2-AZABICYCLO[3.2.0]HEPTANE-3,4-DIONES (3): LEWIS ACID CATALYSED RING EXPANSION OF 3-ETHOXY-Δ^2-AZABICYCLO[3.2.0]HEPTAN-4-ONES: SYNTHESIS OF 2-ETHOXY-3-AZATROPONES[1]

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Treatment of 2-azabicyclo[3.2.0]heptane-3,4-dione imidic ester (6) with tin(IV) chloride gave the dihydroazatropolone 2-ethyl ethers (7) in moderate yields which were also obtained by reaction of dihydroazatropolones (2) with Meerwein reagent. DDQ oxidation of 7 gave 2-ethoxy-3-azatropones (8), which rearranged, on treatment with water, into ethyl pyridine 2-carboxylate (10). Spectroscopic data of azatropolone 2-ethyl ethers were also described.

For an azatropolone two alkyl ethers, A and B, are possible. Recently, we reported base catalyzed ring expansion of 2-azabicyclo[3.2.0]heptane-3,4-diones (1) to dihydroazatropolones (2) which on methylation followed by dehydrogenation affoded 7-methoxy-2-azatropone (4)[2] (type A). Methylation of 3-azatropolones (5) produced only the same ethers (4). Thus, the corresponding 2-alkyl ethers (type B) are hitherto unknown. Here we report the unequivocal synthesis of the 2-ethyl ethers, via Lewis acid catalysed ring expansion of the imidic esters of 2-azabicyclo[3.2.0]heptane-3,4-diones.

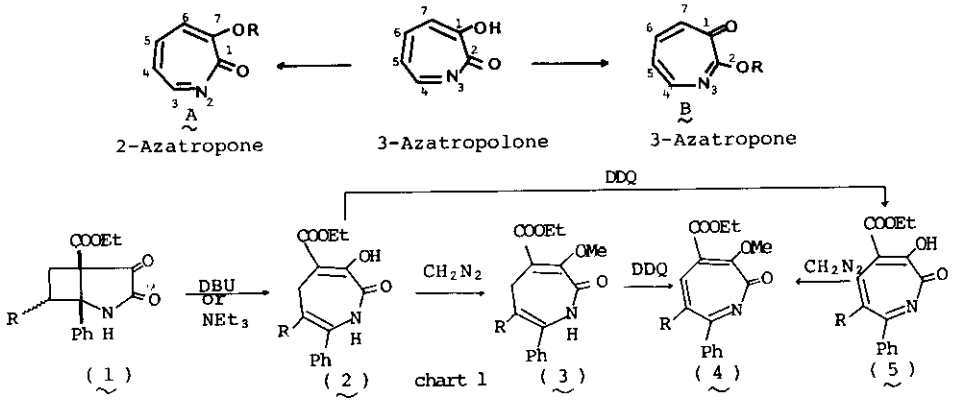
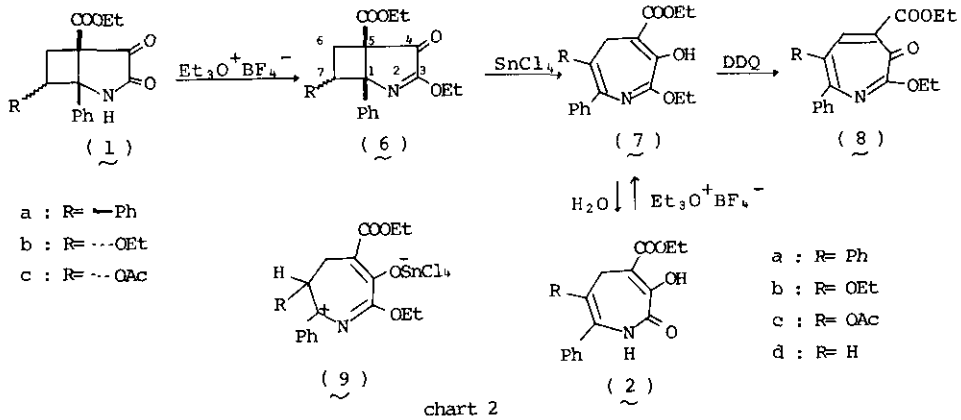


chart 1

The imidic esters (6a~c) were prepared from (1a~c)[3,4] in 65~89% yield with excess Meerwein reagent in CH_2Cl_2 at room temperature and the structures were confirmed spectroscopically.[5] The imidic esters (6), when treated overnight with $SnCl_4$ (1.5 mol eq.) in CH_2Cl_2 at room temperature, gave the dihydroazatropolone 2-ethyl ethers (7) in moderate yields. The spectral data[5] and the following transformations established their structures. They were hydrolysed by 5% HCl in tetrahydrofuran (1:1) to the known dihydroazatropolones (2) which on treatment with Meerwein reagent yield the 2-ethyl ethers identical with the compounds obtained above.

