

PREPARATION OF TRIMETHINIUM SALTS WITH BULKY SUBSTITUENTS*

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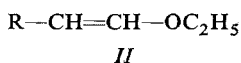
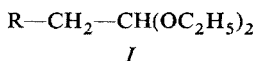
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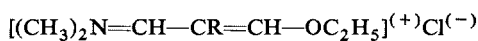
Reaction of 3,3-dimethylbutanal diethylacetal (*Ie*) with dimethylchloromethyleneammonium chloride and the subsequent treatment with dimethylamine afforded the trimethinium salt *IVe* with a tert-butyl group at position 2. The β -diketones *VIIc*–*VIIe* were used as starting compounds in the synthesis of trimethinium salts *VIc*–*VIe* substituted symmetrically at positions 1 and 3 by ethyl, isopropyl, and tert-butyl groups.

In connection with earlier investigations of this Series^{1–3}, it appeared desirable to examine the effect of bulky substituents *a*) on the course of the Vilsmeier–Haack formylation reaction in the aliphatic series and *b*) on the physicochemical properties of the thus-prepared trimethinium salts^{1,3–5}.

The synthesis of β -dialdehydes and their derivatives consisting in reaction of dimethylchloromethyleneammonium chloride⁶ with aliphatic aldehyde dialkylacetals of type *I* may be regarded as a typical and preparatively valuable formylation reaction. It has been convincingly established^{2,7} that the synthesis proceeds through the unsaturated ether *II* as intermediate; the formylating agent is then added to the double bond of this intermediate. Some earlier observations¹ are in accordance with the assumed unfavourable effect of increasing steric requirements of the group R at this stage of the formylation. In order to obtain additional informations in this respect, we have now examined the formylation of 3,3-dimethylbutanal diethylacetal (*Ie*). In this case, the double bond of the assumed intermediate *Iie* is substituted by a tert-butyl group on that carbon atom which is then attacked by the electrophilic cation of the formylating reagent.



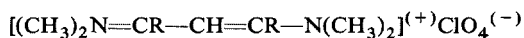
* Part XXX in the series Synthetic Reactions of Dimethylformamide; Part XXIX: This Journal 39, 3327 (1974).



III



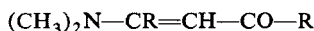
IV



VI



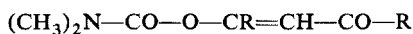
VII



VIII



IX



X

a, R = H; *b*, R = CH₃; *c*, R = C₂H₅; *d*, R = iso-C₃H₇; *e*, R = tert-C₄H₉

We have now observed that the reaction rate is considerably decreased by the presence of the bulky tert-butyl group but, notwithstanding, the required product may be obtained in 71% yield when the reaction time is prolonged (20 h) and the temperature of the chloroform-containing reaction mixture elevated to the boiling point. The reaction course was qualitatively checked by treatment of the assumed intermediate *IIIe* with dimethylamine and precipitation of the corresponding product in the form of the perchlorate *IVe*. With derivatives where R is hydrogen or a primary alkyl group, similar yields¹ may be obtained in the course of 15–30 min.

As it has been reported earlier, the trimethinium salts of type *IV* are readily hydrolysed on the dimethyliminium group. The behaviour of the salt *IVe* was similar in this respect since α-tert-butyl-β-dimethylaminoacrolein (*V*) was obtained by the action of potassium carbonate in water–benzene. The trimethinium salt *IVe* is the most interesting member of the series *IVa* to *IVe* wherein the substituent R is hydrogen, methyl, ethyl, isopropyl, and tert-butyl. The trimethinium salts *IVa* (ref.⁸), *IVb* (ref.⁵), and *IVd* (ref.³) have been reported earlier. In connection with intended detailed investigations on compounds of this type, the remaining derivative *IVc* was therefore prepared along with some symmetrically 1,3-disubstituted salts *VIc* to *VIe* with alkyl groups from ethyl to tert-butyl as substituents of positions 1 and 3; the 1,3-dimethyl derivative *VIb* has been reported earlier⁵. The intermediary enamino ketones *VIIIc*–*VIIIe* were converted into the required salts *VIc*–*VIe* by reaction with dimethyl sulfate and the subsequent amination with dimethylamine⁵; as expected, the yields strongly decreased with increasing bulkiness of alkyl groups. The

required intermediate *VIIIc* may be obtained from dipropionylmethane (*VIIc*) by a direct heating with dimethylamine. On the other hand, the remaining branched diketones *VIIId* and *VIIe* must be first subjected to chlorination and the resulting mixture of the starting diketone and the corresponding chloro derivative *IX* then treated with dimethylamine. The chlorination of diisobutyrylmethane (*VIIId*) which requires milder conditions, was preferably performed with phosgene containing a trace of dimethylformamide while thionyl chloride was used in the case of dipivaloylmethane *VIIe*. In connection with attempts on the alternative synthesis of the enamino ketone *VIIIe*, the reaction of the sodium salt of the diketone *VIIe* with dimethylcarbamoyl chloride^{8,9} has been examined. Instead of the expected compound *VIIIe* however, a stable derivative *Xe* of carbamoic acid was isolated which failed to split off carbon dioxide even on heating with copper at 260°C.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). The IR spectra were recorded on a Zeiss Jena UR-10 apparatus.

