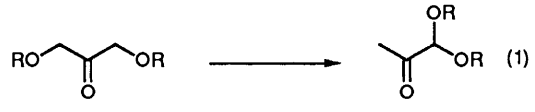
A Study of Rearrangement of some 1,3-Dimethoxyalkan-2-ones

Yin Yu, Guo-qiang Chen, Jun Zhu, Xu-sheng Zhang, Shu-xin Chen, Hui-tong Tang, and Pang Zhang *
Department of Chemistry, Peking University, Beijing, PR of China

1,3-Dialkoxyacetones, 1-alkyl- and 1-(substituted phenyl)-, 1-alkanoyl-1,3-dimethoxyacetones, and methyl 2,4-dimethoxyacetoacetate were shown to undergo acid-catalysed rearrangement to give respectively methylglyoxal dialkyl acetals, 3-substituted methylglyoxal dimethyl acetals, 5-alkyl-3-methoxy- and 4,5-dimethoxyfuran-2(5*H*)-ones. 1-(Substituted aroyl)-1,3-dimethoxyacetones underwent only scission to give substituted ω-methoxyacetophenones. Methyl 2-alkyl-2,4-dimethoxyacetoacetates, 3- and 1-methoxy-, and 1,5-dimethoxypentane-2,4-diones were not affected by similar acid treatment except for the fact that they suffered some limited C–C bond scissions. Implications related to rearrangement mechanisms are discussed.

The rearrangement of glyceraldehyde and 1,3-dihydroxyacetone in both acid and basic aqueous solutions to give methylglyoxal represents the prototype of the well known Lobry de Bruyn–Alberda van Ekenstein transformation.[1] It was reported in 1980 that 2,3-di-*O*-methylglyceraldehyde and 1,3-dimethoxyacetone also gave methylglyoxal when heated in dil. hydrochloric acid.[2] We noticed that samples of 1,3-dimethoxyacetone (**1a**)[3] on storage altered, in a few days, to methylglyoxal dimethyl acetal (**2a**) [equation (1)]. It seemed likely that adventitious acid in these samples had catalysed the rearrangement, and it was found this rearrangement could be effected readily in benzene containing a little toluene-*p*-sulphonic acid (PTSA) and at 50 °C for 24 h. 1,3-Diethoxy- (**1b**) and 1,3-di-isopropoxyacetone (**1c**) were also found to rearrange to give, respectively, methylglyoxal dialkyl acetals (**2b**) and (**2c**), but no rearrangement was observed for 1,3-diphenoxyacetone (**1d**) and 1,3-dihydroxyacetone diacetate (**1e**). These facts led us to investigate the scope of this rearrangement.



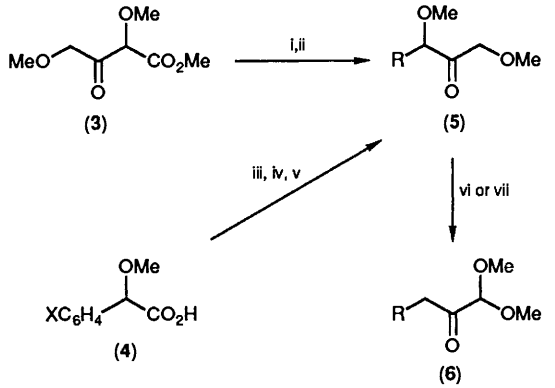
(1) (2)

a, R = Me; **b**, R = Et; **c**, R = Pr^i; no reaction with **d**, R = Ph and **e**, R = Ac.

Reagents and conditions: PTSA, PhH, 50 °C.

Results

Synthesis and Rearrangement of 1-*Alkyl- and* 1-(*Substituted phenyl*)-1,3-*dimethoxyacetones*.—As shown in Scheme 1, alkylation of methyl 2,4-dimethoxyacetoacetate (**3**) with alkyl halides was not successful with sodium methoxide as condensing agent, but could be effected in the presence of potassium carbonate in dimethylformamide (DMF).[4] The alkylated esters were then demethoxycarbonylated in dipolar solvents[5] to give 1-alkyl-1,3-dimethoxyacetones (**5**) (Table 1), which underwent acid-catalysed rearrangement in benzene to yield the respective 3-alkyl methylglyoxal dimethyl acetals (**6**) (Table 2) as expected. Various 1-(substituted phenyl)-1,3-dimethoxyacetones (**5**) were synthesized from substituted 2-methoxy-2-phenylacetic acids (**4**)[6] *via* intermediate formation of 2-methoxy-2-phenylacetyldiazomethanes followed by methanolysis (Table 3). PTSA in methanol was effective in causing rearrangement of compounds (**5**) to yield 3-(substituted phenyl) methylglyoxal dimethyl acetals (**6**) which could be characterized as their *p*-nitrophenylosazones (Table 4). The *p*-nitrophenylosazone of compound (**6f**) could be used for quantitative estimation in the presence of compound (**5f**) with acetic acid–methanol as solvent, for while its phenylosazone was somewhat soluble, its 2,4-dinitrophenylosazone precipitated out of the mixed solvent together with the 2,4-dinitrophenylhydrazone of compound (**5f**). With the help of this method, it was found that 0.8M-hydrogen chloride in methanol at 55 °C for 55 h was sufficient for the completion of the rearrangement.