Interestingly, the 2-azabicyclo[3.2.0]heptane-3,4-diones (1) were not affected under similar acidic condition ($SnCl_4$ in CH_2Cl_2 at r.t.), and the imidic esters were stable to base. We therefore assume that the reaction of 6 proceeds through a cationic intermediate 9.

DDQ oxidation of 7 to the 2-ethoxy-3-azatropone (8) was achieved more readily than that of 2 to 5 or that of 3 to 4. Thus a mixture of 7 and DDQ (1.3 mol eq.) in benzene was heated in a sealed tube, and the resulted product was purified by rapid chromatography on SiO_2 to give the 2-ethoxy-3-azatropone (8), in satisfactory yield. Attempt to direct preparation of 8b from 5b with Meerwein reagent was unsuccessful, only a complex mixture being obtained.



(1) (6) (7) (8)

(9) (2)

chart 2

All 2-ethoxy-3-azatropones (8) prepared above were yellow gum and had λmax around 370~400 nm in their electronic spectra. The maximum is red-shifted relative to the corresponding 3-azatropolones (5) and 7-methoxy-2-azatropones (4)[2] (see Fig 1).

Fig 1

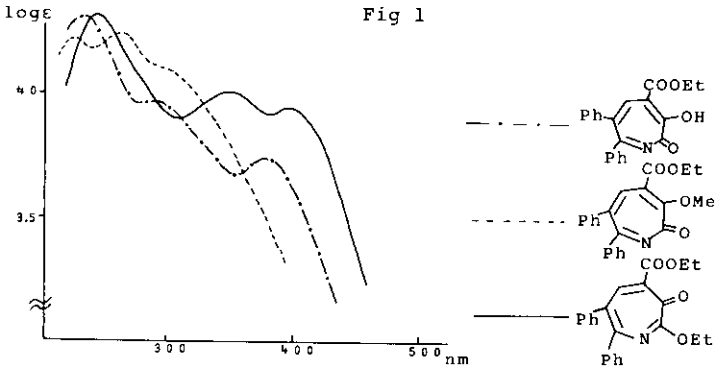


Table 1. Preparation of Dihydroazatropolone 2-Ethyl Ethers (7) and 2-Ethoxy-3-Azatropones (8).

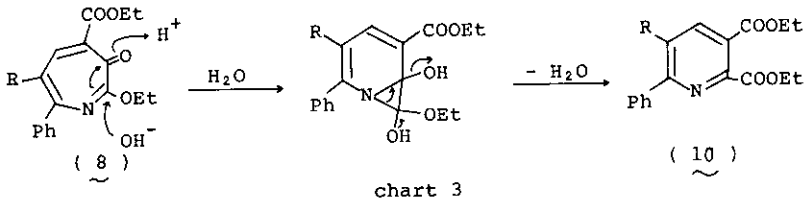
	Dihydroazatropolone 2-Ethyl Ether (7)			2-Ethoxy-3-Azatropone (8)		
	Yield (%)			Condition		
R	from 6	from 2	m.p.	temp.	time	Yield (%)
a: ph	69	94	114-115°	105°	8 min.	77
b: OEt	12[a)]	65	yellow gum	25°	spontaneous	43
c: OAc	43	82	73- 75°	110°	20 min.	60
d: H		50	colorless gum	25°	1~2 min.	82

a) 7b was vulnerable to air oxidation

Table 2. Spectral Data of 2-Ethoxy-3-Azatropones (8).

