

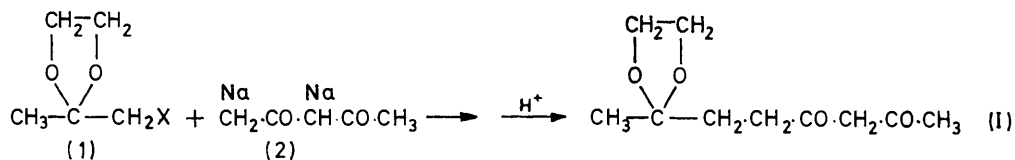
Alkylation of Disodiopentane-2,4-dione with Halogeno-acetals

By **K. Gerald Hampton**,* Department of Chemistry, University of Southern Mississippi, Hattiesburg, Mississippi 39401
Richard E. Flannery, Department of Chemistry, Texas A & M University, College Station, Texas U.S.A.

The alkylation of disodiopentane-2,4-dione with halogeno-acetals was found to be dependent on the leaving halide. Chloroacetaldehyde dimethyl, diethyl, and ethylene acetals failed to yield any alkylation products whereas bromoacetaldehyde dimethyl, diethyl, and ethylene acetals did afford γ -alkylation products. β -Bromopropionaldehyde diethyl acetal and β -chloropropionaldehyde ethylene acetal alkylated disodiopentane-2,4-dione. Copper chelates of the alkylation products were prepared.

It has been observed that 2-chloromethyl-2-methyl- and 2-bromomethyl-2-methyl-1,3-dioxolan do not alkylate disodiopentane-2,4-dione (2)^{1,†} [equation (I)],

Structure (3; $n = 1$, RR = $-\text{CH}_2-\text{CH}_2-$) differs from (1) in the presence of a proton rather than a methyl group, which should mean less steric hindrance. Table I



(X = Cl or Br)

whereas other halogeno-acetals, having the chlorine or bromine atom farther from the acetal group, do so.² In an effort to extend the range of these alkylations and to learn more about the stereochemical requirements we have studied the reaction of the halogeno-acetals (3) with the disodio-compound (2) [equation (II)].

† For convenience these dianions will be represented by one resonance form although they are resonance hybrids of several contributing forms and the oxygen atoms may bear the greater part of the charge.

shows that chloroacetaldehyde dimethyl, diethyl, and ethylene acetals did not react with (2), whereas bromoacetaldehyde dimethyl, diethyl, and ethylene acetals did. This indicates that while steric hindrance is not important in going from (1; $n = 1$) to (3; $n = 1$) when X = Cl, it is when X = Br. Although it is recognized

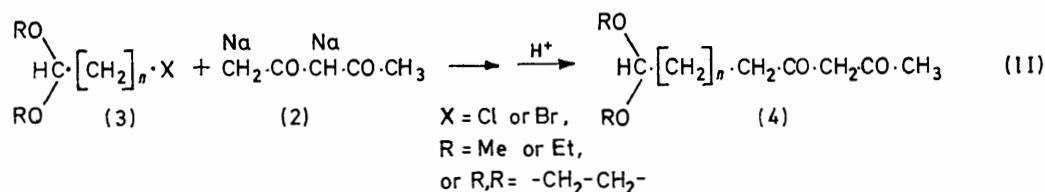
¹ M. L. Miles, C. G. Moreland, D. M. von Schrittz, and C. R. Hauser, *Chem. and Ind.*, 1966, 2098.

² R. E. Flannery and K. G. Hampton, *J. Org. Chem.*, 1972, **37**, 2806.

that alkyl bromides are more reactive than alkyl chlorides, this is one of the first cases reported where a difference in the halogen with the same alkyl group has made a significant difference in the reactivity of the disodio-compound (2). For instance, butyl chloride, bromide, and iodide gave about the same yield in alkylation of (2).

need to use the bromo-compounds for alkylation with (3; $n = 1$).

β -Chloropropionaldehyde ethylene acetal (3; $n = 2$, X = Cl) alkylated (2) although not in high yield. This shows that the lack of reaction of (3; $n = 1$, X = Cl) is not just a leaving group effect, but a combination of



We do not consider that the differences in yield between ethylene and methyl and particularly between ethyl and methyl acetals are large enough to allow quantitative conclusions about the difference in steric effects of the acetal groups in these cases to be reached, although the results fit qualitatively with the methyl group being

leaving group ability and steric hindrance to S_N2 attack. The lack of alkylation product from β -chloropropionaldehyde diethyl acetal may have been due to a competing β -elimination reaction. A vigorous reaction occurred as the chloroacetal was added, but no alkylation product or chloroacetal was recovered.