a, R = Me; **b**, R = Pr^n; **c**, R = Pr^i; **d**, R = Bu^n; **e**, R = Bn; for R = XC_6H_4; **f**, X = H; **g**, X = *p*-MeO; **h**, X = *p*-Me; **i**, X = *p*-Cl; **j**, X = *m*-Cl; **k**, X = *p*-NO_2.

Scheme 1. *Reagents and conditions:* i, RX, K_2CO_3, DMF, 25 °C; ii, LiCl, DMSO, 120–140 °C; iii, $SOCl_2$, 60 °C, 4 h; iv, CH_2N_2, Et_2O, 25 °C; v, MeOH, BF_3, 25 °C; vi, PTSA, PhH, 50 °C; vii, HCl, MeOH, 55 °C.

Rearrangement of 1-*Acyl*-1,3-*dimethoxyacetones* (**7**).—Synthesis of the title diketones (**7**) will be reported † separately. The rearrangement of 1,3-dimethoxypentane-2,4-dione (**7a**) was typical and its transformation product obtained by acid-catalysed rearrangement in benzene was identified by mass and ^{1}H NMR spectroscopy to be 3-methoxy-5-methylfuran-2(5*H*)-one (**12a**),[7,8] the formation of which was suggested to proceed as shown in Scheme 2. The rearrangement results first in the formation of 1,1-dimethoxypentane-2,4-dione (**8a**) which, as a

† 1-Alkanoyl- (**7**) and 1-(substituted benzoyl)-1,3-dimethoxyacetones (**16**) were synthesized by acylation of 1,3-dimethoxyacetone morpholine enamine and, among them, compounds (**7a–d**) were obtained admixed with varied proportions of the isomeric 1,5-dimethoxy-3-alkylpentane-2,4-diones (**20**) which were not affected in the rearrangement.

Table 1. 1-Alkyl-1,3-dimethoxyactones (**5a–e**).

Compd. (5)	B.p. (°C/mmHg) Yield (%)	ν_{max}(cm^{-1})	δ_H
a	78–80/20 47		1.32 (d, 3 H, 3.38 (s, 3 H), 3.42 (s, 3 H), 3.90 (q, 1 H), 4.30 (s, 2 H)
b	97–100/22 72	2 970, 2 900, 1 730, 1 130, 1 100	0.90 (t, 3 H), 1.50 (m, 4 H), 3.30 (s, 3 H), 3.35 (s, 3 H), 3.68 (t, H), 4.20 (s, 2 H)
c	85–89/22 51	2 970, 2 850, 1 730, 1 130, 1 100	0.95 (d, 6 H), 2.02 (m, 1 H), 3.39 (s, 3 H), 3.43 (s, 3 H), 3.44 (t, 1 H), 4.25 (s, 2 H)
d	76–77/0.85 90	2 960, 2 930, 1 730, 1 130, 1 100	0.90–1.70 (m, 9 H,), 3.37 (s, 3 H), 3.42 (s, 3 H), 3.72 (t, 1 H), 4.27 (s, 2 H)
e	156–160/23 92	3 070–3 000, 2 930, 2 830, 1 470, 1 100, 1 030, 760, 705	2.98 (q, 2 H), 3.31 (s, 6 H), 3.95 (t, 1 H), 4.08 (d, 2 H), 7.26 (s, 5 H)

Table 2. 3-Alkyl methylglyoxal dimethyl acetals (**6a–e**).

Compd. (6)	B.p. (°C/mmHg) Yield (%)	ν_{max}(cm^{-1})	δ_H
a	60–62/22 52	2 970, 2 940, 1 730, 1 100, 1 080	1.05 (t, 3 H), 2.57 (q, 2 H), 3.41 (s, 6 H), 4.48 (s, 1 H)
b	85–88/19 60	2 950, 2 930, 1 730, 1 120, 1 070	0.94 (t, 3 H), 1.45 (m, 4 H), 2.50 (t, 2 H), 3.40 (s, 6 H), 4.45 (s, 1 H)
c	84–86/19 64	2 950, 1 730, 1 070	0.92 (d, 6 H), 1.21 (m, 1 H), 2.40 (d, 2 H), 3.40 (s, 6 H), 4.41 (s, 1 H)
d	88–90/21 68	2 960, 2 930, 1 730, 1 120, 1 080	0.85 (t, 3 H), 1.27–1.35 (m, 6 H), 2.50 (t, 2 H), 3.40 (s, 6 H), 4.40 (s, 1 H)
e	148–152/27 60	3 070–3 000, 1 740, 1 120, 1 080, 760, 705	2.89 (s, 4 H), 3.36 (s, 6 H), 4.42 (s, 1 H), 7.21 (s, 5 H)

Table 3. 1-(Substituted phenyl)-1,3-dimethoxyacetones (**5f–k**).

