Tetrahedron. Vol 31, pp. 2145 to 2149. Pergamon Press 1975. Printed in Great Britain

AZIRIDINE TRANSITION STATES

THERMAL REARRANGEMENT OF (ANILINODIAROYL-)-METHYLMERCAPTOACETIC ACIDS

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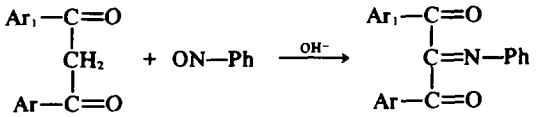
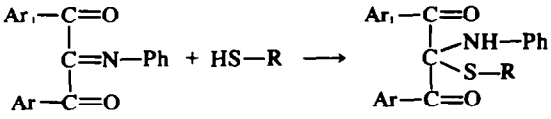
(*Received in UK* 3 *March* 1975; *Accepted for publication* 18 *April* 1975)

The addition of some nucleophiles to C=N double bonds of Schiff bases of vicinal polyketoacids has been previously investigated.[1-4] In the present investigation we directed our attention to the anil derivatives of vicinal polyketones. The 2-mono-anils of 1,3-diarylpropane-1,2,3-trione were obtained by the condensation of 1,3-diaroylmethanes with nitrosobenzene:[5]



Compounds **1–5**

The structure of these 2-mono-anils was fully confirmed by elemental and spectral analysis (Table 1). The 2-mono-anils of 1,3-diarylpropane-1,2,3-trione treated with nucleophiles containing sulphydryl groups, such as thiols and thioacids, formed the corresponding adducts (compounds **6–14**, Table 2):



Compounds **6–14**

where: R-alkyl or aryl (compounds **11–12**), carboxymethylene (compounds **6–10**), carbomethoxymethylene (**13**), sodium carboxymethylene (**14**).

The adducts of mercaptoacetic acid proved to be the most interesting (compounds **6–10**, Table 2). It might be expected that these adducts would undergo an intramolecular condensation to thiazolidone derivatives[6-7] under heating in xylene. However, the intramolecular condensation did not occur but the adducts rearranged into N-aroyl-ω-anilinoacetophenones.

The structure of the N-aroyl-ω-anilinoacetophenones (compounds **15–23**, Table 3) was established by means of elemental analysis, and by spectral and synthetical methods.

The IR spectra of the adducts with mercaptoacetic acid, i.e. (anilinodiaroyl-)-methylmercaptoacetic acids (compounds **6–10**) showed three sharp CO bands and one sharp amine band at approximately 1650, 1680, 1710 and 3365 cm^{-1} respectively (Table 2). This suggests that one of the CO groups must be H-bonded with the carboxylic group, whereas the amine NH group remains free. The importance of the participation of the carboxylic group or rather its acidic H atom is supported by the fact that neither the adducts with thiols (**11–12**) nor the adduct with mercaptoacetic acid methyl ester (**13**) rearranged under the conditions mentioned above. Similarly, the sodium salt of (anilinodiphenyl-)-methylmercaptoacetic acid (**14**) did not rearrange. We suggest the following mechanism. The CO group of the (anilinodiaroyl-)-methylmercaptoacetic acid molecule which has a suitable steric orientation may be protonated in the first step of the reaction, facilitating the polarization of this CO group, and promoting a nucleophilic attack of the free electron pair of the amine nitrogen. This process is probably connected with a nearly synchronous detachment of the mercaptoacetic acid fragment. The latter partly polymerizes and partly decomposes. The dipolar aziridine transition state (I) formed in this way and containing a quaternary nitrogen atom isomerizes into the more stable intermediate (II). This intermediate may be stabilized by the cleavage of the aziridine ring forming the end-product: The aziridine transition states proposed for the thermal rearrangement of (anilinodiaroyl-)-methylmercaptoacetic acids are similar to those considered for typical Beckmann,[8] Neber,[9] Baumgarten,[10] Leseticky and Prochazka,[11] or Sheehan and Frankenfeld[12] rearrangements.

