Tetrahedron. Vol 32, pp. 2549 to 2558 Pergamon Press 1976 Printed in Great Britain

NOVEL ALDEHYDE SYNTHESES BASED ON SELECTIVE REDUCTION OF *s*-TRIAZOLE DERIVATIVES†

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(*Received in UK 2 February* 1976; *Accepted for publication 27 April* 1976)

Abstract—Methods are described for synthesising *s*-triazolium halides (**5**) and converting these into aldehydes RCHO, RCH_2CHO, RCH_2CH_2CHO in which R can contain double bonds, halogen, nitro, keto and ester substituent; have one or two side chains on the α-carbon, or can be alicyclic. A general method for converting α-hydroxyacids to aldehydes is suggested.

In the development of a simple and selective method for the synthesis of aldehydes, it has been observed that compound **1A** is readily reduced to **2A** which is the key-step in the conversion of benzoic acid to benzaldehyde.[2] A practical aldehyde synthesis involves reduction of type **3** compounds and subsequent hydrolysis via compounds **4**[3] to the desired aldehydes.

The *s*-triazolium (**5**) salts,[4,5] are even more promising starting compounds and a general method for the synthesis of **5** chlorides, depends on the reactions of S-methyl-1,4-diphenylisothiosemicarbazide[4] (**6**)‡ with acid chlorides or, in the presence of $POCl_3$, with carboxylic acids. Treatment of the reaction mixtures with aqueous KI furnished the corresponding iodides whose isolation proved easier (Table 1).

An alternative mode of preparation of type **5** salts consists in deprotonation and subsequent alkylation of **5** (R = R′R″CH–) iodides (Table 1). Deprotonation to yield compounds—which, as a type, have been assigned the structure of anhydrobases **7b**[6,7] but which, at least, do react as *C*-ylids **7a**—may be easily achieved with NaH in anhyd DMF. If R′ in the cation **5** (R = R′R″CH–) is a haloalkyl group, intermolecular alkylation takes place after deprotonation as in the synthesis of **5** (R = cyclopropyl) iodide. The compounds **7** are, in general, rather unstable and have not been isolated although **7** (R′ = R″ = Ph), proved stable. By treatment with aqueous HCl and KI the latter is reconverted into **5** ($R = Ph_2CH$–) iodide, and in TFA soln its NMR spectrum is identical with that of the cation **5** ($R = Ph_2CH$–).

A variety of heterocyclic cations are readily converted into dimers of nucleophilic carbenes which, at elevated temperatures, react as the monomeric carbenes.[8–12] Accordingly, the easily accessible **5** (R = H) iodide was deprotonated to yield the nucleophilic carbene **8** for which there is no indication of the existence of a stable high melting dimer **9**. In contrast to other nucleophilic carbenes, compound **8** may be readily alkylated to yield type **5** cations ($R \neq H$).

When the carbene **8** reacts with trimethylene bromochloride, the resulting **5** ($R = Cl–CH_2–CH_2–CH_2$–) bromide is deprotonated by the unreacted carbene to yield compound **7** (R′ = $Cl–CH_2–CH_2$–, R″ = H) which subsequently undergoes intramolecular alkylation to yield the cation **5** (R = cyclopropyl).

Treatment of the *s*-triazolium (**5**) salts with $NaBH_4$ furnished the corresponding *s*-triazolines **10** (Table 2.).

Attack of the nucleophilic $H:^{\ominus}$ ions takes place exclusively at position 5 of the cations **5** because, as shown by the limiting structures **5a** and **b**, the positive charge is mainly localized in the N(1)–C(5)–N(4) moiety, because no stable neutral primary product could result from attack at C(3). Interchange of the C(3) and C(5) substituents does not alter the site of attack of nucleophiles. Compound **11** furnishes the *s*-triazolinium-5-olate **12** and the *s*-triazoline **13** when treated with NaOH and $NaBH_4$, respectively. Proof of structure for compound **13** comes from its NMR spectrum and its reaction with 6-(2-aminophenyl)-3-methylthio-*as*-triazin-5(2H)-one[14] which furnishes compound **14** (R = H)[15] and thereby proves the presence of a formaldehyde equivalent in **13**.

Acid hydrolysis of the *s*-triazolines **10** furnished the aldehydes R–CHO§ (Table 3) in 40–80% yields, based on the carboxylic acids R–COOH or their chlorides originally introduced. Neither the *s*-triazoline (**10**), nor the *s*-triazolium (**5**) salt intermediates need be isolated in pure form.

The selectivity of the reduction step is high. As shown by several examples listed in Table 3, halogen substituents, nitro and ester groups and C=C double bonds remain unchanged. Our method is furthermore suitable for the conversion of dicarboxylic into aldehydic acids. The reduction may be carried out selectively even in the presence of ketone carbonyl groups. Further indication of the selectivity of the reduction step is the observation that **5** (R = Ph) may be successfully reduced even in the presence of a tenfold molar excess of propanal or butanal.

The present aldehyde synthesis as well as that described in Ref. 3 has advantages over the well known methods developed by Meyers *et al.*[16,17,29] in the simplicity of both the preparation and reduction of the cations **5** (and **3**), and the ease of deprotonation of the cations **5** as well as the use of carbenes **8** as intermediates (see, however, Ref. 30). The advantage of the presently described aldehyde synthesis over our earlier method[3] is that the salts **5** are much more readily and cheaply accessible than the salts **3**; decomposition of the *s*-triazolines **10** to yield the aldehydes is, on the other hand, somewhat more tedious than the decomposition of the compounds **4**.

A typical carbene reaction (*cf.* Ref. 8) of compound **8** is

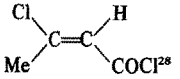
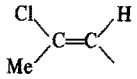
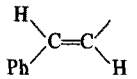
†Part of this work has been published in preliminary communications, see Refs. 1*a–c*.

‡Tautomeric structure unknown.

§A simple example of this reaction for R = Ph has been described in literature.[4]