Compd. (5)	B.p. (°C/mmHg) Yield (%)	δ_H	2,4-Dinitrophenylhydrazone m.p. and *m/z*
f	90–91/0.5 61	3.31 (s, 3 H), 3.35 (s, 3 H), 4.22 (d, 2 H), 4.82 (s, 3 H), 7.36 (s, 5 H)	139–140 °C analysis: see Experimental section
g	13	3.31 (s, 3 H), 3.33 (s, 3 H), 3.79 (s, 3 H), 4.20 (s, 2 H), 4.78 (s, 1 H), 6.83–7.34 (m, 4 H)	129–130 °C $C_{18}H_{20}N_4O_7$ *m/z* 404 (M^+)
h	28	2.34 (s, 3 H), 3.31 (s, 3 H), 3.34 (s, 3 H), 4.21 (d, 2 H), 4.79 (s, 1 H), 7.21 (d, 4 H)	107–108 °C $C_{18}H_{20}N_4O_6$ *m/z* 388 (M^+)
i	42	3.32 (s, 3 H), 3.36 (s, 3 H), 4.24 (d, 2 H), 4.81 (s, 1 H), 7.33 (s, 4 H)	96–97 °C $C_{17}H_{17}ClN_4O_6$ *m/z* 408 (M^+)
j	46	3.33 (s, 3 H), 3.37 (s, 3 H), 4.25 (d, 2 H), 4.80 (s, 1 H), 7.28–7.38 (m, 4 H)	96–97 °C $C_{17}H_{17}ClN_4O_6$ *m/z* 408 (M^+)
k	18	3.36 (s, 3 H), 3.44 (s, 3 H), 4.30 (d, 2 H), 4.96 (s, 1 H), 7.56–8.29 (m, 4 H)	135–136 °C $C_{17}H_{17}N_5O_8$ *m/z* 419 (M^+)

1,3,4-tricarbonyl equivalent, cyclizes by acid catalysis *via* its enol by a series of intermediates involving 2-methoxy-5-methylfuran-3(2*H*)-one (**9a**) followed by addition of methanol and dehydration to give 2,3-dimethoxy-5-methylfuran (**10a**). In a synthetic study related to dimethoxyfurans,[9] 2,3-dimethoxyfuran was found to be very labile and its formation had to be detected by trapping with ethyl propiolate. It was, therefore, most likely that the furan (**10a**) underwent an immediate 1,4-addition with a molecule of water, generated in the reaction, to yield the dihydrofuran (**11a**) which then demethanolates to give ultimately the furan-2-one (**12a**). Other dimethoxy diones (**7b–f**) underwent the same transformation to give, respectively, the furanones (**12b–f**) as reported in Table 5.

Methyl 2,4-dimethoxyacetoacetate (**3**) rearranged similarly and the methyl 4,4-dimethoxyacetoacetate (**13**) thus formed underwent a similar cyclization in HCl–MeOH with concomitant formation of the enol methyl ether to give the known 4,5-dimethoxy-furan-2(5*H*)-one (**14**)[10] in low yield. Methyl 2-alkyl-2,4-dimethoxyacetoacetates (**15**) prepared for the synthesis of 1-alkyl-1,3-dimethoxyacetone (**5**) (Scheme 1) were unaffected under the conditions that caused the non-alkylated ester (**3**) to rearrange. Additional exceptions to this rearrangement were the 1-(substituted aroyl)-1,3-dimethoxy-

* See footnote on previous page.

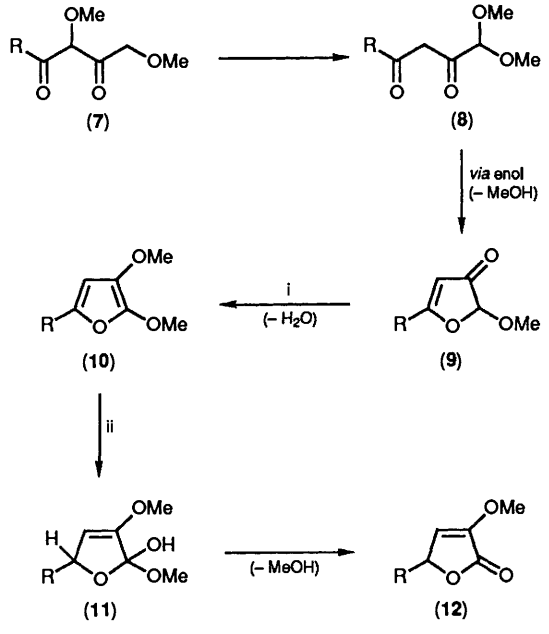
Table 4. 3-(Substituted phenyl) methylglyoxal dimethyl acetals (**6f–k**)[a].

