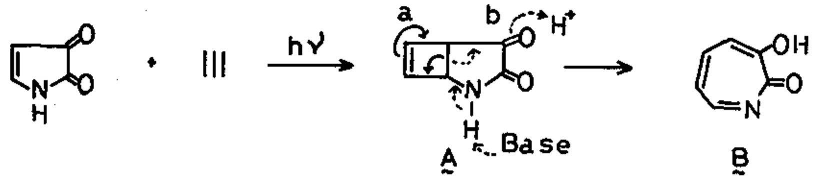
Azatropolones, the compounds of new ring system, were synthesized by thermal cleavage of 2-azabicyclo[3.2.0]hept-6-one derivatives, and their chemical and spectral properties were described. Particularly azatropolones were susceptible to solvolysis furnishing pyridine-2-carboxylates.

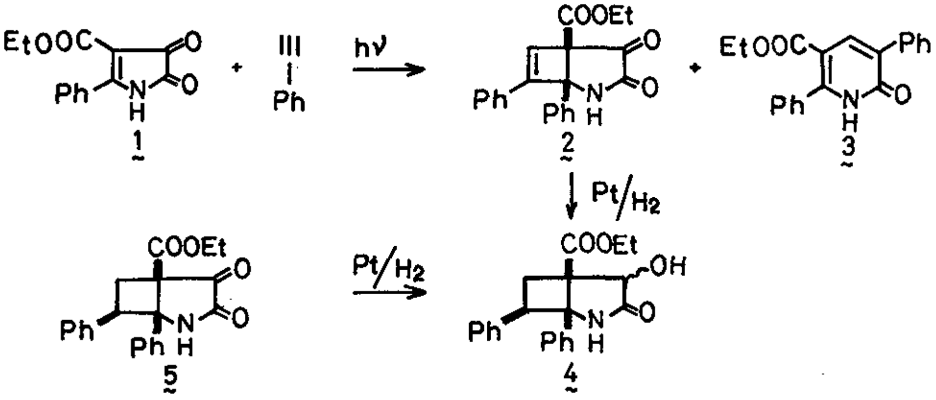
Recently the synthetic utility of dioxopyrrolines as versatile synthons in heterocyclic chemistry has been demonstrated by the syntheses of hydroindoles[2~4], 2-azabicyclo[3.2.0]heptane-3,4-diones[5,6], pyranopyrroles[3,7], and dihydropyridones[6,8] through the photo and thermal cycloaddition reactions to olefins. Our study was now extended to the synthesis of a new ring system, azatropolone which has never been reported previously.

A possible synthetic precursor to an azatropolone is an azabicyclo[3,2,0]heptenedione (A) which may be prepared by the photocycloaddition reaction of a dioxopyrroline to an appropriate acetylene and be convertible to an azatropolone (B) by the ring opening at C_1-C_5 bond by means of electrocyclic (a) or acid-base catalized (b) processes as illustrated in Scheme 1.



Scheme 1

Irradiation of a mixture of 2-phenyl-3-ethoxycarbonyl-Δ^2-pyrroline-4,5-dione (1) and phenylacetylene in dimethoxyethane with high pressure mercury lamp (100W, pyrex filter) at 0°C for 30 min yielded the cyclobutene (2)(55%), colorless prisms, mp 179-183°, ν_{max}^{Nujol} 1770, 1750, 1730 cm^{-1}; λ_{max}^{EtOH} 257(18,100), 328 sh (5,650), 414(3,700) and $\lambda_{max}^{Dioxane}$ 254(18,000), 383(700), 403 nm (650); δ 6.50(s, C_6-H) together with the known pyridone (3)[8](9%).