3,3-Dimethylbutanal Diethylacetal (*Ie*)

To magnesium shavings (13.6 g; 0.56 gramatom) activated with iodine vapours, there was added a mixture of neopentyl chloride (10 g; 0.094 mol), ether (20 ml), and 1,2-dibromoethane (0.5 ml). When the reaction began, a solution of neopentyl chloride (50 g; 0.467 mol) in ether (200 ml) was added dropwise over 3.5 h. The reaction mixture was then gently refluxed for additional 2 h, cooled down, and treated with a solution of triethyl orthoformate (96 ml; 0.68 mol) in ether (200 ml). The whole mixture was kept at room temperature for 24 h, refluxed for 5.5 h, and decomposed with a solution of ammonium chloride (240 g) in water (1000 ml). The product was isolated by extraction with ether, drying of the extract over anhydrous magnesium sulfate, and rectification. Yield, 44.4 g (45%) of compound *Ie*, b.p. 71.5–72.0°/23 Torr, n_D^{20} 1.4059. For $C_{10}H_{22}O_2$ (174.3) calculated: 68.92% C, 12.72% H; found: 68.76% C, 12.45% H.

3,3-Dimethylbutanal dinitrophenylhydrazone. M.p. 146–147°C; reported¹⁰, m.p. 146–147°C.

N,N-Dimethyl-N-(2-tert-butyl-3-dimethylaminoprop-2-enylidene)ammonium Perchlorate (*IVe*)

A mixture of 3,3-dimethylbutanal diethylacetal (5.22 g; 0.03 mol) and 2M N,N-dimethylchloromethylenammonium chloride in chloroform (37 ml) was refluxed for 20 h, cooled down, diluted with ethanol (15 ml), treated with 4.4M ethanolic dimethylamine (70 ml), and kept at room temperature for 4 h. The solvents were then removed under diminished pressure, the residue dissolved in water (20 ml), and the solution precipitated with sodium perchlorate (4.2 g) in water (10 ml). The precipitate was collected with suction and dried to afford 6.05 g (71%) of compound *IVe*, m.p. 156–159°C. Recrystallisation from 4 : 1 benzene-acetonitrile at 50–60°C (bath temperature) raised the m.p. to the value of 163–165°C. For $C_{19}H_{23}ClN_2O_4$ (282.8) calculated: 46.75% C, 8.18% H, 12.52% Cl, 9.90% N; found: 47.07% C, 8.29% H, 12.55% Cl, 9.74% N.

2-Tert-butyl-3-dimethylaminoacrolein (*V*)

The salt *IVe* (0.5 g) was added into a stirred mixture of saturated aqueous potassium carbonate (10 ml), water (10 ml), and benzene (10 ml), placed on a steam bath. After 2 h, the mixture was cooled down, extracted with 2 : 1 benzene-ethanol, the extract dried over anhydrous potassium carbonate, the solvents evaporated, and the residue purified by two distillations (at 0.5 Torr/bath temperature 70–75°C). Yield, 0.11 g (40%) of compound *V*. For $C_5H_{17}NO$ (155.2) calculated: 69.63% C, 11.04% H, 9.02% N; found: 69.21% C, 11.19% H, 8.79% N.

N,N-Dimethyl-N-(2-ethyl-3-dimethylaminoprop-2-enylidene)ammonium Perchlorate (*IVc*)

The title compound *IVc*, m.p. 98–99°C (ethanol), was obtained in 65% yield from 2-ethyl-3-dimethylaminoacrolein¹ analogously to the reported preparation⁵ of the methyl derivative *IVb*. For $C_9H_{19}ClN_2O_4$ (254.7) calculated: 42.45% C, 7.51% H, 13.90% Cl, 10.99% N; found: 42.65% C, 7.34% H, 13.82% Cl, 10.72% N.

5-Dimethylamino-4-hepten-3-one (*VIIIc*)

A mixture of dipropionylmethane^{11,12} (*VIIIc*; 12.8 g; 0.1 mol) and 2M dimethylamine in benzene (150 ml) was sealed into ampoules and heated in an autoclave at 140°C for 7 h. The solvent and unreacted diketone were removed by rectification. Yield, 5 g of compound *VIIIc*, b.p. 80–85°C (bath temperature) at 0.4 Torr. For $C_9H_{17}NO$ (155.2) calculated: 69.93% C, 11.04% H, 9.02% N; found: 69.60% C, 11.07% H, 9.24% N.