TABLE 1
Alkylations of disodiopentane-2,4-dione with halogeno-acetals

Halogeno-acetal	Amount (mol) *	Product	Reaction time (h)	B.p. [°C] (mmHg)	Yield (%)
Chloroacetaldehyde dimethyl acetal	0.1	None	2		0
Chloroacetaldehyde diethyl acetal	0.1	None	2		0
Chloroacetaldehyde ethylene acetal	0.1	None	2		0
Bromoacetaldehyde dimethyl acetal	0.1	4,6-Dioxoheptanal dimethyl acetal	2	67—69 (0.25)	49
Bromoacetaldehyde diethyl acetal	0.1	4,6-Dioxoheptanal diethyl acetal	2	80—83 (0.6)	46
Bromoacetaldehyde ethylene acetal	0.1	4,6-Dioxoheptanal ethylene acetal	2	110—115 (0.1)	38
β -Bromopropionaldehyde diethyl acetal	0.05	5,7-Dioxo-octanal diethyl acetal	24	75 (0.45)— 105 (0.85)	35
β -Chloropropionaldehyde diethyl acetal	0.05	None	1½		0
β -Chloropropionaldehyde ethylene acetal	0.05	5,7-Dioxo-octanal ethylene acetal	2	85—86 (0.05)	20

* 1 : 1 Ratio of disodiopentane-2,4-dione to acetal in each reaction.

TABLE 2
Alkylations of disodiopentane-2,4-dione with halogeno-acetals. Product and copper chelate analyses

n	R	Product (4)			Copper chelate of product			
		Calc.	C (%)	H (%)	M.p. (°C)	C (%)	H (%)	Cu (%)
1	Me	Calc.	57.4	8.55	107—108	49.4	6.9	14.5
		Obs.	57.45	8.6		49.3	6.95	14.4
1	Et	Calc.	61.05	9.35	128—129	53.5	7.75	12.85
		Obs.	60.75	9.15		53.3	7.7	13.15
1	-CH ₂ -	Calc.	58.1	7.5	150—152	49.8	6.05	14.65
		Obs.	57.85	7.8		49.65	6.1	14.75
2	-CH ₂ -	Calc.	60.0	8.0	148—149	52.0	6.55	13.75
		Obs.	58.8 *	7.75 *		51.9	6.5	13.65

* This is the best of three analyses.

smaller than ethyl, leading to the higher yield. In attempts to force the reaction of chloroacetaldehyde dimethyl acetal with (2) by using more vigorous conditions, solvents such as di-isopropylamine, 1,2-dimethoxyethane, and pyridine (all of higher b.p. than ammonia) were used, but starting materials were recovered and no alkylation product was observed; this emphasizes the

The structures of the β -diketone acetals were deduced by analogy with previous alkylation studies, by analysis (see Table 2), and by i.r. and n.m.r. spectra. Although we were unable to get a satisfactory analysis of 5,7-dioxo-octanal diethyl acetal, the copper chelate gave the expected figures, which indicates that the acetal was impure and/or underwent some decomposition.

Each of the i.r. spectra of the four copper chelates showed absorption bands for the carbon-carbon double bond (6.52–6.60 μm) and for the carbonyl bond (6.10–6.45 μm). It has been reported that the copper chelates of pentane-2,4-dione and similar β -diketones unsubstituted at the methylene group show i.r. bands at 6.10–6.45 and 6.52–6.60 μm whereas the chelates of their 3-substituted derivatives exhibit only the former band.³

This study shows that alkylation of dicarbanions of β -diketones can be used to introduce functional as well as alkyl and aryl groups. The reaction is dependent, for acetal halides, on leaving group and steric hindrance interaction.

EXPERIMENTAL

M.p.s were taken on a Thomas-Hoover apparatus. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee, and Chemalytics, Inc., Tempe, Arizona. The i.r. spectra were recorded on Beckman IR-8 and Perkin-Elmer Grating 237B spectrophotometers using potassium bromide pellets for solids and sodium chloride plates for liquids. The ^1H n.m.r. spectra were obtained on a Varian A60 spectrometer; samples were either neat or dissolved in carbon tetrachloride with tetramethylsilane as internal standard.