Compd. (6)	M.p. (°C) Yield (%)	δ_H	Formula *m/z*	*p*-Nitrophenylosazone,[b] m.p. (°C)
f		see Experimental section		271–273
g[a]	138–139 93	3.89 (s, 3 H), 6.18 (s, 1 H), 6.50 (s, 1 H), 6.89–7.92 (m, 4 H), 9.20 (s, 1 H)	$C_{10}H_{10}O_3$ *m/z* 178 (M^+)	289–290
h[a]	166–168 96	1.41 (s, 3 H), 6.18 (s, 1 H), 6.56 (s, 1 H), 7.13–7.81 (m, 4 H), 9.19 (s, 1 H)	$C_{10}H_{10}O_2$ *m/z* 162 (M^+)	275–276
i[a]	150–152 92	6.11 (s, 1 H), 6.69 (s, 1 H), 7.24–7.83 (m, 4 H), 9.24 (s, 1 H)	$C_9H_7ClO_2$ *m/z* 182 (M^+)	275–276
j[a]	116–118 77	6.09 (s, 1 H), 6.72 (s, 1 H), 7.25–7.87 (m, 4 H), 9.25 (s, 1 H)	$C_9H_7ClO_2$ *m/z* 182 (M^+)	263–264
k[a]	168–170 93	6.19 (s, 1 H), 6.84 (s, 1 H), 7.58–8.70 (m, 4 H), 9.33 (s, 1 H)	$C_9H_7NO_4$ *m/z* 193 (M^+)	160–161

[a] Isolated and characterized as 3-(substituted phenyl) methylglyoxals. [b] Elemental analyses not reported.

Table 5. 5-Alkyl-3-methoxyfuran-2(5*H*)-ones (**12a–f**).

Compd. (12)	B.p. (°C/mmHg) Yield (%)	δ_H	Formula *m/z*
a	78–81/0.4 30	1.43 (d, 3 H), 3.81 (s, 3 H), 5.08 (q, 1 H), 6.10 (d, 1 H)	$C_6H_8O_3$ *m/z* 128 (M^+)
b	89–92/0.4 29	0.99 (t, 3 H), 1.75 (octet, 2 H), 3.81 (s, 3 H), 4.90 (sextet, 1 H), 6.22 (d, 1 H)	$C_7H_{10}C_3$ *m/z* 142 (M^+)
c	94–95/0.3 38	0.8–1.80 (m, 7 H), 3.80 (s, 3 H), 4.90 (sextet, 1 H), 6.13 (d, 1 H)	$C_8H_{12}O_3$ *m/z* 156 (M^+)
d	102–104/0.4 37	0.8–1.80 (m, 11 H), 3.74 (s, 3 H), 4.85 (sextet, 1 H), 6.08 (d, 1 H)	$C_{10}H_{16}O_3$ *m/z* 184 (M^+)
e	m.p. 61–62 38	1.00 (q, 6 H), 1.95 (m, 1 H), 3.80 (s, 3 H), 4.75 (q, 1 H), 6.10 (d, 1 H)	$C_8H_{12}O_3$ *m/z* 156 (M^+)
f	m.p. 88–89 39	3.00 (d, 2 H), 3.73 (s, 3 H), 5.10 (m, 1 H), 6.00 (d, 1 H), 7.29 (m, 5 H)	$C_{12}H_{12}O_3$ Found (requires): C, 70.4 (70.6); H, 6.0 (5.9)

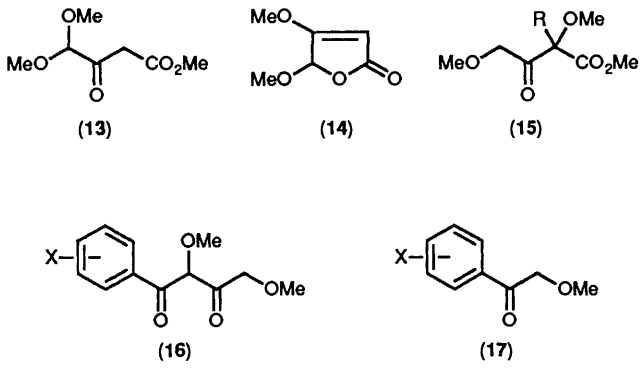


a, R = Me; **b**, R = Et; **c**, R = Pr^n; **d**, R = Am^n; **e**, R = Pr^i; **f**, R = Bn.