Table 1. Synthesis of *s*-triazolium (5) chlorides and iodides

Starting compound	Product 5 R =	Method[a]	Anion	Yield %	Product M.p., °C recryst. from	Formula Mol. wt	Calc/found C%	H%	N%
MeCOCl		A	Cl	94	240–2 EtOH–ether	*b*			
	Me	A		92	259–60	*b*			
		B	I	82	i-PrOH				
5 (R = H) I^-		E[c]		97					
EtCOOH		C		94					
EtCOCl		A		67	217	$C_{17}H_{18}IN_3S$			9.93
5 (R = Me) I^-	Et	D[c]	I	83	i-PrOH	423.32	*e*		10.08
5 (R = H) I^-		E[d]		66					
PrCOOH		C		98					
PrCOCl	Pr	A	I[f]	42	240–2	$C_{18}H_{20}IN_3S$	49.43	4.61	9.61
5 (R = Me) I^-		D[d]		76	EtOH	437.35	49.37	4.50	9.70
i-PrCOOH		C		82	243–5	$C_{18}H_{20}IN_3S$	49.43	4.61	
5 (R = Et) I^-	i-Pr	D[c]	I	54	EtOH	437.35	49.48	4.62	*g*
					221–3	$C_{19}H_{22}IN_3S$			9.31
5 (R = H) I^-	Bu	E[h]	I	76	i-PrOH	451.38	*i*		9.60
t-BuCOCl		A		31	268–70	$C_{19}H_{22}IN_3S$	50.56	4.91	9.31
5 (R = i-Pr) I^-	t-Bu	D[c]	I	62	aqu MeOH	451.38	50.95	4.99	9.60
$Cl(CH_2)_3COCl$	Cl–$(CH_2)_3$–	A	I	70	320[d]	$C_{18}H_{19}ClIN_3S$			
		B		60	MeOH	471.80	*j*		
MeOOC–$(CH_2)_2$–COOH		C		87	244–6	$C_{19}H_{20}IN_3O_2S$			8.73
5 (R = Me) I^-	MeOOC–CH_2–CH_2–	D[k]	I	77	MeOH	481.36	*k*		9.11
5 (R = H) I^-		E[l]		43					
MeOOC–$(CH_2)_4$–COCl–	MeOOC–$(CH_2)_4$–	A	I	63	147	$C_{21}H_{24}IN_3O_2S$	49.51	4.75	
		B		68	i-PrOH	509.41	49.45	4.65	
$AcOCH_2COCl$	AcO–CH_2–	B	I	34	182–3 EtOH	$C_{18}H_{18}IN_3O_2S$ 467.33			8.89 9.09
$HOOC(CH_2)_4COOH$	–$(CH_2)_4$–	C[n]	I	52	308–10 aqu AcOH	$–C_{34}H_{34}I_2N_6S_2$ 844.61	48.35 48.75	4.06 4.41	
PhCOOH	Ph	C	I	93	>360[o] EtOH	*p*			
PhCOCl	Ph	A	Cl	95	320[d]	*p*			
		B		83	EtOH				
2-MeC_6H_4COCl	2Me–C_6H_4–	A	I	67	268–70 EtOH	$C_{22}H_{20}IN_3S$ 485.38			8.66 8.93
4-ClC_6H_4COOH	4Cl–C_6H_4–	C	I	95	246–8 $MeNO_2$	$C_{21}H_{17}ClIN_3S$ 505.82			8.31 8.36
4-$O_2NC_6H_4COOH$	4NO_2–C_6H_4–	C	I	91	264–5[d] $MeNO_2$	$C_{21}H_{17}IN_4O_2S$ 516.37	*q*		10.85 10.85
4-MeOOCC$_6$H$_4$COOH	4-MeOOC–C_6H_4–	C	I[r]	41	220[d]	$C_{23}H_{20}IN_3O_2S$	52.18	3.81	7.93
4-MeOOCC$_6$H$_4$COCl		A		95	MeOH-ether	529.40	52.32	3.99	7.93

$3,4,5\text{-}(MeO)_3C_6H_2COOH$	$3,4,5\text{-}(MeO)_3C_6H_2$–	C	I	76	242–4 EtOH	$C_{24}H_{24}IN_3O_3S$ 561.44	*s*		7.48 6.99
$PhCH_2COOH$		C		95					
$PhCH_2COCl$	$PhCH_2$	A	I	63	194–6	$C_{22}H_{20}IN_3S$	*u*		8.66
5 (R = H) I^-		E[t]		72	EtOH	485.39			8.72
$Ph_2CHCOOH$	Ph_2CH	C	I[v]	66	>100[d] —	$C_{28}H_{24}IN_3S$ 561.48	*w*		
PhC_2H_4COOH		C		98	240–2	$C_{23}H_{22}IN_3S$	55.31	4.44	8.42
PhC_2H_4COCl	Ph–CH_2–CH_2–	A	I[x,x]	76	aqu. EtOH	499.42	55.44	5.14	8.38
Nicotinic acid	3-Pyridil	C	I	98	318–20[d] MeOH–ether	$C_{20}H_{17}IN_4S$ 472.36	50.85 50.76	3.63 3.81	11.86 11.73
		A	I	30	266–8[d] MeOH	$C_{18}H_{17}ClIN_3S$ 469.79			8.94 8.68
Trans-cinnamic acid		C	I	95	>240[d] EtOH	$C_{23}H_{20}IN_3S$ 497.40	*y*		8.47 8.70

[a] See text. [b] Identical with an authentic sample.[5] [c] Alkylating agent MeI. [d] Alkylating agent EtI. [e] I, Calc.: 29.98, Found: 30.26°. [f] Treatment of the iodide in MeOH with excess 20% aqu $NaBF_4$ soln furnished the tetrafluoroborate, m.p. 179° (from i-PrOH), in 81% yield. [g] I, Calc.: 29.02, Found: 28.94%. [h] Alkylating agent BuI. [i] I, Calc.P 28.12; Found: 28.60%. [j] Found: Cl, 7.13; I, 27.02. Calc.: Cl, 7.52; I, 26.90%. [k] Alkylating agent $ClCH_2COOMe$. [l] Alkylating agent $ClCH_2CH_2COOMe$. [m] Found: I, 26.50; S, 6.38. Calc.: I, 26.37; S, 6.66%. [n] Both carboxyl groups did react to yield 5,5' - tetramethylene - bis(3 - methylthio - 1,4 - diphenyl - *s* - triazolium) diiodide. [o] Change of crystal form above 300°. [p] Identical with an authentic sample.[4] [q] S, Calc.: 6.21. Found: 6.61%. [r] Found: I, 23.84; S, 5.72. Calc.: I, 23.89, S. 6.06%. [s] I, Calc.: 22.61. Found: 22.45%. [t] Alkylating agent $PhCH_2Cl$. [u] Found: I, 26.22; S, 6.61. Calc.: I, 26.15; S, 7.08%. [v] Obtained through compound **7** (R' = R'' = Ph) (see text) by dissolving the latter in aqu. methanolic HCl and adding excess 20% aq KI soln. [w] I, Calc.: 22.60, Found: 22.45%. [x] Treatment of the iodide in MeOH with excess 20% aq $NaBF_4$ soln furnished the tetrafluoroborate, m.p. 222–4° (from EtOH), in 40% yield. [y] I, Calc.: 25.51, Found: 25.42%. [z] I, Calc.: 25.41. Found: 25.08%.

Table 2. $NaBH_4$ reduction of the triazolium (**5**) salts

R	Solvent used for extraction[a]	Yield %	Product (**10**) M.p., °C recryst. from	Formula Mol. wt.	Calc/found C%	H%	N%	S%
Me	pentane	97	75–6 i-PrOH	$C_{16}H_{17}N_3S$ 283.39			14.83 14.77	11.31 11.50
Et	ether	90	90–1 i-PrOH	$C_{17}H_{19}N_3S$ 297.41	68.65 69.18	6.44 6.51	14.13 14.46	
Pr	pentane	89	65–6 i-PrOH	$C_{18}H_{21}N_3S$ 311.44			13.49 13.50	
t-Bu	—	76	82–3 i-PrOH	$C_{19}H_{23}N_3S$ 325.46	70.12 70.47	7.12 6.95	12.81 12.72	
cyclopropyl	—[b]	98	80.81 i-PrOH	$C_{18}H_{19}N_3S$ 309.42	69.86 70.13	6.19 6.30	13.58 13.81	
MeOOC–$(CH_2)_4$–	ether	85	63–4 i-PrOH	$C_{21}H_{25}N_3O_2S$ 383.50				8.36 8.30
Ph	—	99	109–10 i-PrOH	[c]				
4-ClC_6H_4–	—[d]	99	106–7 i-PrOH	$C_{21}H_{18}ClN_3S$ 379.90	[e]		11.06 11.25	8.44 8.50
4-$O_2NC_6H_4$–	—[d]	97	134–5 i-PrOH	$C_{21}H_{18}N_4O_2S$ 390.45			14.35 14.15	8.21 8.51
4-$MeOOCC_6H_4$–	—[d]	96	112 MeOH	$C_{23}H_{21}N_3O_2S$ 403.49	68.46 68.96	5.25 5.83	10.41 10.45	7.95 8.33
3,4,5-$(MeO)_3C_6H_4$–	—[f]	90	126–7 EtOH	$C_{24}H_{25}N_3O_3S$ 434.52			9.67 9.67	7.38 7.53
p-phenylene	—[g]	80	182–3 DMF–MeOH	$C_{36}N_{32}N_6S_2$ 612.80	70.50 70.33	5.25 5.18		
$PhCH_2$–	—[h]	98	105–6 i-PrOH	$C_{22}H_{21}N_3S$ 359.48			11.69 11.39	8.92 9.04
3-pyridyl	—	97	126 i-PrOH	$C_{20}H_{18}N_4S$ 346.44			16.17 16.25	9.25 9.18