When a substituent was located in one of the aroyl rings

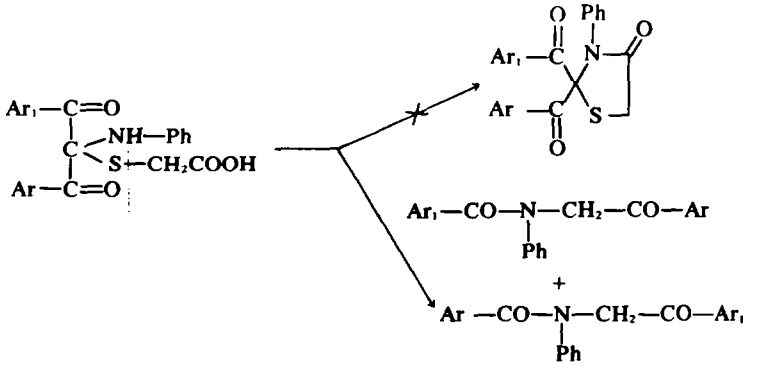
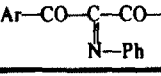


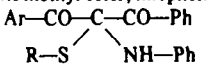
Table 1. Analyses and Spectral Data of the 2-mono-anils of 1,3-diarylpropane-1,2,3-trione



No	Ar	M.p.	Yield	Formula	Elemental Analyses	I.R. data, ν cm^{-1}	M.S. data, m/e, % of base peak
1	Ph	82-4°	60%	$C_{21}H_{15}NO_2$ /313.36/	Calc.C 80.5 H 4.8 N 4.5 -	1650 /C=N/, 1672[a] /C=O/	313 /$M^{\oplus}$/,105 /$ArCO^{\oplus}$,100%/
					Found 80.9 5.0 4.8 -		
2	p-C_6H_4Cl	76-8°	58%	$C_{21}H_{14}ClNO_2$ /347.80/	Calc.C 72.6 H 4.0 N 4.0 Cl 10.1	1648 /C=N/, 1675[a] /C=O/	347 /$M^{\oplus}$/,139 /$ArCO^{\oplus}$,96%/,
					Found 72.9 4.4 4.6 10.2		105 /$PhCO^{+}$,100%/
3	p-$C_6H_4CH_3$	78-9°	55%	$C_{22}H_{17}NO_2$ /327.39/	Calc.C 80.7 H 5.2 N 4.3 -	1645 /C=N/, 1675[a] /C=O/	327 /$M^{\oplus}$/,119 /$ArCO^{\oplus}$,100%/,
					Found 80.3 5.3 4.4 -		105 /$PhCO^{\oplus}$,75%/
4	p-C_6H_4Br	79-80°	60%	$C_{21}H_{14}BrNO_2$ /391.76/	Calc.C 64.3 H 3.6 N 3.6 Br 20.4	1649 /C=N/, 1678[a] /C=O/	391 /$M^{\oplus}$/,183,185 /$ArCO^{\oplus}$,82.8%,
					Found 64.7 3.3 4.0 20.3		86.7%/,105 /$PhCO^{\oplus}$,100%/
5	m-C_6H_4Cl	74-5°	55%	$C_{21}H_{14}ClNO_2$ /347.80/	Calc.C 72.6 H 4.0 N 4.0 Cl 10.1	1650 /C=N/, 1665[a] /C=O/	347 /$M^{\oplus}$/,139 /$ArCO^{\oplus}$,51.1%/,
					Found 72.9 4.0 4.1 10.2		105 /$PhCO^{\oplus}$,100%/

[a] Broad bands

Table 2. Analyses and spectral data of the adducts of the 2-mono-anils of 1,3-diarylpropane-1,2,3-trione with mercaptoacetic acid, its methyl ester, thiophenol and 1-butanethiol