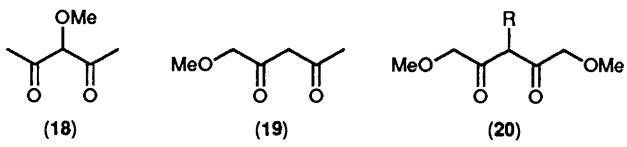
Scheme 2. *Reagents:* i, MeOH; ii, water.

acetones (**16**)* which underwent scission of the C(2)–C(3) bond on treatment with acidic methanol to give substituted ω-methoxyacetophenones (**17**) and methyl methoxyacetate.

Attempted Rearrangement of some Mono- and Dimethoxyacetylacetones.—3- (**18**) and 1-Methoxy- (**19**), and various 3-alkyl-1,5-dimethoxypentane-2,4-diones (**20**), were found to be unaffected under the acid-catalysed rearrangement conditions. Thus, 1-alkanoyl-1,3-dimethoxyacetones (**7a–d**) were recovered admixed with various proportions of compounds (**20a–d**)* on rearrangement; the latter products remained unchanged and could be separated from the furanones (**12a–d**) [formed from substrates (**7a–d**)] by distillation.



a, X = H; **b**, X = *p*-Me; **c**, *p*-MeO; **d**, X = *p*-NO_2.



* See footnote on page 2239.

Discussion

1,3-Dimethoxyalkan-2-ones represented by structures (**1**), (**3**), (**5**), and (**7**) were shown to rearrange to give 3-substituted methylglyoxal dimethyl acetals and those containing a 4-oxo or 4-ester group rearranged further to yield furan-2(5*H*)-one derivatives. They are related to the well known Lobry de Bruyn–Alberda van Ekenstein transformation products which are generally considered to arise by an allyl rearrangement *via* their enols. Yet, some of the facts reported in this paper seem not fit into such a dissociative process. Thus, 1,3-dihydroxyacetone diacetate (**1e**) was not affected under the conditions specified, although it is known that allyl acetates easily undergo acid-catalysed allylic rerrangement.[11] It is also known that in contrast to methyl 2,4-dimethoxyacetoacetate (**3**), which rearranges, its 2-alkyl derivatives (**15**) do not alter on similar treatment, though they contain tertiary methoxy groups, while a tertiary allyl ether tends to suffer ready acid-catalysed S_N1 dissociation.[11] Lastly, why should 3-methoxypentane-2,4-dione (**18**) and 1,3-dimethoxypentane-2,4-dione (**7a**) behave differently? Further studies are in progress.

Experimental

All solvents were purified, dried, and distilled prior to use. The usual drying agent for organic extracts was anhydrous sodium sulphate. Silica gel of various grades was employed for TLC analyses and for column chromatography. Solvents were removed under reduced pressure using a rotary evaporator and a water-pump with bath temperature kept at 40–45 °C. M.p.s were determined on a micromelting-point apparatus and both m.p.s and b.p.s are uncorrected. ^{1}H NMR spectra were recorded on a Varian FT-80A (80 MHz) spectrometer for solutions in $CDCl_3$ with tetramethylsilane as internal standard. IR spectra were obtained in a Specord-IR-75 (Carl Zeiss) or a 5MX (Nicolet) spectrophotometer. Ordinary mass spectra were measured with a ZAB-HS (VG) instrument. Light petroleum refers to that fraction boiling over the range 35–60 °C.

Rearrangement of 1,3-*Dialkoxyacetones* (**1**).—*General procedure.* A solution of a 1,3-dialkoxyacetone (50 mmol) and PTSA monohydrate (20 mg, 0.1 mmol) in benzene (20 ml) was kept at 50 °C for 24 h. The reaction mixture was successively washed with dil. aq. sodium hydrogen carbonate (once) and water (once), dried, and evaporated, and the product was distilled under reduced pressure to give acetals (**2**) and recovered diethers (**1**).

1,3-Dimethoxy- (**1a**),[3] 1,3-diethoxy- (**1b**),[3] and 1,3-di-isopropoxy-acetone (**1c**)[3] gave methylglyoxal dimethyl (**2a**),[12] diethyl (**2b**),[13] and di-isopropyl acetal (**2c**)[14] in 62, 59, and 45% yields, respectively, calculated on consumed substrates (**1**), and the products were characterised as methylglyoxal phenylosazone.[15] Both 1,3-diphenoxyacetone (**1d**)[16] and 1,3-dihydroxyacetone diacetate (**1e**)[17] were recovered on attempted rearrangement.