[a] See text. [b] The reduction of the starting **5** (120 mmole) was performed in 1:2 (v/v) DMF–MeOH mixture (225 ml). The reaction mixture was heterogeneous throughout. [c] The product was identical with an authentic sample obtained as described in literature.[4] [d] The reduction of the starting **5** (20 mmole) was performed in methanol (80 ml) with slightly alkaline aq $NaBH_4$ soln. Crystallization of the product started before acidification with AcOH and did not need addition of water for completion. [e] Cl, Calc.: 9.33, Found: 9.73%. [f] The reduction was performed in 2:1 (v/v) DMF–MeOH mixture. [g] The starting *p*-phenylenebis(*s*-triazolium) salt was prepared in 89% yield (crude product) according to Method C; it resisted all attempts of recrystallization. The reduction product started to separate before acidification with AcOH. Addition of water was not necessary for completion of separation of the product. [h] As [d], but water had to be added in order to complete separation of the product.

Table 3. Decomposition of the triazolines **10**

R	Method[a]	R–CHO Yield, %	m.p. °C (recryst) b.p. °C/Torr	Identified as[b]
Me	F	60		**14**[15 c]
Et	F	90		**14**[c,d]
Pr	F	72[e]	— 75/760	DNP, m.p. 122°C[f]
i-Pr	F	87[g]	— 62–3/760	DNP, m.p. 182°C[h]
t-Bu	F	75	— 75/760	DNP, m.p. 210°C[i]
cyclopropyl	F	63[e]	— 62–4/5	DNP, m.p. 186–7°C[j]
Cl–$(CH_2)_3$–	H	61[g,k]	— 62–4/5	DNP, m.p. 132–3°C[l]
MeOOC–C_4H_8–	H[m]	64	— 72–4/1[n]	**14**[o]
Ph	G H[p]	89 91	— 178–80/760	**14**[15]
2-MeC_6H_4–	H	78[g,q]	— 88–9/119	DNP, m.p. 193°C[r]
4-ClC_6H_4–	H	81	47–48 (pentane)[s]	
4-$NO_2C_6H_4$–	H	91	— 105–6 (water)[t]	

Table 3. (*Contd.*)

R	Method[a]	R–CHO Yield, %	m.p. °C (recryst) b.p. °C/Torr	Identified as[b]
4-MeOOCC$_6$H$_4$–	H	77	64–5[u]	**14**[v]
3,4,5-(MeO)$_3$C$_6$H$_2$–	G	91	75–6 (water)[w]	
Trans-cynnamoyl	H[m]	83	250–2/760[z]	**14**[z]
p-phenylene	H[y]	87	114–5[aa]	

[a] See text. [b] DNP = 2,4-dinitrophenylhydrazone. [c] The distillate was collected in a flask cooled in an ice-bath and containing 1-equivalent of 6 - (2 - aminophenyl - 3 - methylthio - *as* - triazin - 5(2H) - one,[14] dissolved in a 10:1 v/v EtOH–AcOH mixture. The yield stated refers to the resulting type **14** condensation product. [d] **14** (R = Et), m.p. 226–228° (from nitromethane). Found: C, 56.66; H, 5.49; N, 20.25. Calc. for $C_{13}H_{14}N_4OS$ (274.34): C, 56.91; H, 5.14; N, 20.43%. [e] Distilled product. [f] Lit.[20a] m.p. 123°. [g] Overall yield of the reduction an decomposition steps. [h] Lit.[20a] m.p. 187°. [i] Lit.[20a] m.p. 209°. [j] Lit.[21] b.p. 98°, m.p. 186–7°. [k] Ether and methylene dichloride were used as the solvents for the extraction of the triazoline **10** and the aldehyde, respectively. [l] Lit.[22] m.p. 135°. [m] Ether was used as the solvent for extraction of the aldehyde. [n] Lit.[23] b.p. 69° at 0.6 Torr. [o] **14** (R = MeOOC–C$_4$H$_6$–), m.p. 178–179° (from MeOH). Found: C, 55.91; H, 5.48; S, 9.07. Calc. for $C_{17}H_{20}N_4O_3S$ (360.43). C, 56.65; H, 5.59; S, 8.90%. [p] Extraction with benzene. [q] Ether was used as the solvent for extraction both of the triazoline **10** and the aldehyds. [r] Lit.[20c] m.p. 194°. [s] Lit.[24] m.p. 47°. [t] Lit.[20c] m.p. 106°. [u] Lit.[25] m.p. 63°. [v] **14** (R = 4-MeOOC–C$_6$H$_4$–), m.p. 255–6° (from DMF). Found: N, 14.55; S, 8.27. Calc. for $C_{15}H_{16}N_4O_3S$ (380.42): N, 14.73; S, 8.43%. [w] Lit.[26] m.p. 75°. [z] Lit.[20d] b.p. 252°. [x] **14** (R = *trans*-cinnamyl), m.p. 233–4° (from DMF). Found: N, 14.27; S, 13.04. Calc. for $C_{15}H_{16}N_4OS$ (380.42): N, 14.73; S, 12.62%. [y] Extraction with pentane. [aa] Terephthalaldehyde, lit.[27] m.p. 116°.

its reaction with benzaldehyde to yield, via **15**, compound **16** which has been obtained also by reacting phenylglyoxal with compounds **6**, or by reacting the carbene with benzoyl chloride, and reducing the resulting **5** (R = PhCO–) iodide with $NaBH_4$. [Ethanolysis of **5** (R = PhCO), on the other hand, results in elimination of the benzoyl group.]

The intermediate **15** may alternatively be generated by deprotonation of **5** (R = PhCHOH–) iodide, obtained by deacetylation of **5** (R = PhCHOAc). **5** (R = MeCHOH) was similarly obtained. The related **5** (R = Et–CHOBz–) iodide was obtained in good yields by treating compound **7** (R′ = Et, R″ = H) with dibenzoyl peroxide. Attempts to generalize the latter reaction has failed since the desired products were obtained only in low yields. When the solution was acidified immediately after generation of **15**, benzaldehyde and **5** (R = H) iodide were obtained, and no compound **16** could be isolated, which demonstrates that the first step of the reaction of the carbene with aldehydes is reversible.

Heating of **5** (R = PhCHOH– and MeCHOH–) iodide at 170° or treatment with Et_3N at r.t. results in decomposition to yield benzaldehyde and acetaldehyde, respectively, and **5** (R = H) iodide. [**5** (R = Et–CHOBz–) iodide reacts similarly with methanolic Et_3N.] The above reaction sequence is a novel method for the degradation of α-hydroxyacids to the aldehydes containing one carbon atom less.

EXPERIMENTAL

1,4-Diphenylthiosemicarbazide. The following procedure is an improved version of that reported in the literature.[18]

The mixture of thiocarbanilide (412 g; 1.8 mole), phenylhydrazine (200 ml; 2.0 mole) and EtOH (800 ml) was refluxed until a clear soln resulted (1 hr). On cooling, separation of the crystalline product started. (Cooling of the mixture at this point is necessary; otherwise, the considerable heat of crystallization incurs heavy losses of material.) The heterogeneous mixture was refluxed for further 4 hr to yield 406 g (92.7%) of the title compound, m.p. 179° (non-recrystallized product), lit.[18] 181°.