No	Ar	R	M.p.	Formula	Elemental Analyses	I.R. data, ν cm^{-1}	N.M.R[b] data, δ ppm
6	Ph	CH_2CO_2H	149-52°	$C_{23}H_{19}NO_4S$ /405.48/	Calc. C 68.1 H 4.7 N 3.5 S 7.9 - Found 67.9 4.6 3.5 7.9 -	1655, 1690 /C=O/, 1710 /$C=O_{ac}$/, 3365 /NH/, 2570-2860[a] /OH_{ac}/	2.92 /s,2H,CH_2/, 6.21 /s,1H,NH/, 8.17 /s,1H,OH_{ac}/
7	p-C_6H_4Cl	"	153-5°	$C_{23}H_{18}ClNO_4S$ /439.92/	Calc. C 62.9 H 4.1 N 3.2 S 7.3 Cl 8.0 Found 62.6 4.6 3.2 7.6 8.1	1652,1682 /C=O/, 1710 /$C=O_{ac}$/, 3365 /NH/, 2570-2980[a] /OH_{ac}/	2.90 /s,2H,CH_2/, 6.19 /s,1H,NH/, 8.23 /s,1H,OH_{ac}/
8	p-$C_6H_4CH_3$	"	134-5°	$C_{24}H_{21}NO_4S$ /419.50/	Calc. C 68.8 H 5.0 N 3.3 S 7.6 - Found 68.3 5.2 3.4 7.6 -	1652,1680 /C=O/, 1712 /$C=O_{ac}$/, 3362 /NH/, 2575-2985[a] /OH_{ac}/	2.93 /s,2H,CH_2/, 2.27 /s,3H,CH_3/, 6.23 /s,1H,NH/, 8.20 /s,1H,OH_{ac}/
9	p-C_6H_4Br	"	150-1°	$C_{23}H_{18}BrNO_4S$ /483.88/	Calc. C 57.0 H 3.7 N 2.9 S 6.6 Br 16.5 Found 56.5 4.1 3.1 6.8 16.3	1652,1680 /C=O/, 1710 /$C=O_{ac}$/, 3365 /NH/, 2580-2980[a] /OH_{ac}/	2.92 /s,2H,CH_2/, 6.18 /s,1H,NH/, 8.23 /s,1H,OH_{ac}/
10	m-C_6H_4Cl	"	125-7°	$C_{23}H_{18}ClNO_4S$ /439.92/	Calc. C 62.9 H 4.1 N 3.2 S 7.3 Cl 8.0 Found 62.9 3.9 3.1 7.4 7.5	1658,1682 /C=O/, 1710 /$C=O_{ac}$/, 3360 /NH/, 2570-2875[a] /OH_{ac}/	2.93 /s,2H,CH_2/, 6.20 /s,1H,NH/, 8.21 /s,1H,OH_{ac}/
11	Ph	/CH_2/$_3CH_3$	140°	$C_{25}H_{25}NO_2S$ /403.55/	Calc. C 74.4 H 6.2 N 3.5 S 7.9 - Found 74.6 6.3 4.0 8.3 -	1668[a] /C=O/, 3325, 3360 /NH/	0.78 /t,3H,CH_3/, 1.35 /m,4H,CH_2/, 2.21 /t,2H,SCH_2/, 6.28 /s,1H,NH/
12	Ph	Ph	145°	$C_{27}H_{21}NO_2S$ /423.54/	Calc. C 76.6 H 5.0 N 3.3 S 7.5 - Found 76.9 5.1 3.7 7.8 -	1670[a] /C=O/, 3362, 3375 /NH/	6.09 /s,1H,NH/
13	Ph	$CH_2CO_2CH_3$	138°	$C_{24}H_{21}NO_4S$ /419.50/	Calc. C 68.7 H 5.0 N 3.3 S 7.6 - Found 68.8 5.1 3.7 7.4 -	1652,1688 /C=O/, 1740 /$C=O_{ac}$/ 3378 /NH/	2.97 /s,2H,CH_2/, 3.21 /s,3H,CH_3/, 6.26 /s,1H,NH/
14	Ph	CH_2CO_2Na	230-3° d.	$C_{23}H_{18}NaNO_4S$ /427.47/	Calc. C 64.6 H 4.2 N 3.2 S 7.5 - Found 64.2 4.7 3.0 7.1 -	1655,1685 /C=O/, 1718 /$C=O_{ac}$/, 3365 /NH/	-

ac - acid, d. - decomposition

[a] Broad bands [b] s - singlet, t-triplet, m-multiplet

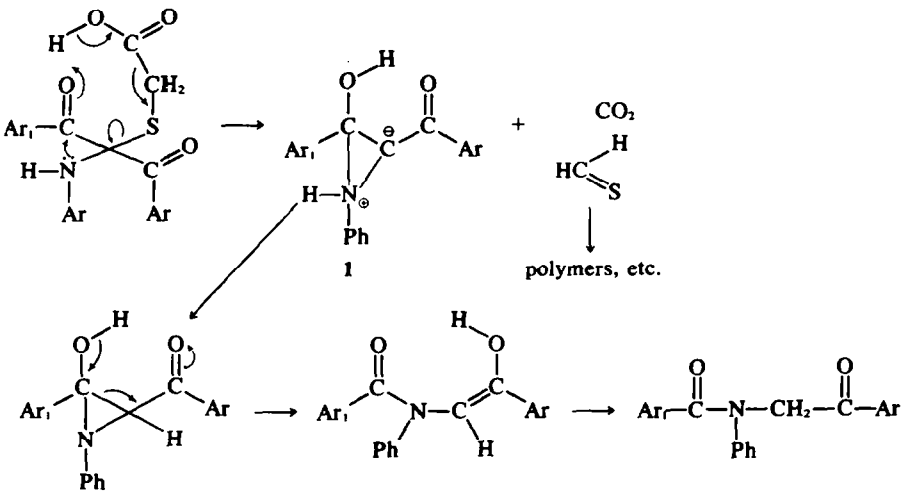
Table 3. Analyses and spectral data of the N-aroyl-ω-acetophenones