1-*Alkyl*-1,3-*dimethoxyacetones* (**5**).—*General procedure.* To a solution of methyl 2,4-dimethoxyacetoacetate (**3**)[18] (5 g, 28.6 mmol) and methyl iodide or an alkyl bromide (86.8 mmol) in DMF (10 ml) was added anhydrous potassium carbonate (11 g, 80 mmol) and the mixture was stirred at ambient temperature for 48 h.[4] The reaction mixture was filtered, DMF was evaporated off, and the residue was dissolved in diethyl ether and then washed with water and dried. Diethyl ether was removed under reduced pressure and the methyl 2-alkyl-2,4-dimethoxyacetoacetate (**15**) was distilled under reduced pressure, and the product was collected within a 1–5 °C boiling-point range. The latter product (9.2 mmol) and lithium chloride monohydrate (0.017 g, 2.8 mmol) were dissolved in dimethyl sulphoxide (DMSO) (30–40 ml) and the solution was heated at 120–140 °C and stirred for 10 h.[5] Diethyl ether (30 ml) and water (25 ml) were added to the cooled mixture and the organic layer was separated, washed once with water, and dried. The organic solvent was evaporated off and the product was distilled under reduced pressure to give the corresponding product (**5**) (Table 1), which was too volatile to be weighed; the mass spectrum did not show a molecular ion, but the methoxyacetyl ion *was* observed.

Rearrangement of 3-*Alkyl*-1,3-*dimethoxyacetones* (**5**).— *General procedure.* A compound (**5**) (20 mmol) and PTSA monohydrate (0.5 g) were dissolved in benzene (25 ml) and the solution was stirred at ambient temperature for 24 h [10 h for (**5e**)]. The reaction mixture was washed successively with 5% aq. sodium hydrogen carbonate and water, and dried. Evaporation of solvent and distillation of the residue under reduced pressure yielded 3-alkyl methyl glyoxal dimethyl acetals (**6**) (Table 2) which were again too volatile to be weighed and which did not yield molecular ions in their mass spectra.

1-(*Substituted phenyl*)-1,3-*dimethoxyacetones* (**5g–k**).— *General procedure.* A 2-methoxy-2-(substituted phenyl)acetic acid (**4**)[6] (60 mmol) and freshly distilled thionyl chloride (20 ml) were warmed together at 60 °C for 4 h. Excess of thionyl chloride was removed by evaporation and the residual acid chloride was taken up in diethyl ether (100 ml), to which (stirred) a *ca.* 0.3M-diazomethane solution in diethyl ether[19] (300 ml) was added slowly; the mixture was maintained at between −2 and 0 °C for 90 min and then at ambient temperature for 1 h. Anhydrous methanol (100 ml) was added to the stirred mixture and the organic solvent was removed by evaporation as far as possible. The diazoketone was added to anhydrous methanol (200 ml) containing boron trifluoride–diethyl ether (1 ml) and the mixture was set aside for 1 h at ambient temperature. The solvent was again removed by evaporation and the product was distilled under reduced pressure or subjected to chromatographic separation on silica gel with elution with diethyl ether–light petroleum (1:2) to give a compound (**5g–k**) (Table 3).

Rearrangement of 1-(*Substituted phenyl*)-1,3-*dimethoxyacetones* (**5g–k**).—*General procedure.* Typically a solution of compound (**5f**) (6.5 g, 33.5 mmol) in methanol (50 ml) was treated with 18% (4.8M) hydrogen chloride in methanol (10 ml) and the product was stirred at 55 °C for 55 h. The reaction mixture was evaporated, diethyl ether (60 ml) was added, the mixture was washed successively with saturated aq. sodium hydrogen carbonate and water, and was then dried. Diethyl ether was removed and the product was distilled to give compound (**6f**) (4.2 g, 65%), b.p. 73–76 °C/0.2 mmHg. It was further purified chromatographically on silica gel; ν_{max}(film) 3 060, 3 030, 2 945, 2 860, 1 740, 1 500, 1 400, 1 080, and 700 cm^{-1}; δ_H 3.40 (s, 6 H, OMe), 3.86 (s, 2 H, CH_2), 4.53 (s, 1 H, CH), and 7.26 (s, 5 H, Ph); it yielded no molecular ion, but a characteristic ion at *m/z* 75 [$(MeO)_2CH^+$] *was* observed; *p*-nitrophenylosazone, m.p. 271–273 °C (Found: C, 60.0; H, 4.3; N, 19.8. $C_{21}H_{18}N_6O_4$ requires C, 60.3; H, 4.3; N, 20.1%).

With compounds (**5g–k**), exactly one-third of the rearranged mixture was added to freshly prepared 0.05M-*p*-nitrophenylhydrazine in 1:1 acetic acid–water (40 ml) and the mixture was warmed. The separated osazone was filtered off and recrystallized (from DMF–EtOH). The remaining two-thirds was partially evaporated, water (10 ml) was added, and the mixture was kept at 80 °C for 2 h, then was extracted with benzene (10 ml) twice, and the combined benzene extracts were washed with water and dried ($MgSO_4$). Evaporation of benzene

yielded crystalline substituted benzylglyoxals, which were recrystallized from benzene (Table 4).