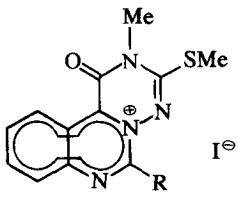
S - Methyl - 1,4 - diphenylisothiosemicarbazide (**6**). 1,4 - Diphenylthiosemicarbazide (406 g; 1.67 mole) was stirred into anhyd DMF (700 ml), the mixture was placed in an ice-bath, and freshly distilled dimethylsulfate (170 ml; 1.81 mole) was immediately added dropwise at a rate to maintain the temp. at 15–20°. The ice-bath was removed, and the mixture was stirred for another hr during which period its temp. rose to 40°. The brownish-green soln was poured into the aqueous (2 l.) soln of $NaOAc \cdot 3H_2O$ (540 g; 3.9 mole), and the resulting oil was taken up in ether or benzene (600 ml). The aqueous layer was extracted with two portions (400 ml, each) of ether or benzene, the combined organic solns were washed with water (two portions, 300 ml, each), dried ($MgSO_4$) and evaporated to dryness *in vacuo* at 40°. The residue was triturated with i-PrOH (270 ml) and, allowed to stand in a refrigerator overnight to yield 338–365 g (78–85%) of the title compound, m.p. 78–79°, which was washed with ice-cold i-PrOH (100 ml) and pentane (750 ml) until colourless.

Synthesis of s-*triazolium* (**5**) *salts* (*Table* 1)

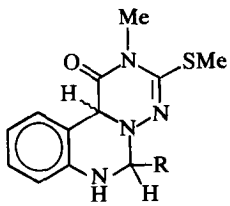
Method A. Mixtures of compound **6** (25.7 g; 0.1 mole), the appropriate acid chlorides (0.1 mole) and anhyd dioxane (100 ml) were refluxed for 20 min. After cooling, anhyd ether (300 ml) was added to yield the **5** *chlorides* either as crystalline or oily products. In the latter case, the mixtures were chilled (0°), the solvent was decanted and the oily product was triturated with ether. The solvent was again decanted and the oil was taken up in MeOH (50–150 ml). 20% KI aq (100–300 ml) was added to precipitate the crystalline **5** *iodides.*

Method B. As above, but the dioxane (20 ml) soln of the acid chloride was added to the dioxane soln of compound **6** dropwise (15 min) at 0° under stirring, and the mixture was allowed to stand for 24 hr at r.t.

Method C. $POCl_3$ (12 ml; 0.13 mole) was added under vigorous stirring to mixtures of compound **6** (25.7 g; 0.1 mole), the appropriate carboxylic acids (0.1 mole) and anhyd. pyridine (70 ml) at such a rate that the mixtures started and were kept boiling. The hot mixtures were stirred for 1 min. Anhyd. MeOH (70 ml) was added dropwise. The warm solns were treated with 20% KI aq (140 ml) and chilled (0°) to yield the **5** iodides. When the latter separated as oils, water (300 ml) was added and the mixtures were extracted with $CHCl_3$. The oily residues, obtained after conventional work-up of the $CHCl_3$ solns were triturated with ether (100 ml) until they turned crystalline.



1
(1a: R = Ph)



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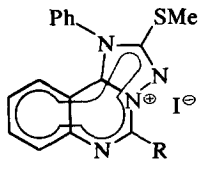
(2a: R = Ph)



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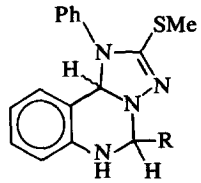

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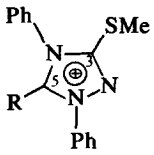

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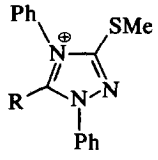

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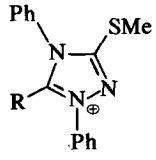

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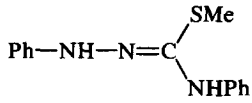

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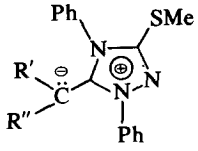

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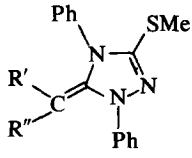

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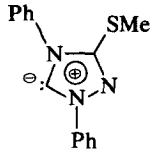

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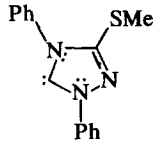

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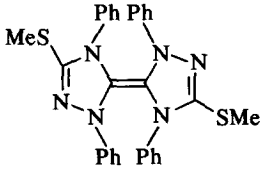

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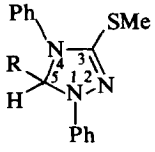

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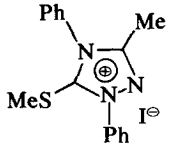

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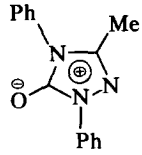

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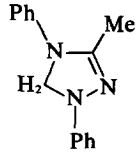

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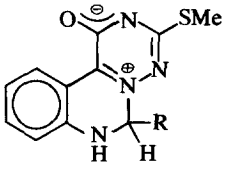

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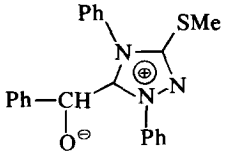

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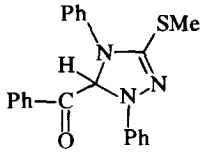

16

Method D. 80% NaH dispersions in mineral oil (0.2 mole) were stirred under ice cooling into mixtures of the **5** iodides (R = R′R″CH–) (0.1 mole) and anhyd DMF (100 ml). The mixtures were stirred for 15 min at 0° and for another 15 min at r.t. until the evolution of H_2 ceased, and again chilled (0°). The excess NaH and the NaI were filtered off and washed with anhyd DMF (two portions, 20 ml, each). Alkyl halides (R‴–X) (0.1 mole) were added to the combined filtrate and washings and the mixtures were kept overnight in a refrigerator. 20% KI aq (150 ml), AcOH (15 ml) and water (300 ml) were added successively, and the resulting oily **5** iodides were worked up as in Method C. The crude crystalline **5** iodides (R = R′R″R‴C–) which were usually contaminated with about 10–20% of the starting **5** iodide (R = R′R″CH–), were either purified by recrystallization or directly converted into the aldehydes R′R″R‴C–CHO without further purification.

Method E. Mixtures of **5** iodide (R = H) (39.5 g; 0.1 mole) and anhyd DMF (160 ml) were treated with 80% NaH dispersions in mineral oil (0.15 mole), alkyl halides (R′X) (0.1 mole), and finally with AcOH (15 ml) and 20% KI aq soln (300 ml) as in Method D. The resulting crude crystalline **5** iodides (R ≠ H) were filtered off and dissolved in $CHCl_3$ (200 ml). Alternatively, water (300 ml) was added to the mixtures containing the crude oily iodides, and the product was extracted with $CHCl_3$ (three portions, 100 ml, each). The $CHCl_3$ solns were filtered (in order to remove unreacted starting material which is almost insoluble in *cold* $CHCl_3$), washed with water, dried ($MgSO_4$) and evaporated to dryness. The residues, when triturated with ether, turned crystalline.

NMR spectra of the **5** *iodides.* In addition to the signals corresponding to the R groups, the $CDCl_3$ spectra exhibit two multiplets centered around δ 8.4–8.1 (4*H*, *o*-protons of the N–Ph groups) and 7.8–7.5 (6H, *m*- and *p*-protons of the N–Ph groups), respectively, and a singlet at about 2.8–2.7 ppm (3H, S–Me). In DMSO-d_6 and TFA solns the multiplets of the *o*- and of the remaining aromatic protons are merged.