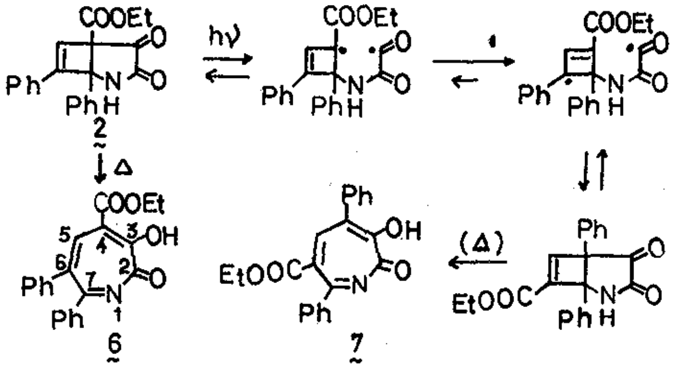


Scheme 2

Catalytic hydrogenation of 2 over Pt in acetic acid gave the tetrahydro-derivative (4), mp 252-255°, (monoacetate, mp 218-222°), identical with the compound (4) obtained by reduction of the known cyclobutane (5)[5], thus confirming the structure.

Heating of 2 in an aprotic solvent (boiling xylene, 2 hr), it was converted into the isomeric compound (6) in 60% yield, yellow needles, mp 151-154°, which was purified by rapid chromatography over silica gel (CH_2Cl_2 elution) followed by recrystallization from dry ether-CH_2Cl_2: $M^+=347$ for $C_{21}H_{17}O_4N$; ν_{max}^{Nujol} 3200, 1735, 1715, 1690, 1660, 1610, 1600 cm^{-1}; λ_{max}^{EtOH} 232 sh (18,300), 325(11,000), 395(9,000) and $\lambda_{max}^{Dioxane}$ 227(19,000), 286(9,400), 377 nm (5,400); δ 8.0(s, C_5-H).

Further irradiation of 2 or prolonged irradiation (8 hr) of a mixture of 1 and phenylacetylene afforded the pyridone (3)(10%) and a new isomer (7)(5%), yellow needles, mp 191-194° which had the similar spectral properties with 6: $M^+=347$ for $C_{21}H_{17}O_4N$; ν_{max}^{Nujol} 3180, 1700, 1650, 1590 cm^{-1}; λ_{max}^{EtOH} 375(6,100) and $\lambda_{max}^{Dioxane}$ 230(18,600), 328(12,200), 365 nm (11,000); δ 7.68(s, C_5-H).



Scheme 3

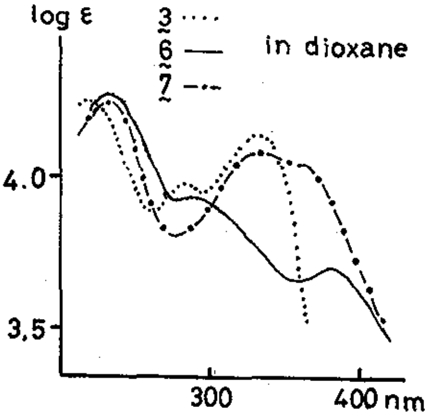
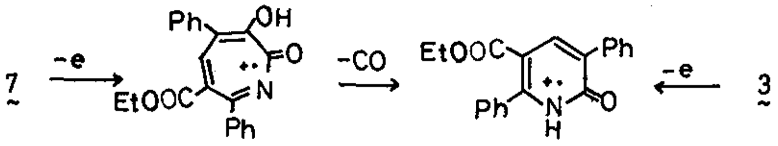


Fig. 1

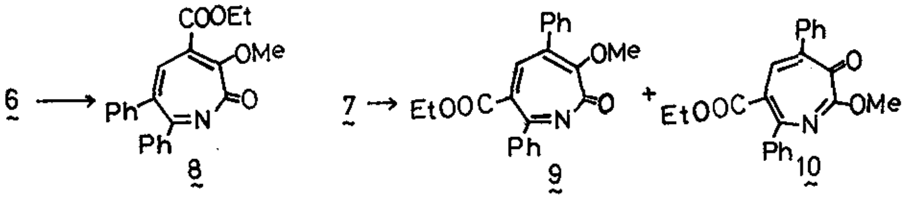
We consider that 6 and 7 are isomeric azatropolones formed by the route shown in Scheme 3 from the following reasons. 1) They have the expected molecular formula, $C_{21}H_{17}O_4N$. 2) They showed a positive test with ferric chloride solution (yellowish green). 3) In the UV spectra they have the absorptions at longer wave length than that of the pyridone (3)(Fig 1). 4) In the ^1H-NMR spectra they exhibited signals, except $CO_2C_2H_5$, only at aromatic region, among which one proton appeared at fairly low field (δ 8.0 for 6, and δ 7.68 for 7). 5) In the mass spectra either compound showed elimination of CO from the molecular ion, as always seen in the fragmentation of α-tropolones. Particularly the fragmentation pattern of 7 below m/e 319(M^+-CO) was almost superimposable with that of the pyridone (3) except a few peaks. This fact confirms the structure of azatropolone 7 (Scheme 4). Our assignments were supported by the chemical reactions described below.