$Ar_1—CO—N(Ph)—CH_2—CO—Ar$

No	Ar_1	Ar	Yield[b]	M.p.	Formula	Elemental Analyses	IR data, ν cm^{-1}	NMR data, δ ppm	MS data, m/e, % of base peak
15[a]	Ph	Ph	60%	152°	$C_{21}H_{17}NO_2$ /315.37/	Calc. C 80.0 H 5.3 N 4.4 - Found 79.8 5.2 4.5 -	1648 /C=O$_{am}$/ 1692 /C=O/	5.23 /s,2H,CH_2/	315 /M$^{\oplus}$/, 105 /$Ar_1CO^{\oplus}$, $ArCO^{+}$, 100%/, 210 /$Ar_1CON^{\oplus}(Ph)=CH_2$, $ArCOCH=\overset{\oplus}{N}HPh$, 40.2%/
16	p-C_6H_4Cl	Ph	22%	187°	$C_{21}H_{16}ClNO_2$ /349.82/	Calc. C 72.2 H 4.6 N 4.0 Cl 10.0 Found 72.2 4.5 4.0 10.1	1642 /C=O$_{am}$/ 1690 /C=O/	5.25 /s,2H,CH_2/	349 /M$^{\oplus}$/, 244 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 23.5%/, 210 /$ArCOCH=\overset{\oplus}{N}HPh$, 6.5%/, 139 /$Ar_1CO^{\oplus}$, 100%/, 105 /$ArCO^{\oplus}$, 23.6%/
17	Ph	p-C_6H_4Cl	20%	148°	$C_{21}H_{16}ClNO_2$ /349.82/	Calc. C 72.2 H 4.6 N 4.0 Cl 10.0 Found 72.2 4.6 4.3 10.0	1645 /C=O$_{am}$/ 1690 /C=O/	5.19 /s,2H,CH_2/	349 /M$^{\oplus}$/, 210 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 27.3%/, 139 /$ArCO^{\oplus}$, 5.3%/, 105 /$Ar_1CO^{\oplus}$, 100%/
18	p-$C_6H_4CH_3$	Ph	28%	160°	$C_{22}H_{19}NO_2$ /329.40/	Calc. C 80.2 H 5.8 N 4.3 - Found 79.7 5.9 4.8 -	1650 /C=O$_{am}$/ 1698 /C=O/	5.31 /s,2H,CH_2/ 2.40 /s,3H,CH_3/	329 /M$^{\oplus}$/, 224 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 19.6%/, 105 /$ArCO^{\oplus}$, 8.0%/, 210, /$ArCOCH=\overset{\oplus}{N}HPh$, 1.0%/, 119 /$Ar_1CO^{+}$, 100%/
19	Ph	p-$C_6H_4CH_3$	22%	126°	$C_{22}H_{19}NO_2$ /329.40/	Calc. C 80.2 H 5.8 N 4.3 - Found 80.0 5.8 4.1 -	1658 /C=O$_{am}$/ 1695 /C=O/	5.31 /s,2H,CH_2/ 2.25 /s,3H,CH_3/	329 /M$^{\oplus}$/, 224 /$ArCOCH=\overset{\oplus}{N}HPh$, 2.1%/, 119 /$ArCO^{\oplus}$, 17.6%/, 210 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 20.2%/, 105 /$Ar_1CO^{\oplus}$, 100%/
20	p-C_6H_4Br	Ph	28%	161°	$C_{21}H_{16}BrNO_2$ /393.78/	Calc. C 63.9 H 4.1 N 3.5 Br 20.3 Found 63.8 4.1 3.3 20.7	1645 /C=O$_{am}$/ 1692 /C=O/	5.26 /s,2H,CH_2/	393 /M$^{\oplus}$/, 289, 287 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 54.5%, 52.8%/, 185, 183 /$Ar_1CO^{\oplus}$, 96.6%, 100%/, 210 /$ArCOCH=\overset{\oplus}{N}HPh$, 6.6%/, 105 /$ArCO^{\oplus}$, 72.8%/
21	Ph	p-C_6H_4Br	32%	214°	$C_{21}H_{16}BrNO_2$ /393.78/	Calc. C 63.9 H 4.1 N 3.5 Br 20.3 Found 63.5 4.2 3.3 20.6	1645 /C=O$_{am}$/ 1695 /C=O/	5.22 /s,2H,CH_2/	393 /M$^{\oplus}$/, 289, 287 /$ArCOCH=\overset{\oplus}{N}HPh$, 1.1%, 1.6%/, 185, 183 /$ArCO^{\oplus}$, 8.4%, 9.3%/, 210 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 74.0%/, 105 /$Ar_1CO^{\oplus}$, 100%/
22	m-C_6H_4Cl	Ph	20%	114°	$C_{21}H_{16}ClNO_2$ /349.82/	Calc. C 72.2 H 4.6 N 4.0 Cl 10.0 Found 72.2 4.6 3.8 9.9	1645 /C=O$_{am}$/ 1695 /C=O/	5.23 /s,2H,CH_2/	349 /M$^{\oplus}$/, 244 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 76.7%/, 139 /$Ar_1CO^{\oplus}$, 100%/, 210 /$ArCOCH=\overset{\oplus}{N}HPh$, 8.2%/, 105 /$ArCO^{+}$, 74.7%/
23	Ph	m-C_6H_4Cl	21%	136°	$C_{21}H_{16}ClNO_2$ /349.82/	Calc. C 72.2 H 4.6 N 4.0 Cl 10.0 Found 72.2 4.8 4.2 10.2	1660 /C=O$_{am}$/ 1695 /C=O/	5.18 /s,2H,CH_2/	349 /M$^{\oplus}$/, 244 /$ArCOCH=\overset{\oplus}{N}HPh$, 4.5%/, 139 /$ArCO^{\oplus}$, 6.8%/, 210 /$Ar_1CON^{\oplus}(Ph)=CH_2$, 28.3%/, 105 /$Ar_1CO^{\oplus}$, 100%/

