

5,5-Dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane; A New Brominating Agent for Saturated and α,β -Unsaturated Carbonyl Compounds

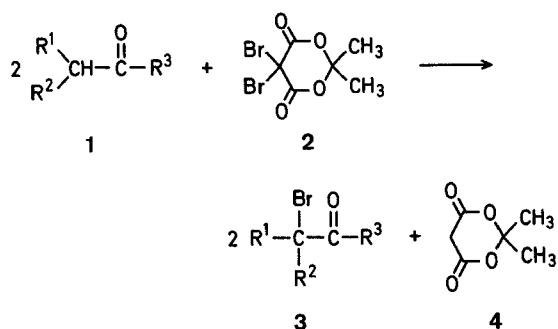
R. BLOCH

Laboratoire des Carbocycles, Equipe de Recherche Associée au C.N.R.S., Université de Paris-Sud, Bâtiment 420, F-91405 Orsay, France

The ability of bromomalononic derivatives to act as bromonium ion sources is well known. However, if bromo- and dibromo-malonitrile are suitable reagents for the bromination of active methylene compounds^{1,2}, they are not active enough to introduce a bromine atom at the α -carbon of monocarbonyl compounds. The purpose of this work is to show that the cyclic malonic ester 5,5-dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**2**) can monobrominate saturated aldehydes and ketones with excellent yields and the α' -carbon atom of α,β -unsaturated ketones with high selectivity.

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R³ = H, alkyl, alkenyl, aryl

The dibromoester **2** is a white solid, stable for months at 0°, which can be easily prepared in two steps from malonic acid via Meldrum's acid **4**³. The bromination is usually carried out by stirring at room temperature an ether solution of **1** and **2** in 2:1 molar ratio. The bromo-ketone or -aldehyde **3** is simply isolated by washing away the Meldrum's acid **4** with an aqueous solution of sodium hydrogen carbonate. The results of some typical experiments are summarized in the Table.

The reaction of the dibromoester **2** with saturated carbonyl compounds needs no catalyst and thus may be useful for the bromination of sensitive ketones or aldehydes (no strong

Table. Bromination of Carbonyl Compounds **1** with 5,5-Dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**2**)

Carbonyl Compound 1	Products 3 ^a	Reaction conditions solvent/time/temperature	Yield ^b [%]	m.p. or b.p./torr	Lit. m.p. or b.p./torr	Reference
a		ether/3 h/r.t.	83 ^c	50–51°	49–50°	2
b		ether/2 h/r.t.	82 ^d	—	—	9
c		ether/3 h/r.t.	77 ^d	—	—	10
d		ether/3 h/r.t.	55°	42–43°/120	41–42°/105	4b
e		ether/3 h/r.t.	84	86–87°/18	81–83°/15	4b
f		ether/11 h/r.t.	86	89–90°/18	90–91°/20	11
g		ether/3 h/r.t.	94	85–86°	82–84°	2
h		ether/7 h/r.t.	57	—	—	8
i		ether + HBr (10 μl)/24 h/reflux	75°	46°	46–47°	6
j		CCl4/5 h/reflux ^f	76°	47.5–48°	47.5°	12
k		CCl4/2 h/reflux ^f ether + HBr (10 μl)/48 h/reflux ^f	40 45	—	—	7

^a All products identified by I.R., N.M.R.

^b Yields after distillation or column chromatography. Compounds **3b**, **3c**, **3h**, and **3k** are liquids purified by column chromatography. No boiling points are available for these products in the literature and **3b**, **3c**, and **3h** are mixtures of isomers.

^c A small amount of dibromocompound is also present.

^d Product distribution estimated by ¹H-N.M.R. spectroscopy.

^e Low yield of distilled product due to its high volatility.

^f A 1:1 molar ratio of reagents was used in order to accelerate the reaction.