3 - *Methylthio* - 1,4 - *diphenyl* - *s* - *triazolium* (**5**, R = H) *iodide*

MeI (44 ml, 0.7 mole) was added under cooling to a soln of 1,4-diphenylthiosemicarbazide (150 g; 0.62 mole) in dry DMF (200 ml). The mixture was stirred for 30 min. Triethyl orthoformate (99 ml; 0.62 mole) was added, and the mixture was kept overnight at 0° to yield 175 g (71%) of the crystalline title compound, m.p. 244–245° (from DMF), which was filtered off and washed with cold DMF, MeOH and ether. (Found: C, 45.64; H, 3.69; N, 10.85. Calc. for $C_{15}H_{14}IN_3S$ (395.27); C, 45.58; H, 3.57; N, 10.63%).

5 - (1 - *Ethyl* - 3 - *methoxycarbonylpropyl*) - 3 - *methylthio* - 1,4 - *diphenyl* - s - *triazolium* (**5**, R = MeOOC–CH_2–CH_2–CHEt-*iodide*

Compound **5** (R = Pr) iodide (40 g; 91 mmole) reacted in anhyd DMF (100 ml) with 80% NaH dispersion in mineral oil (160 mmole) and with $ClCH_2CH_2COOMe$ (10.4 ml; 0.1 mole), dissolved in anhyd DMF (20 ml), according to Method D. The mixture was poured into a mixture of 20% NaCl aq (200 ml), AcOH (10 ml) and ice (100 g). The small amount of insoluble material was removed after the mixture had been kept for 1 hr at 0°. Water (200 ml) was added and the organic product was extracted with $CHCl_3$ (three portions, 100 ml, each). The combined $CHCl_3$ solns were washed with water, dried and evaporated to dryness *in vacuo*. The residue was extracted twice with water (200 and 50 ml) at r.t., and the insoluble oil was discarded. The combined aqueous solns were treated with 20% NaI aq (100 ml) and cooled to 0°. The aqueous layer was decanted from the gummy product, and the latter was dissolved in EtOAc (50 ml) by gentle heating. The soln was concentrated *in vacuo* to about 20 ml and allowed to stand at 0° to yield 16 g (33%) of the title compound, m.p. 168–170° (from i-PrOH). (Found: C, 49.84; H, 5.43; N, 7.89. Calc. for $C_{22}H_{26}IN_3O_2S$ (523.44): C, 50.48; H, 5.01; N, 8.03%).

5 - *Cyclopropyl* - 3 - *methylthio* - 1,4 - *diphenyl* - s - *triazolium* **5**, R = *cyclopropyl*) *iodide*

(a) Intramolecular alkylation was achieved by treating **5** (R = Cl–CH_2–CH_2–CH_2–) iodide (61 g; 130 mmole) in anhyd DMF (450 ml) with a 80% NaH dispersion in mineral oil (260 mmole), and then with the mixture of KI (80 g), water (1500 ml) and AcOH (30 ml), and work-up under the conditions described in Method D. 42 g (75%) of the title compound, m.p. 252–254° (from MeOH), were obtained. (Found: C, 49.70; H, 4.37; I, 28.40; 9.97. Calc. for $C_{18}H_{18}IN_3S$ (435.33): C, 49.66; H, 4.17; I, 29.16; N, 9.65%).

(b) **5** iodide (R = H) (10 g; 25.4 mmole) was converted into the carbene **8**, and the latter was treated with trimethylene bromochloride (1.2 ml; 12 mmole) according to Method E. The mixture was allowed to stand for 2 hr at r.t. 20% KI aq (80 ml) and AcOH (10 ml) were added. The crystalline product was filtered off, washed with water, triturated with $CHCl_3$ (30 ml) and filtered again to yield 5.8 g (58%) of starting substance. The combined filtrates were diluted with water (200 ml), and extracted with $CHCl_3$ to yield, after conventional work-up and trituration with ether, 2.2 g of a crystalline product. The latter was stirred with $CHCl_3$ (30 ml) at r.t., and the insoluble material was filtered off. The dry residue of the filtrate was triturated with ether to yield 1.75 g (34%, based on non-recovered starting material) of the title compound, identical with the product obtained as described under (a).

5 - *Diphenylmethylene* - 3 - *methylthio* - 1,4 - *diphenyl* - 4,5 - *dihydro* - s - *triazole* (**7**, R' = R'' = Ph)

Diphenylacetic acid (8.3 g; 39 mmole), compound **6** (10 g; 39 mmole) and $POCl_3$ (5.6 ml; 60 mmole) reacted in anhyd pyridine (30 ml) according to Method C. MeOH (30 ml) and 20% KI aq (60 ml) were added, and the oily **5** iodide (R = Ph_2CH) was isolated by $CHCl_3$ extraction and was dissolved in MeOH (150 ml). 10% Na_2CO_3 aq (50 ml) was added dropwise at 0° while stirring to yield 12 g (71%) of the title compound, yellow crystals, m.p. 204–205° from nitromethane. (Found: C, 77.96; H, 5.31; N, 9.37. Calc. for $C_{28}H_{23}N_3S$ (433.55): C, 77.66; H, 5.35; N. 9.69%); NMR (TFA): δ 7.15–6.3, m, 20H, ArH's; 5.6, s, 1H, $\rangle$CH; 2.3, s, 3H, S-Me.

Reaction with HCl *and* KI. The above product (0.8 g; 1.84 mmole) was dissolved in the mixture of MeOH (10 ml) and conc HCl (3 ml), and treated with an aqueous soln (60 ml) of NaI (10 g). The resulting oily product gradually solidified. The aqueous layer was decanted and the product was washed with water to yield 0.9 g (93%) of **5** (R = Ph_2CH–) iodide, m.p. 87–104° (unrecrystallized; d) which, according to the IR and NMR spectra, proved chemically pure. (Found: I, 22.45. Calc. for $C_{28}H_{24}IN_3S$ (561.48): I, 22.60%), NMR ($CDCl_3$): δ 7.9–7.75, m, 4H, N-Ph, *o*-H's; 7.45–7.40, m, 6H, N-Ph, *m*- and *p*-H's; 7.2, s, 10H, Ph_2C; 6.1, s, 1H, $\rangle$C–H; 2.75, s, 3H, S-Me.

$NaBH_4$ *reduction of the* s-*triazolium* (**5**) *salts* (Table 2)

The *s*-triazolium salts (0.1 mole) were dissolved in mixtures of dry DMF (200 ml) and MeOH (200 ml). Aqueous solns (50 ml) of $NaBH_4$ (0.12 mole), made alkaline by the addition of a few drops of 10% NaOH aq, were added under ice-salt-cooling and stirring at such a rate that the temp. did not exceed 3–5°. The excess of the reagent was decomposed by adding AcOH (15 ml); water (400 ml) was added to precipitate the *s*-triazolines **10** either in crystalline form or as oils. In the latter case the products were taken up in suitable organic solvents, and the resulting solns were worked up conventionally. The oily *s*-triazolines thus obtained were mostly hydrolyzed to the corresponding aldehydes without being previously crystallized.

NMR spectra. The $CDCl_3$ NMR spectra of the triazolines exhibit, in addition to the signals of the groups R, a multiplet at about δ 7.4–6.9 (10H, N-Ph groups) and a singlet at 2.6–2.5 (3H, S-Me). The signal of the 5-H is found at 5.9–5.3 (if R = alkyl), its multiplicity depending on the nature of R, and at 6.5–6.1 ppm (s), if R = aryl or hetaryl.

Reduction of **5** (R = Ph) *chloride in the presence of aldehydes*

(a) Compound **5** (R = Ph) chloride (7.0 g; 18 mmole) was dissolved in a mixture of dry MeOH (30 ml) and propanal (4.3 ml, 64.4 mmole), and reduced with a slightly alkaline aqueous (10 ml) soln of $NaBH_4$ (0.66 g; 18 mmole). AcOH (3 ml) was added to yield 6.0 g (97%) practically pure (IR, m.m.p.) **10** (R = Ph), colourless crystals, m.p. 108–110° (from i-PrOH).