am - amide , s - singlet

[a] Ref. /13/ [b] Yields obtained in thermal rearrangement.



of the investigated acids a mixture of both isomeric N-aroyl-ω-anilinoacetophenones was obtained. The ratio of isomers was nearly 1 : 1 in all cases so the influence of the substituents do not seem to be very important.

EXPERIMENTAL

2-Mono-anils of 1,3-diarylpropane-1,2,3-trione (compounds **1–5**). The corresponding diaroylmethane (1 g) and the equimolar amount of nitrosobenzene were dissolved in 5 ml EtOH and 0·01 ml of 33% ethanolic KOH was added. The exothermic, violent reaction occured almost immediately after the base addition and the mixture changed its colour from dark green to orange. The crude product was precipitated after day's standing in a refrigerator. It was purified by crystallization from EtOH, yield 55–60%.

(Anilinodiaroyl-)-methylmercaptoacetic acids (compounds **6–10**). The corresponding 2-mono-anil (1 g) was mixed with 1 ml freshly destilled mercaptoacetic acid. The exothermic process started at once and the 2-mono-anil dissolved. The red oil was diluted with 5 ml of cold EtOH and the pale yellow crystals precipitated. The crude product was purified by crystallization from EtOH, yield 80–85%.

The adducts of the 2-mono-anils of 1,3-diarylpropane-1,2,3-trione with thiols and mercaptoacetic acid methyl ester were prepared using the same method (compounds **11–14**).

Thermal rearrangement. An adduct (1 g) was dissolved in 10 ml dry xylene and the mixture was heated until the liberation of sulphur dihydride had finished (usually 6–8 hr). During this time the starting yellow soln turned deep red and traces of a black oil appeared. Then 0·1 g of Norit was added to the mixture and it was heated again and filtered. The filtrate was diluted with 1 ml petrol ether and put aside into a refrigerator for 1 hr. The crude product consisted of two isomers of the N-aroyl-ω-anilinoacetophenone. They were separated by crystallization from ligroin (b.p. 80–100°), EtOH and EtOAc, yield 20–60%.

N-aroyl-ω-anilinoacetophenones (compounds **15–23**). The corresponding ω-bromoacetophenone (1 g) was mixed with the equimolar amount of aniline in 5 ml EtOH containing 0·5 ml Et_3N. The mixture was heated at 35° for 15 min and put aside into a refrigerator for 1 hr. The ppt was filtered off, washed with cold EtOH and purified by crystallization from light ligroin (b.p. 60–80°), yield 60–65%.

The ω-anilinoacetophenone was mixed with the corresponding aroyl chloride in 5 ml dry benzene and heated on a steam bath for 1 hr. The product obtained after cooling, was purified by crystallization from EtOH or EtOAc, yield 70%.

Apparatus. NMR spectra were recorded on a Tesla BT-476 spectrometer, using $CDCl_3$ as a solvent and TMS as an inner standard. IR spectra were recorded on an UR-10 Zeiss Jena spectrophotometer, using Nujol and Hexachlorobutadiene mulls. Mass spectra were recorded on an LKB-9000S spectrometer in Central Laboratory of Mass Spectroscopy, Cracow.

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