Halogeno-acetals.—Acetals (3; X = Cl or Br, R = Me or Et) and β -chloropropionaldehyde diethyl acetal were commercial samples.

A mixture of bromoacetaldehyde diethyl acetal (78.8 g, 0.40 mol), ethylene glycol (24.8 g, 0.40 mol), and a trace of toluene-*p*-sulphonic acid was heated in an oil-bath at 160° for 2 h. The two liquids were immiscible and no reaction occurred. The mixture was allowed to cool. Two drops of bis-(2-methoxyethyl) ether were added and the mixture was heated. Ethanol distilled off and the residue was distilled under vacuum to afford bromoacetaldehyde ethylene acetal (66 g, 99%), b.p. 75–78° at 20 mmHg. Chloroacetaldehyde ethylene acetal was formed by the same procedure from chloroacetaldehyde dimethyl acetal.

Methylene chloride (100 ml) was cooled to 0° and saturated with HBr (8.5 g). Acrylaldehyde (5.6 g) was dripped into the stirred, cooled solution. Absolute ethanol (4.6 g) was added followed by ethyl orthoformate (16.3 g), and the mixture was set aside for 2 h. Then anhydrous potassium

carbonate was added. The mixture was filtered and the filtrate was distilled to afford β -bromopropionaldehyde diethyl acetal (15.7 g, 74%).⁴

β -Chloropropionaldehyde ethylene acetal was prepared in 58% yield by the procedure of Faass and Hilgert.⁵

Alkylation of the Disodio-derivative (2) with Halogeno-acetals.—A suspension of sodium amide⁶ in freshly distilled liquid ammonia (450 ml) was cooled to -78° in a CO_2 -acetone bath while nitrogen was passed over it. A solution of pentane-2,4-dione (see Table 1 for quantities) in ether (20 ml) was added in small portions from a pressure-compensating addition funnel. The cooling bath was removed, the mixture was allowed to warm to room temperature, and the nitrogen flow was stopped. After 30 min, the acetal halide (see Table 1 for quantities) in ether (30 ml) was added dropwise over 5 min. After stirring (see Table 1 for times), anhydrous ether was added and the ammonia was evaporated off by warming the mixture. The ethereal suspension was cooled in ice and a mixture of ice (50 g) and hydrochloric acid (10 ml) was added and stirred for ca. 0.5 min. Immediately, the layers were separated and the aqueous layer was extracted with ether (3 \times 25 ml). The acidity of the water layer was checked prior to extraction. The combined ethereal extracts were dried (MgSO_4), and evaporated at reduced pressure. The residue was distilled under vacuum. See Table 1 for b.p.s and yields of the products.

A typical n.m.r. spectrum is that for 4,6-dioxoheptanal diethyl acetal: δ 1.14 (6H, t, CH_3C), 2.03 (3H, s, CH_3CO), 2.44 (2H, t, CH_2CO), 3.6 (6H, m, $-\text{OCH}_2$ and $\text{CH}_2\text{C}\cdot\text{O}$), 4.51 (1H, t, $\text{O}\cdot\text{CH}\cdot\text{O}$), and 5.62 (ca. 1H, s, vinyl).

The reaction appears to be more sensitive to solvent purity than previous alkylations of dianions. For instance, when the ammonia was not distilled but introduced directly from the tank, the yield of 4,6-dioxoheptanal dimethyl acetal was 17 instead of 49% (Table 1).

Copper Chelates.—The copper chelates were formed by adding a filtered aqueous solution of copper(II) acetate to the diketone acetal (ca. 1 g). The chelates were recrystallized from methanol (see Table 2).

We thank the Petroleum Research Fund, administered by the American Chemical Society, and the Robert A. Welch Foundation for financial support.

[3/482 Received, 5th March, 1973]

³ R. P. Dryden and A. Winston, *J. Phys. Chem.*, 1958, **62**, 635.

⁴ E. J. Corey, personal communication.

⁵ U. Faass and H. Hilgert, *Chem. Ber.*, 1954, **87**, 1343.

⁶ C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, 1954, **8**, 122.