(b) Compound **5** (R = Ph) chloride (2.2 g; 5.8 mmole) was reduced in the mixture of MeOH (10 ml) and butanal (5.3 ml, 60 mmole) with $NaBH_4$ (0.22 g; 5.8 mmole) as above to yield 1.65 g (82%) **10** (R = Ph), m.p. 108–109° (crude).

Decomposition of the triazolines **10** (Table 3)

Method F. Mixtures of the triazolines **10** (0.1 mole), water (75 ml) and conc H_2SO_4 (15 ml) were subjected to distillation at normal pressure. The aqueous distillates were saturated with NaCl, and the aldehydes were separated or extracted.

Method G. The above mixtures of the triazolines and dil H_2SO_4 were stirred at 70° for 5 min and, without preliminary cooling, extracted with three portions of benzene (75 ml, each). The combined benzene solns were washed with dil H_2SO_4 and water, and dried. The solvent was distilled off *in vacuo*.

Method H. The triazolines **10** (0.1 mole) were stirred for 10 min at r.t. with mixtures of conc HCl and 38% HCHO aq (100 ml, each). The aldehydes R–CHO were filtered off, washed with conc HCl and water, or extracted with suitable organic solvents and isolated after conventional work-up, depending whether they separated initially in crystalline form or as oils. The aldehydes were identified in all cases in form of their 2,4-dinitrophenylhydrazones or of their type **14** condensation products.[15]

Methyl 4 - (2,4 - *dinitrophenylhydrazono*) - *butyrate*

The *s*-triazolium (**5**, R = MeOOC–C_2H_4–) iodide (8.2 g; 17 mmole) was reduced in a mixture af anhyd DMF (20 ml) and MeOH (40 ml) with a slightly alkaline aqueous (10 ml) soln of $NaBH_4$ (0.8 g; 21 mmole) as described above. AcOH (2 ml) and water (150 ml) were added, and the *s*-triazoline was extracted with ether.

The oily residue was dissolved in MeOH (20 ml) and treated with the soln of 2,4-dinitrophenylhydrazine (3.4 g; 17 mmole) in a mixture of 50% H_2SO_4 (20 ml) and MeOH (40 ml) to yield 2.9 g and, after dilution of the filtrate with water, another 0.6 g (total yield 70%) of the yellow crystals of the title compound identical, according to m.p. (131–132°, from DMF–MeOH), m.m.p. and IR spectra, with an authentic product.[19]

E - 2 - *Chlorocrotonaldehyde* 2,4 - *dinitrophenylhydrazone*

Reduction of the *s*-triazolium (**5**, R = *E* - 2 - chloropropenyl) salt (7.1 g; 15 mmole) and decomposition of the excess $NaBH_4$ was performed as above. The crude oily *s*-triazoline was isolated by extraction with pentane, dissolved in EtOH (40 ml) and treated with a warm mixture of 2,4-dinitrophenylhydrazine (3 g; 15 mmole), 50% H_2SO_4 and EtOH (40 ml, each) to yield 3.8 g (89%)

of the title compound, orange coloured crystals, m.p. 186–187° from DMF–MeOH. (Found: C, 42.34; H, 3.34; Cl, 12.29. Calc. for $C_{10}H_9ClN_4O_4$ (284.66): C, 42.19; H, 3.19; Cl. 12.46%).

Phenylacetaldehyde 2,4-dinitrophenylhydrazone

Compound **10** (R = $PhCH_2$) (0.5 g; 1.4 mmole) was dissolved in EtOH (10 ml) and treated with a mixture of 2,4-dinitrophenylhydrazine (275 mg; 1.4 mmole), 50% H_2SO_4 (4 ml) and EtOH (10 ml). The mixture was heated to its b.p. and, after addition of water (5 ml), allowed to cool to yield 0.32 g (68%) of the title compound, 20^d m.p. 121° (from MeOH).

Nonanal

A mixture of nonanoyl chloride (21 ml; 116 mmole), **6** (30 g; 116 mmole) and dry dioxane (100 ml) was refluxed for 20 min and evaporated to dryness *in vacuo*. The resulting oil was dissolved in MeOH (100 ml) and treated with the slightly alkaline (50 ml) soln of $NaBH_4$ aq (6.5 g; 172 mmole) and then with dil. aqueous AcOH. The crude oily yellowish *s*-triazoline **10** (R = n-C_8H_{17}) was extracted with ether and stirred for 10 min with a mixture of conc HCl and 38% aqueous HCHO soln (30 ml, each) at r.t. The supernatant oil was separated, washed with 20% HCl (10 ml) and taken up in pentane to yield 10.2 g (62%) of crude nonanal. Fractional distillation *in vacuo* gave 7.3 g (44%; based on the nonanoyl chloride introduced) of pure product, b.p. 91–92° at 22 torr which was identified in form of its condensation product **14** (R = n-C_8H_{14}), m.p. 165° (from 2-propanol), obtained in 95% yield in the usual manner[15] with 6 - (2 - aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one. (Found: N, 15.30; S, 9.01. Calc. for $C_{19}H_{26}N_4OS$ (358.50): N, 15.63; S, 8.94%).

Ethyl 6-formylhexanoate

The oily **5** [R = EtOOC-$(CH_2)_5$] chloride, obtained from ethyl 6-(chlorocarbonyl)hexanoate (6.0 g; 29 mmole) according to Method A, was dissolved in MeOH (50 ml) and reduced with the slightly alkaline (15 ml) soln of $NaBH_4$ (1.5 g; 40 mmole) as described above. The crude *s*-triazoline was isolated after treatment with dil. aqueous AcOH by extraction with ether and decomposed with conc. HCl and 38% HCHO aq (10 ml, each) as above. The title compound, 2.3 g (46%, based on the acyl chloride introduced) was isolated by extraction with pentane and identified in form of its condensation product **14** [R = EtOOC-$(CH_2)_5$-], m.p. 148° (from EtOH), obtained in 84% yield in the usual manner.[15] (Found: C, 58.77; H, 6.26; N, 14.17; S, 8.50. Calc. for $C_{19}H_{24}N_4O_3S$ (388.48): C, 58.74; H, 6.23; N, 14.42; S, 8.25%).

3-Pyridinecarboxaldehyde

The crude crystalline **5** (R = 3-pyridyl) iodide, obtained from nicotinic acid (14.4 g; 116 mmole) according to Method C, was dissolved in a mixture of DMF (150 ml) and MeOH (300 ml) under gentle heating, and chilled. The resulting suspension was treated with a slightly alkaline (90 ml) soln of $NaBH_4$ (5.7 g; 150 mmole) as described above. A clear soln resulted temporarily from which crystalline needles soon started to separate.

Dil. aqueous AcOH was added, and the resulting **10** (R = 3-pyridyl) was decomposed by stirring with 20% HCl (60 ml) and PhCHO (50 ml; 0.5 mole) for 15 min at 80°. Water (80 ml) was added, and the aqueous layer was extracted with ether and concentrated to 20 ml *in vacuo*. Water (20 ml) was added and the soln was neutralized with cryst K_2CO_3. The small amount of gummy impurities was filtered off, and the filtrate was extracted with $CHCl_3$ to yield 7.8 g (63%) of crude or, after distillation at reduced pressure, 6.9 g (55%) of pure 3-pyridinecarbaldehyde, b.p. 93–95° at 14 Torr.