Rearrangement of 1-*Alkanoyl*-1,3-*dimethoxyacetones* (**7**).—Typically, a solution of compound (**7a**)* (20 mmol) in 8% hydrogen chloride–methanol (30 ml) was stirred at 50 °C for 20 h. Chloroform (100 ml) was added and the solution was washed thrice with water and dried. Evaporation of chloroform and distillation of the residue under reduced pressure gave 3-methoxy-5-methylfuran-2(5*H*)-one (**12a**). Its mass spectrum was identical with that reported:[8] *m/z* (M^+) 128 (50), 43 (100), 85 (55), 57 (34), and 42 (7); ν_{max}(film) 3 100, 2 980, 2 940, 1 770, 1 650, 1 450, 1 320, 1 250, 1 130, and 990 cm^{-1}. Other data and those of compounds (**12b–f**) are collected in Table 5.

Rearrangement of Methyl 2,4-*Dimethoxyacetoacetate* (**3**).—Hydrogen chloride (10 g) was introduced into a solution of ester (**3**) (10 g, 57 mmol) in methanol (50 ml) and the mixture was stirred at 50 °C for 24 h. Most of the methanol was evaporated off and ethyl acetate (40 ml) was added; the mixture was neutralized with 5% aq. sodium hydrogen carbonate and the aqueous layer was extracted further with diethyl ether (4 × 10 ml). The organic extracts were combined, washed with a little water, and dried. Evaporation of diethyl ether yielded 4,5-dimethoxyfuran-2(5*H*)-one (**14**) as needles which were recrystallized from ethyl acetate (0.6 g, 15%), m.p. 75–77 °C (lit.,[9] 71–73 °C) (Found: C, 50.1; H, 5.6. Calc. for $C_6H_8O_4$: C, 50.0; H, 5.6%); ν_{max}(film) 3 130, 3 000, 2 960, 1 800, 1 750, and 1 640 cm^{-1}; δ_H 3.55 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 5.14 (s, 1 H, CH), and 5.59 (s, 1 H, =CH). It was further identified by hydrolysis with 0.1M-hydrochloric acid to give 5-hydroxy-4-methoxyfuran-2(5*H*)-one.[20]

Rearrangement of 1-(*Substituted benzoyl*)-1,3-*dimethoxyacetones* (**16**). *General procedure*. A solution of a dione (**16**) (5 mmol) in 10% hydrogen chloride–methanol (10 ml) was treated as in the rearrangement of compounds (**7**). The substituted ω-methoxyacetophenones (**17**) were isolated directly or as their 2,4-dinitrophenylhydrazones:

ω-Methoxyacetophenone (**17a**) (71%), b.p. 115–117 °C/14 mmHg (lit.,[21] 118–120 °C/15 mmHg); 2,4-dinitrophenylhydrazone, m.p. 180–181 °C; δ_H 3.64 (s, 3 H, OMe), 4.78 (s, 2 H, CH_2), 7.40–7.82 (m, 5 H, ArH), 8.25 (d, 1 H, ArH), 8.28 (d, 1 H, ArH), 9.14 (d, 1 H, ArH), and 12.80 (s, 1 H, NH).

ω-Methoxy-*p*-methylacetophenone (**17b**) (75%), isolated as 2,4-dinitrophenylhydrazone, m.p. 196–198 °C; δ_H 2.41 (s, 3 H, Me), 3.63 (s, 3 H, OMe), 4.76 (s, 2 H, CH_2), 7.45 (m, 1 H, ArH), 8.25 (d, 1 H, ArH), 8.28 (d, 1 H, ArH), 9.14 (d, 1 H, ArH), and 12.80 (s, 1 H, NH).

ω,*p*-Dimethoxyacetophenone (**17c**) (82%), m.p. 43–45 °C; δ_H 3.49 (s, 3 H, OMe), 3.87 (s, 3 H, OMe), 4.64 (s, 2 H, CH_2), and 6.87–7.98 (q, 4 H, ArH).

ω-Methoxy-*p*-nitroacetophenone (**17d**) (70%), m.p. 118–120 °C; δ_H 3.51 (s, 3 H, OMe), 4.69 (s, 2 H, CH_2), and 8.14–8.39 (q, 4 H, ArH).

3-*Methoxypentane*-2,4-*dione* (**18**).—*Improved preparation*. To a solution of 3-diazopentane-2,4-dione[22] (25 g, 0.2 mol) in methanol was added freshly prepared zinc–copper powder[23] (12 g) and the mixture refluxed for 3 h. The catalyst was removed by filtration, the methanol was evaporated off, and the product was distilled under reduced pressure and redistilled to give the dione (**18**) (9.0 g, 36%), b.p. 79–81 °C/20 mmHg (lit.,[24] ~ 50 °C/6 mmHg; 20%); ν_{max}(film) 1 740, 1 720, and 1 620 cm^{-1}; δ_H 2.16 and 2.22 (2 s, 6 H, Me), 3.44 and 3.56 (s, 3 H, OMe), 4.30 and 14.24 (s, 1 H, OH), indicating 70% enolization.