Scheme 4

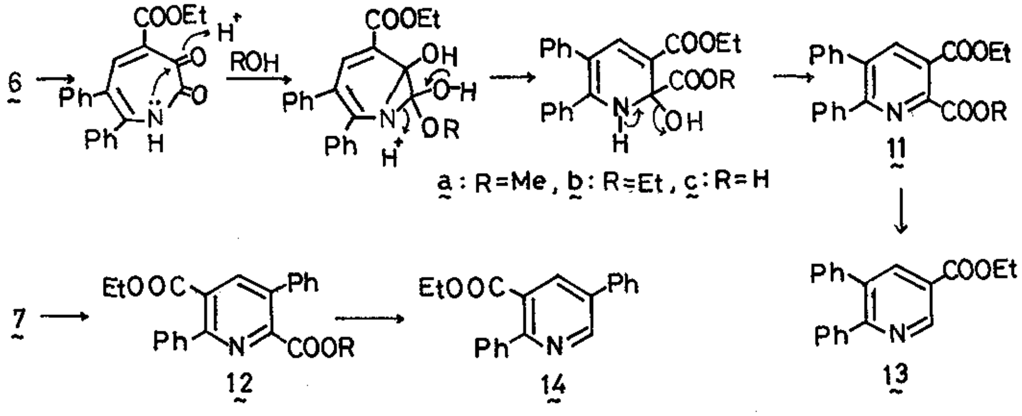
The compound 6 and 7 are fairly acidic[9] and rapidly comsumed CH_2N_2 to yield O-methyl derivatives. Thus the reaction of 6 in dry CH_2Cl_2 gave the methyl-ether (8)[10], (70%) [yellow needles, mp 131-134°, $C_{22}H_{19}NO_4$; ν_{max}^{Nujol} 1735, 1700, 1620, 1600 cm^{-1}; $\lambda_{max}^{Dioxane}$ 253(17,000), 300(12,300); δ 4.17(s, OMe), 7.92(s, C_5-H)] and 7 gave two isomeric methyl-ethers (9) and (10), $C_{22}H_{19}NO_4$, in the ratio of about 3:2 corresponding two enol forms of the azatropolone[10]

[9: pale yellow needles, mp 102-105°, ν_{max}^{Nujol} 1720, 1680, 1665, 1620, 1595 cm^{-1}; $\lambda_{max}^{Dioxane}$ 255(20,000), 300 sh (10,500), 350 sh nm (7,350); δ 4.03(s, OMe), 8.30(s, C_5-H). 10: yellow needles, mp 133-135°, ν_{max}^{Nujol} 1720, 1700, 1650, 1620 cm^{-1}; $\lambda_{max}^{Dioxane}$ 232(16,700), 280(10,100), 355 nm (13,200); δ 4.05(s, OMe), 7.80(s, C_5-H)].



Scheme 5

The azatropolones 6 and 7 were unstable in protic solvents, in which their yellow color faded gradually. The half-life (T½) of 6 in MeOH at 10°C was ca.200 min and that of 7 ca.18 min when measured from the rate of decrease of the absorptions at 395 nm and at 375 nm, respectively. Thus 6 and 7 on warming in MeOH yielded new colorless compounds, (11a) and (12a) in quantitative yields, respectively. [11a: mp 103-105°; ν_{max}^{Nujol} 1750, 1725, 1590 cm^{-1}; λ_{max}^{EtOH} 247(17,200), 300 sh nm (9,900); δ 4.03(s, COOMe), 8.27(s, C_4-H). (12a): mp 113-114°; ν_{max}^{Nujol} 1745, 1730 cm^{-1}; λ_{max}^{EtOH} 270 nm (19,700); δ 3.77(s, COOMe), 8.15(s, C_4-H)]. Although they are isomeric to the methyl-ethers (8), (9) and (10), profound changes of their UV or IR spectra indicated that the skeletal rearrangement had taken place. We conclude that the compounds are the methyl pyridine-2-carboxylates (11a) and (12a), respectively, produced by a benzylic acid type rearrangement of the azatropolones probably via diketo-forms (Scheme 6).