Type **14** condensation product (R = 3-pyridyl) obtained in 95% yield in the usual manner:[15] red crystals, m.p. 247–248° (d; from anhyd DMF). (Found: C, 59.03; H, 4.18; N, 21.24; S, 10.07. Calc. for $C_{16}H_{13}N_5OS$ (323.37): C, 59.43; H, 4.05; N, 21.66; S, 9.91%).

(2 - Oxocyclopentyl)butanal bis(2,4 - dinitrophenylhydrazone)

The crude **5** [R = (2-oxocyclopentyl)propyl]iodide obtained from 2-oxocyclopentanebutyric acid (4.0 g; 24 mmole) according to Method C, was reduced in dry MeOH (30 ml) with slightly alkaline (10 ml) $NaBH_4$ (0.76 g; 20 mmole) at −20°. The resulting brownish oily **10** (isolated, after treatment with dil aqueous AcOH, by extraction with ether) was treated with the warm mixture of 2,4-dinitrophenylhydrazine (7.1 g; 36 mmole), 50% H_2SO_4 aq and EtOH (60 ml, each) to yield 2.5 g (21%) of the title compound, m.p. 220° from DMF–MeOH. (Found: C, 49.49; H, 4.29; N, 21.51. Calc. for $C_{21}H_{22}N_8O_8$ (514.45): C, 48.02; M, 4.31; N, 21.78%).

Pentanal

An anhyd DMF soln of **5** (R = Bu) iodide was prepared according to Method E starting with **5** (R = H) iodide (30 g; 76 mmole) and BuI (8.6 ml, 76 mmole), and kept for 24 hr in a refrigerator. Dry MeOH (100 ml) was added, and $NaBH_4$ reduction was performed as described above. The triazoline **10** (R = Bu) was isolated, after acidification with dil AcOH by extraction with ether and decomposedd without purification according to Method F to yield 5.2 g (79%) of pure pentanal, b.p. 101–103°, lit. 20^a 102°, identified in form of its 2,4-dinitrophenylhydrazone m.p. 97–98°, lit. 20^a 98°.

3 - Methyl - 5 - methylthio - 1,4 - diphenyl - s - triazolium iodide (**11**)

A mixture of 2,4-diphenylthiosemicarbazide[13] (18 g; 74 mmole), anhyd DMF (30 ml) and MeI (5 ml; 80 mmole) was stirred for 1 hr at 0°. Triethyl orthoacetate (15 ml; 80 mmole) was added, and the mixture was kept overnight in a refrigerator to yield 18 g (60%) of **11**, m.p. 147° from anhyd DMF-anhyd ether. (Found: C, 47.36; H, 3.86; I, 30.51; N, 10.50. Calc. for $C_{16}H_{16}IN_3S$ (409.30): C, 47.95; H, 3.94; I, 31.01; N, 10.27%).

Alkaline hydrolysis of compound **11**

Compound **11** (5.0 g; 12 mmole) was dissolved in a mixture of anhyd DMF and MeOH (40 ml, each) under gentle heating. The soln was chilled at 0°, and to the resulting suspension 4% NaOH aq (20 ml) was added dropwise under stirring and cooling. AcOH (5 ml) and water (200 ml) were added to the resulting soln to yield 2.5 g (81%) of **12**, m.p. 135° from MeOH. (Found: C, 71.51; H, 4.72. Calc. for $C_{15}H_{13}N_3O$ (251.27): C, 71.70; H, 5.21%); IR (KBr): first band in the double bond region 1580 cm^{-1}.

$NaBH_4$ reduction of compound **11**

The title compound (5.0 g; 12 mmole) was reduced in anhyd DMF–MeOH (1:2) suspension (75 ml) with $NaBH_4$ as described for the reduction of the salts **5**. Dil AcOH was added to the resulting clear soln to yield 2.5 g (82%) of **13**, m.p. 68° from i-PrOH.† (Found: C, 75.60; H, 6.48. Calc. For $C_{15}H_{15}N_3$ (237.29): C, 75.92; H, 6.37%); NMR (CCl_4): δ 7.4–6.8, m, 10H, ArH's–, 5.15, s, 2H, CH_2; 2.05, s, 3H, CH_3.

Cleavage of compound **13**

A mixture of **13** (0.3 g; 1.3 mmole), 6 - (2 - aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one (0.23 g; 1.0 mmole) and 20% HCl aq (5 ml) was heated to its b.p. The resulting red soln was poured into an aqueous (30 ml) soln of crystalline NaOAc (10 g), and the crude product obtained was recrystallized from DMF (3 ml) to yield 0.17 g (55%) of **14** (R = H), identical, according to m.p. (238–240°; d) and IR spectra with an authentic product.[15]

Reaction of the carbene **8** *with benzaldehyde*

A mixture of the DMF soln of the carbene, obtained from **5** (R = H) iodide (6.0 g; 15 mmole) according to Method E, and benzaldehyde (1.5 ml, 15 mmole) was kept for 2 days at r.t. and acidified with a few drops of AcOH. Water (300 ml) was added, and the product was isolated by extraction with $CHCl_3$, and triturated with water until it turned solid to yield, after recrystallization from EtOH (50 ml), 2.6 g (48%) of **16**, identical according to m.p. (149–150°, from $MeNO_2$), m.m.p. and IR spectra with an authentic sample (see below).

Reaction of the carbene **8** *with benzoyl chloride*

HCl *free* PhCOCl (2.9 ml, 25 mmole was added at 0° under stirring to the anhyd DMF soln of the carbene, obtained,

†**5** $I^{\ominus}$ (R = Me) was reduced under the same conditions to yield 52% of **7** (R = Me).

according to Method E, from **5** (R = H) iodide (10 g; 25 mmole). The mixture was stirred for another 5 min and poured onto a mixture of ice (60 g) and 20% KI aq (60 ml). The oily crude product was isolated according to Method E. Trituration of the dry residue with the mixture of EtOH (50 ml) and Et_2O (20 ml) furnished 8.6 g (70%) of **5** (R = PhCO–) iodide, m.p. 212–214° ($MeNO_2$–anhyd ether). (Found: N, 8.29. Calc. for $C_{22}H_{16}IN_3OS$ (499.37): N, 8.42%).

Ethanolysis

The above product (6.0 g; 12 mmole) was refluxed with EtOH (40 ml) for 1 hr. A clear soln was formed temporarily from which 3.2 (67%) of **5** (R = H) iodide separated and identified by m.p., m.m.p. and IR spectra with an authentic sample. The ethanolic filtrate was diluted with water (5 vols) and extracted with ether to yield 1.3 g (72%) of ethyl benzoate, identified by its IR spectrum.

$NaBH_4$ *Reduction of compound* **5** (R = PhCO) *iodide*

An anhyd DMF soln of the title compound, obtained from **5** (R = H) iodide (10 g; 25 mmole) as described above, was treated with thoroughly pulverized $NaBH_4$ (1.0 g, 27 mmole) and worked up as described above for the reduction of type **5** salts, to yield a gradually solidifying oil. Trituration with hot EtOH (50 ml) converted the latter into 3.5 g (40%) of a red powder (**16**) which, according to m.p. (149–150°, from $MeNO_2$), m.m.p. and IR spectra, proved identical with an authentic sample.

Authentic 5 - *benzoyl* - 3 - *methylthio* - 1,4 - *diphenyl* - 4,5 - *dihydro* - s - *triazole* (**16**)

A mixture of phenylglyoxal (0.67 g; 5 mmole), **6** (1.0 g; 3.9 mmole) and EtOH (10 ml) was refluxed for 10 min to yield 1.1 g (79%) of the red coloured title compound, m.p. 149–150° from $MeNO_2$. (Found: N, 11.62; S, 8.46. Calc. for $C_{22}H_{19}N_3S$ (357.46): N, 11.76; S, 8.97%).