		NMR(δ, ppm)			
Comp.	IR (cm^{-1})	C6-H	C5-H	UV $\lambda_{max}^{dioxane}$	(ε)
8a:	1720	8.17(s)		240	(21,200)
	1655			349	(9,800)
	1620			398	(8,600)
8b:	1723	8.00(s)		247	(10,600)
	1660			355	(5,100)
	1640			395	(5,300)
8c:	1765	7.88(s)		225	(11,500)
	1725			258sh	(9,500)
	1660			345	(7,300)
	1620			385sh	(6,100)
8d:	1725	8.03	6.90	240	(10,400)
	1660			258sh	(9.000)
	1620	(d, J=10 Hz)	(d, J=10 Hz)	370	(12,500)

The 2-ethoxy-3-azatropones, similar to the 3-azatropolones, were unstable in aqueous solvent. When 8 was treated with silica gel-H_2O or heated in aqueous acetone in presence of catalytic amount of sodium acetate, it quantitatively changed into the ethyl pyridine 2-carboxylate (10)[5], identical with that obtained on treatment of 2 or 4 with ethanol[6], no pyridine 2-carboxylic acid being formed. The conversion of 8 to 10 is explained by hydration to -C=N- double bond, benzilic acid type rearrangement followed by dehydration, thus supporting our proposed mechanism of an azatropolone to pyridine 2-carboxylate.[2]



(8) (10)

chart 3

References and Note

1. Dioxopyrrolines XVII, Part XVI: T. Sano, Y. Horiguchi, and Y. Tsuda, Heterocycles, in press.
2. T. Sano, Y. Horiguchi and Y. Tsuda, Heterocycles, 1979, 12, 1427.
3. T. Sano and Y. Tsuda, Heterocycles, 1976, 4, 1229.
4. see Part XVI.
5. 6a: mp.137-139°; IR: 1760, 1740, 1640 cm^{-1}; NMR:δ 2.38(1H, dd, J=6, 4 Hz, C_6-H), 3.58(1H, dd, J=4, 6 Hz, C_6-H), 3.78(1H, t, J=6 Hz, C_7-H).
   6b: mp.68-71°; IR: 1770, 1760, 1735 cm^{-1}; NMR:δ 1.93(1H, dd, J=14, 5 Hz, C_6-H), 3.37(1H, dd, J=14, 8 Hz, C_6-H), 4.71(1H, dd, J=5, 8 Hz, C_7-H).
   6c: mp.106-108°; IR: 1759, 1750, 1630 cm^{-1}; NMR:δ 2.05(1H, dd, J=14, 5 Hz, C_6-H), 3.57(1H, dd, J=14, 9 Hz, C_6-H), 5.85(1H, dd, J=5, 9 Hz, C_7-H).
   7a: IR: 1665, 1630, 1600 cm^{-1}; NMR:δ 2.90(2H, s, C_5-H); $\lambda_{max}^{dioxane}$ 234(ε 20,600), 268(ε 17,800), 345sh(ε 2,100)nm.
   7b: IR: 1730, 1660, 1620 cm^{-1}; NMR:δ 2.90(2H, s, C_5-H); $\lambda_{max}^{dioxane}$ 255sh(ε 10,700) nm.
   7c: IR: 1765, 1660, 1630 cm^{-1}; NMR:δ 2.97(2H, s, C_5-H); $\lambda_{max}^{dioxane}$ 228sh(ε 12,000), 253(ε 16,500), 335sh(ε 1,500)nm.
   7d: IR: 1658, 1620 cm^{-1}; NMR:δ 2.68(2H, d, J=7 Hz, C_5-H), 5.85(1H, t, J=7 Hz, C_6-H); $\lambda_{max}^{dioxane}$ 223(ε 13,600), 258(ε 17,300), 335sh(ε 1,300)nm.
   10b: mp.84-85°;IR: 1745, 1725 cm^{-1}; NMR:δ 7.57(1H, s, C_4-H); λ_{max}^{EtOH} 239(ε 14,800), 264sh(ε 10,100), 315(ε 12,500)nm.
   10c: gum; IR: 1765, 1725, 1600 cm^{-1}; NMR:δ 8.0(1H, s, C_4-H); λ_{max}^{EtOH} 262(ε 9,500), 293(ε 10,600)nm.
   10d: gum; IR: 1740, 1730 cm^{-1}; NMR:δ 8.28(1H, d, J=9 Hz, C_5-H), 7.82(1H, d, J=9 Hz, C_4-H); λ_{max}^{EtOH} 268sh(ε 15,000), 290(ε 18,900)nm.
6. Y. Tsuda, N. Kaneda, T. Sano, Y. Horiguchi, and Y. Iitaka, Heterocycles, 1979, 12, 1423.

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