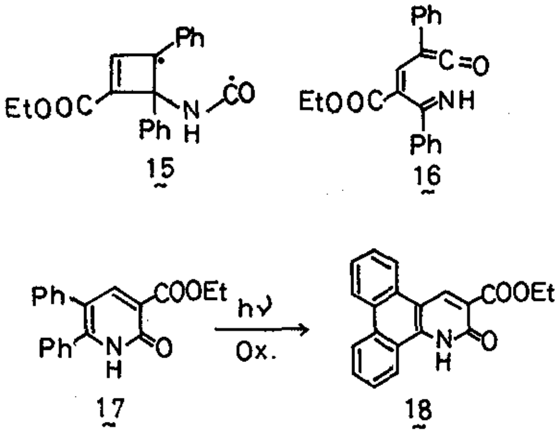
Scheme 6

Similar treatments of **6** with EtOH and aq. acetone yielded the corresponding ethyl ester (**11b**), and the carboxylic acid (**11c**), respectively, [**11b**: mp 128-130°; ν_{max}^{Nujol} 1740, 1720, 1585 cm^{-1}; λ_{max}^{EtOH} 247(15,600), 300 sh nm (9,200); δ 8.23(s, C_4-H). **11c**: colorless gum; $\nu_{max}^{CH_2Cl_2}$ 1770, 1730 cm^{-1}; λ_{max}^{EtOH} 243 and 300 sh nm.] and **7** gave the acid (**12c**) with water, [**12c**: colorless gum, $\nu_{max}^{CH_2Cl_2}$ 1775, 1730 cm^{-1}; δ 8.15(s, C_4-H)]. Methylation of **11c** and **12c** with CH_2N_2 gave **11a** and **12a**, respectively.

Supporting our structural assignments of these pyridine-2-carboxylates, the acids (**11c**) and (**12c**) were decarboxylated on heating with SiO_2 at 120° for a few hrs, to yield **13**, [mp 79-82°; ν_{max}^{Nujol} 1720, 1595 cm^{-1}; λ_{max}^{EtOH} 243(17,500), 300 nm (9,700); δ 8.31 (d, J=2 Hz, C_4-H) and 9.28(d, J=2 Hz, C_2-H)], and **14**, [mp 137-138°; ν_{max}^{Nujol} 1718 cm^{-1}; λ_{max}^{EtOH} 273(22,500), 373 nm (1,100); δ 8.25(d, J =2.5 Hz, C_4-H), 8.97(d, J=2.5 Hz, C_2-H)].

Interestingly heating of the cyclobutene (2) in MeOH or EtOH with NaOAc under reflux for 2 hrs directly produced the pyridine-2-carboxylates (11a) and (11b), in ca.50% yield respectively. This suggests that intermediary azatropolone (6) was formed by acid-base catalysed reaction.

Brief comment must be made on the pyridone (3) which might be formed by one of the following three routes in photolyses of 2: 1) from the azatropolone (7), 2) from the nor-biradical (15), or 3) from the imino-ketene (16). We have no evidence at present which course is the actual one. The possible isomeric pyridone (17) was not found, instead the pyrido-phenanthrene (18)[11] was isolated in minute amount together with 3 and 7. Such an oxidative photocyclization of 6π-electron system is a well known process.



Scheme 7

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8. Part IX (see Ref. 1).
9. The pKa's could not be accurately determined because of their instability in protic solvents.
10. X-ray analysis of the corresponding 4'-bromo-derivative is now completed. The result and the tautomerism of the azatropolones will be discussed in a separate paper.
11. mp 228-230°, M^+=317 for $C_{20}H_{15}NO_3$; ν_{max}^{Nujol} 1730, 1710, 1650 cm^{-1}; λ_{max}^{EtOH} 242(41,000), 305(9,500), 343 nm (5,900); δ 7.86(s, C_4-H).

Received, 23th February, 1978