Synthesis of **5** (R = PhCHOH–) *iodide*

(a) A mixture of O-acetylmandelyl chloride (12.4 g; 58.4 mmole) and **6** (15 g; 58.4 mmole) reacted in anhyd dioxane (50 ml), and the resulting oily **5** (R = PhCHOAc–) chloride was converted into the corresponding iodide (16 g; 53%), m.p. 224–225° (from EtOH; d) according to Method A.

(b) *Deacetylation.* The above product (8.0 g; 15 mmole) was refluxed for 1 hr with a mixture of MeOH (50 ml), H_2O (30 ml), conc HCl (20 ml) and $NaHSO_3$ (2 g). The yellow soln was evaporated to dryness *in vacuo*, and the residue was triturated with water (30 ml). The water was decanted, and the oily product was dissolved in MeOH (40 ml). 20% KI aq (60 ml) was added, and the mixture was chilled (0°) to yield 6.2 g (80%) of **5** (R = PhCHOH–) iodide, m.p. about 160° and, after resolidification, 238–240°. (Found: I, 25.23; N, 6.06. Calc. for $C_{22}H_{20}IN_3OS$ (501.39): I, 26.32; N, 6.39%).

Reaction with NaH *in anhyd DMF*

The above product (3.0 g; 6 mmole) was dissolved in anhyd DMF (20 ml) and treated under continuous stirring and ice-cooling with a mineral oil dispersion of NaH (15 mmole). The mixture was stirred for another 5 min, and the insoluble inorganic material was filtered off and washed with DMF.

(a) The combined filtrate and washings were allowed to stand for 48 hr at r.t., whereby they gradually turned red. After acidification with a few drops of AcOH, water (150 ml) was added, and the product was isolated by extraction with $CHCl_3$. Recrystallization from EtOH (25 ml) furnished 0.76 g (35%) of **16**.

(b) The combined filtrate and DMF washings were immediately acidified with AcOH (3 ml). 20% KI aq (30 ml) was added to precipitate 1.8 g (76%) of **5** (R = H) iodide. The filtrate of the latter was stirred with 6 - (2 - aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one for 30 min at r.t. to yield 1.55 g (80%) of the orange crystals of the type **14** condensation product of PhCHO, identified by its m.p. (251–252°, from DMF), m.m.p. and the IR spectra with an authentic product.[15]

Preparation of **5** (R = MeCHOH–) *iodide*

A mixture of **6** (10 g; 39 mmole), O-acetyllactyl chloride (5.9 g; 39 mmole) and dry dioxane (50 ml) was refluxed for 20 min. Water (170 ml) and conc HCl (50 ml) were added, and refluxing was continued for another 2 hr. The mixture was evaporated to dryness *in vacuo*, the residue was triturated with ether (100 ml) and, after the latter had been decanted, dissolved in MeOH (150 ml). Warm 20% KI aq was added, and the mixture was chilled (0°) to yield 10.5 g of the title compound, m.p. 191–192° (from EtOH); a second crop, 1.3 g, total yield 68%, was obtained by extraction with CH_2Cl_2 of the mother liquor of the first, after dilution with water. (Found: N, 9.86. Calc. for $C_{17}H_{18}IN_3OS$ (439.32): N, 9.57%).

Synthesis of **5** (R = Et–CHOBz–) *iodide*

Compound **5** (R = Pr) iodide (7.5 g; 17.2 mmole) was converted into the ylide according to Method D. The soln was diluted with CH_2Cl_2 (80 ml) and the soln of dibenzoylperoxide (4.15 g; 17.2 mmole) in dry CH_2Cl_2 (20 ml) was added dropwise at −70° under vigorous stirring. Stirring at −70° was continued for another hr at −70°. The mixture of conc H_2SO_4 (2 ml) and H_2O (15 ml) and, subsequently, the (15 ml) soln of $Na_2S_2O_4$ (1.75 g) were added, and, under continuous stirring, the temp. was allowed to rise to 0°. The mixture was poured into 20% NaI aq (80 ml). Water (250 ml) was added, and the product was isolated by extraction with CH_2Cl_2. The extract was triturated with ether (80 ml), the mixture was chilled (0°) and the solvent was decanted. This treatment was repeated once more, and the residue was recrystallized from i-PrOH (80 ml) to yield 7.1 g (74%) of the title compound, m.p. 198–199°. (Found: I, 22.66; N, 7.51. Calc. for $C_{25}H_{24}IN_3O_2S$ (557.45): I, 22.77; N, 7.54%).

Degradations of **5** (R = R'CHOH–, R' = Ph, Me) *iodides*

(a) Compound **5** (R = PhCHOH–) iodide (3.0 g; 6 mmole) was heated at 170° until the initial melt resolidified. The product was triturated with anhyd ether (10 ml), filtered and washed with ether (two portions, 5 ml each) to yield 2.3 g (93%) of **5** (R = H) iodide, m.p. 244–245°.

6 - (2 - Aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one[14] (1.4 g; 6 mmole), AcOH (3 ml) and EtOH (30 ml) were added to the ether soln, and the mixture was stirred for 30 min to yield 1.45 g (75%) of the type **14** condensation product (R = Ph)[15] of benzaldehyde, m.p. 251–252° (from DMF).

(b) A mixture of **5** (R = PhCHOH–) iodide (3.0 g; 6 mmole), anhyd DMF (10 ml) and Et_3N (1 ml; 7.2 mmole) was allowed to stand for 1 hr at r.t. Dilution with dry ether (20 ml) and chilling (0°) caused the needles of **5** (R = H) iodide (2.1 g; 89%), m.p. 244–246°, to precipitate.

AcOH (3 ml) and 6 - (2 - aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one[14] (1.4 g; 6 mmole) were added to the filtrate. The mixture was stirred for 30 min to yield 1.1 g (57%) of **14** (R = Ph),[15] m.p. 251–252° (from DMF).

(c) Compound **5** (R = MeCHOH–) iodide (10 g; 23 mmole) was dissolved in warm MeOH (50 ml). Et_3N (1 ml; 7.2 mmole) was added, and the mixture was allowed to stand for 1 hr at r.t. to yield 8.0 g (89%) of **5** (R = H) iodide, m.p. 244–246°.

6 - (2 - Aminphenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one[14] (5.4 g; 23 mmole) and AcOH (10 ml) were added to the filtrate. The mixture was stirred for 30 min at r.t. to yield 4.4 g (73%) of the type **14** condensation product[15] (R = Me) of acetaldehyde, m.p. 248–252° (dec; from DMF).

Degradation **5** (R = Et–CHOBz–) *iodide*

(a) The title compound (3.0 g; 5.4 mmole) was stirred with anhyd Et_3N (0.42 ml; 3 mmole) in dry MeOH (20 ml) for 1 hr. A colourless ppt separated. AcOH (20 ml) and anhyd ether (40 ml) wer added, and the mixture was chilled (0°) to yield 1.6 g (75%) of **5** (R = H) iodide, m.p. 246–248° (d).

The filtrate was stirred for 1 hr with 6 - (2 - aminophenyl) - 3 - methylthio - *as* - triazin - 5(2H) - one[14] (1.26 g; 5.4 mmole) to yield 1.2 g (81%) of the red crystals of the type **14** condensation product (R = Et) of propanal, identical according to m.p. (222–224°; d), m.m.p. and IR spectra with an authentic product.[15]

(b) In another experiment water (150 ml) was added to the

filtrate of **5** (R = H) iodide to yield, after conventional work-up of the organic layer, 0.51 g (70%) of methyl benzoate, b.p. 194–199°, identical according to the IR spectra with an authentic sample.

Acknowledgements—The author is indebted to Dr. I. Balogh-Batta and Dr. P. Kolonits and staffs for the microanalyses and the spectra respectively.

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