2,6-Dimethyl-5-dimethylamino-4-hepten-3-one (*VIIIa*)

Diisobutyrylmethane^{12,13} (15.6 g; 0.1 mol) containing a trace of dimethylformamide was cooled down to –10°C and treated with liquid phosgene (9.9 g; 0.1 mol). The mixture was stirred at room temperature for 20 h under a reflux condenser packed with Dry Ice. The phosgene was then

TABLE I
Trimethinium Salts *VI*

Salt R	M.p., °C (yield, %)	Formula (m. w.)	Calculated/Found			
			% C	% H	% Cl	% N
<i>VIc</i> C_2H_5	65–66.5 ^a (42)	$C_{11}H_{23}ClN_2O_4$ (282.8)	47.07 47.00	8.25 8.22	12.54 12.71	9.90 9.72
<i>VIa</i> i- C_3H_7	114–115 ^b (35)	$C_{13}H_{27}ClN_2O_4$ (301.8)	50.23 50.23	8.76 8.53	11.41 11.53	9.01 9.13
<i>VIe</i> t- C_4H_9	165–166 ^c (6)	$C_{15}H_{31}ClN_2O_4$ (338.9)	53.20 53.04	9.10 9.29	10.53 10.60	8.28 7.98

^a Ethanol-ether (4 : 1), –40°C; ^b ethanol, –40°C; ^c repeatedly ethanol-ether at –40°C, then ethanol without cooling.

evaporated and the residue distilled. The distillate containing about 25% of the chloro derivative *IXd* was added to 2M dimethylamine in benzene (250 ml), the mixture sealed into ampoules, and heated in an autoclave at 150°C for 8 h. The mixture was then shaken with saturated aqueous potassium hydrogen carbonate, the benzene layer evaporated, and the residue rectified to afford 4 g (22%) of compound *VIIIId*, b.p. 65–70°C (bath temperature) at 0.4 Torr. For $C_{11}H_{21}NO$ (183.3) calculated: 72.08% C, 11.55% H, 7.64% N; found: 72.16% C, 11.64% H, 7.69% N.

2,2,6,6-Tetramethyl-5-dimethylamino-4-hepten-3-one (*VIIIe*)

A mixture of dipivaloylmethane (5.4 g; 0.03 mol) containing a trace of dimethylformamide, and thionyl chloride (21.3 ml; 0.3 mol) was heated at 80°C for 7 h. The crude chloro derivative *IXe* was isolated by distillation at about 90–100°C/13 Torr. A mixture of the distillate and 2M dimethylamine in benzene (225 ml) was then heated in an autoclave at 150°C for 7 h and processed as in the preceding paragraph to afford 2.5 g (40%) of compound *VIIIe*, b.p. 60–65°C (bath temperature) at 0.3 Torr; reported¹⁴, b.p. 49°C/0.2 Torr. The analytical sample was obtained by precipitation with picric acid in ether, decomposition of the picrate with aqueous triethanolamine, extraction with ether, and rectification. For $C_{13}H_{25}NO$ (211.4) calculated: 73.88% C, 11.92% H, 6.63% N; found: 74.29% C, 11.85% H, 6.54% N.

Preparation of Trimethinium Salts *VIc*, *VIId*, and *VIe*

An equimolar mixture of the dimethylamino derivative *VIII* and dimethyl sulfate was heated at 90°C for 8 h, cooled down, the oil washed repeatedly by trituration with light petroleum, the residual solvent removed under diminished pressure, and the oil dissolved in chloroform. A mixture of this solution and 2M dimethylamine in benzene (tenfold molar excess) was stirred at room temperature for a week and then evaporated under diminished pressure. The residue was diluted with about four volumes of water and treated with saturated aqueous sodium perchlorate (2 equivalents). The emulsion of the perchlorate was extracted with dichloromethane, the extract evaporated, and the residue triturated with ether to afford the perchlorate in the form of a crystalline precipitate. For purification, physical constants, yields, and analyses of the particular perchlorates see Table I.

2,2,6,6-Tetramethyl-5-(N,N-dimethylcarbamoyloxy)-4-hepten-3-one (*Xe*)

Sodium hydride (0.5 g; 0.02 mol) was added with stirring to a mixture of dipivaloylmethane (*VIIe*; 1.85 g; 0.01 mol) and ether (30 ml). When the reaction was complete, the ether was evaporated under diminished pressure and the residue was treated with N,N-dimethylcarbamoyl chloride (3.25 g; 0.03 mol). The mixture was stirred at 120–125°C for 4 h and then briefly heated to 140°C. The product was extracted with hot toluene, the extract filtered, the filtrate evaporated, and the residue rectified to yield 2.4 g of an oil, b.p. 70–90°C (bath temperature) at 0.4 Torr. The oil was purified by chromatography on silica gel (90 g) in 50 : 1 benzene-ethanol and the solid (2 g) sublimed to afford 1.6 g (62%) of compound *Xe*, m.p. 56.5–58.5°C. For $C_{14}H_{25}.NO_3$ (255.4) calculated: 65.85% C, 9.87% H, 5.49% N; found: 65.94% C, 9.76% H, 5.66% N. IR spectrum (chloroform): $\nu(C=C-CO)$ 1689 cm^{-1} , $\nu(C=O)$ 1739 cm^{-1} , $\nu(C=C)$ 1618 cm^{-1} . UV spectrum (ethanol): λ_{max} 236 nm (log ϵ 3.95). Mass spectrum: M^+ 255.

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