3-Cyano-5-methoxy-4,6-dimethyl-2-pyridone (87%),* m.p. 261–262 °C; δ_H 2.26 (s, 3 H, Me), 2.30 (s, 3 H, Me), and 3.58 (s, 3 H, OMe) (Found: M^+, 178. $C_9H_{10}N_2O_2$ requires *M*, 178).

Attempted Rearrangements of 3- (**18**) *and* 1-*Methoxy*- (**19**), *and* 3-*Alkyl*-1,5-*dimethoxypentane*-2,4-*dione* (**20**).—Compounds (**18**), (**19**), and (**20**) were kept separately in benzene (10 ml) containing PTSA (50 mg) as reported for compound (**4a**) and each one was recovered in *ca.* 70% yield and identified by their 2-pyridones.* Compounds (**18**) and (**19**) were also kept separately in methanol containing hydrogen chloride as reported for compound (**7a**) and the products isolated were methoxyacetone and methyl methoxyacetate, respectively (with *ca.* 40% recovery), which were characterized, respectively, as the 2,4-dinitrophenylhydrazone, m.p. 162–163 °C (lit.,[25] 162–163 °C) and spectroscopically.

Acknowledgements

We are grateful to the National Natural Science Foundation and the National Commission of Education for financial grants.

References

1 J. C. Speck, Jr., *Adv. Carbohydr. Chem.*, 1958, **13**, 63.
2 M. Fedoronko, P. Temkovic, V. Mihalov, and I. Tvaroska, *Carbohydr. Res.*, 1980, **87**, 51.
3 J. Kenner and G. N. Richards, *J. Chem. Soc.*, 1953, 2240.
4 D. A. White, *Synth. Commun.*, 1977, **7**, 559.
5 A. P. Krapcho, *Synthesis*, 1982, 805, 893.
6 E. D. Bergmann, D. Ginsberg, and D. Lavie, *J. Am. Chem. Soc.*, 1950, **72**, 5012; W. Reeve and E. L. Compere, Jr., *ibid.*, 1961, **83**, 2755.
7 A. Rossi and H. Schinz, *Helv. Chim. Acta*, 1948, **31**, 1740.
8 C. C. Bonini, C. Iavarone, C. Trogolo, and G. A. Poulton, *Org. Mass Spectrom.*, 1981, **16**, 68.
9 E. McDonald, A. Suksamrarn, and R. D. Wylie, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1893.
10 F. Farina, M. C. Maestro, M. R. Martin, M. V. Martin, and F. Sanchez, *J. Chem. Res.*, 1980, (*S*) 188; (*M*) 2662.
11 R. H. Dewolfe, in 'Comprehensive Chemical Kinetics,' eds. C. H. Bamford and O. F. H. Tipper, Elsevier, London, 1973, vol. 9, ch. 5, pp. 417–487.
12 E. E. Royals and A. G. Robinson, *J. Am. Chem. Soc.*, 1956, **78**, 4161.
13 E. A. Braude and E. A. Evans, *J. Chem. Soc.*, 1955, 3328.
14 H. R. Guest, D. G. MacDowell, and R. W. McNamee, U.S.P. 2 421 559/1947 (*Chem. Abstr.*, 1947, **41**, 5548e).
15 G. Heller, *Justus Liebig's Ann. Chem.*, 1910, **375**, 288.
16 J. Munch-Peterson, *Acta Chem. Scand.*, 1951, **5**, 525.
17 P. H. Bentley and W. McCrae, *J. Org. Chem.*, 1970, **35**, 2082.
18 D. D. Pratt and R. Robinson, *J. Chem. Soc.*, 1925, **127**, 169.
19 J. A. Moore and D. E. Reed, *Org. Synth.*, Coll. Vol. 5, 1973, p. 351.
20 R. Tschesche and H.-J. Hoppe, *Chem. Ber.*, 1971, **104**, 3573.
21 D. D. Pratt and R. Robinson, *J. Chem. Soc.*, 1923, **123**, 748.
22 M. Regitz and A. Leidhegener, *Chem. Ber.*, 1966, **99**, 3128.
23 R. D. Smith and H. E. Simmons, *Org. Synth.*, Coll. Vol. 5, 1973, p. 857.
24 J. P. Fackler, Jr., and F. A. Cotton, *Inorg. Chem.*, 1963, **2**, 102.
25 R. P. Mariella and J. C. Leech, *J. Am. Chem. Soc.*, 1949, **71**, 3558.

Paper 0/00251H
Received 15*th January* 1990
Accepted 2*nd February* 1990

* See footnote on page 2239.