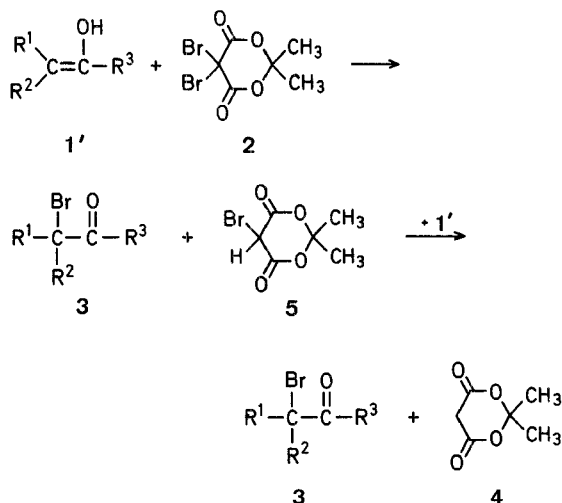
base or acid is present). Furthermore, the direct bromination of aldehydes sometimes occurs with difficulty⁴ and the efficiency of the method described here compares favorably with the recently reported preparation of α -bromoaldehydes via silyl enol ethers⁵.

The direct bromination of α,β -unsaturated ketones leads usually to a complex mixture arising from addition of bromine to the double bond and from allylic displacement. Since α' -bromo- α,β -unsaturated ketones are useful intermediates, several syntheses have been reported during the past years, including the use of selective brominating reagents^{2,6,7} or bromination of silyl enol ethers⁸. As shown in the Table, 5,5-dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**2**) is able to brominate α,β -unsaturated ketones without affecting the double bond or any allylic positions. The reaction rate is strongly dependent on the nature of the substrate and, in the case of slightly enolisable ketones, it can be enhanced by the addition of a small amount of acid (HBr) or by heating (CCl₄, reflux). If in some cases (ketones **1i** and **1j**) a small amount of the dibromo derivative is formed, no compound arising from allylic displacement is observed.

In all cases the bromination reaction seems to proceed via the enol form **1'** of the carbonyl compounds since:

- The reaction is catalysed by acids;
- The rate is closely related to the ease of enolisation (compare aldehydes **1e** and **1f** or ketones **1g** and **1k**);
- A mixture is obtained from asymmetric ketones, corresponding roughly to the enol thermodynamic equilibrium.

When the reaction is monitored by N.M.R. spectroscopy, it is observed that the reagent **2** releases its two bromine atoms in two steps, the first step giving rise to 5-bromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**5**).



However, **5** is a less effective brominating agent than the dibromoester **2**, precluding its use in a few cases (ketones **1j** and **1k**).

1-Bromocyclohexanecarboxaldehyde (**3f**):

Cyclohexanecarboxaldehyde (**1f**; 1.12 g, 0.01 mol) and 5,5-dibromo-2,2-dimethyl-4,6-dioxo-1,3-dioxane (**2**; 1.51 g, 0.005 mol) are dissolved in anhydrous ether (20 ml) and the resultant solution is stirred at room temperature for 11 h (the reaction is then complete, as shown by N.M.R. spectroscopy). The ethereal solution is washed with saturated aqueous sodium hydrogen carbonate solution (20 ml) and, after decantation, the aqueous phase is

extracted twice with ether (10 ml). The organic phase is dried with sodium sulfate and concentrated under vacuum yielding 1.85 g of crude bromoaldehyde. Bulb-to-bulb distillation affords pure **3f**; yield: 1.64 g (86%); b.p. 89–90°/18 torr.

C₇H₁₁BrO calc. C 44.00 H 5.80 Br 41.82
(175.1) found 43.93 5.73 41.84

I.R. (film): $\nu = 1730 \text{ cm}^{-1}$.

¹H-N.M.R. (CCl₄): $\delta = 9.32$ (s, 1H); 1.4–2.2 ppm (m, 10H).

6-Bromo-4,4-dimethylcyclohex-2-enone (**3j**):

A solution of 4,4-dimethylcyclohex-2-enone (**1j**; 1.24 g, 0.01 mol) and dibromoester **2** (3.02 g, 0.01 mol) in carbon tetrachloride (20 ml) is refluxed for 5 h (complete reaction, monitored by T.L.C.). The solution is then treated as above and the residue (2.0 g) subjected to column chromatography [silicagel, 60 g; eluent ether/pentane 1:9] to give (a) 6-bromo-4,4-dimethylcyclohex-2-enone (**3j**); yield: 1.52 g (75%); m.p. 47.5–48° (Lit.¹² m.p. 47.5°); and (b) 6,6-dibromo-4,4-dimethylcyclohex-2-enone; yield: 0.170 g (6%).

¹H-N.M.R. (CCl₄): $\delta = 6.15$ (d, 1H); 5.87 (d, 1H); 3.10 (s, 2H); 1.34 ppm (s, 6H).

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