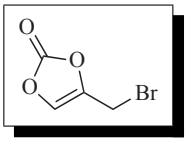
4-(Bromomethyl)-1,3-dioxol-2-one



[80715-25-9] $C_4H_3BrO_3$ (MW 178.97)
InChI = 1S/C4H3BrO3/c5-1-3-2-7-4(6)8-3/h2H,1H2
InChIKey = KFZJRSPXJHVSCX-UHFFFAOYSA-N

(highly functionalized/oxygenated reagent for allylation of carbonyl compounds; synthetic equivalent of 1-hydroxyacetone enolate; synthetic equivalent of a hydroxyacetophenone enolate; alkylating agent)

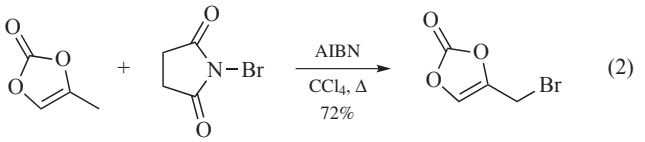
Physical Data: bp 100–110 °C/1 mmHg; *d* 1.8 g cm^{-3}.

Stability: soluble in most organic solvents.

Form Supplied in: viscous yellow oil; not commercially available.

Preparative Methods: obtained in two steps, starting from hydroxyacetone. Reaction of hydroxyacetone with triphosgene affords 4-methyl-1,3-dioxol-2-one (eq 1).[1] Free-radical bromination of 4-methyl-1,3-dioxol-2-one with NBS gives the title reagent (eq 2).[1–3] This latter reaction can also be performed in dichloroethane (although in inferior yield of 52%), as the use of carbon tetrachloride, which until recently was a common solvent for this type of transformations, is strongly discouraged.

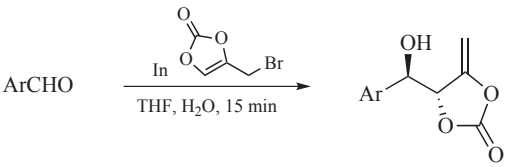
(1)



(2)

Handling, Storage, and Precautions: decomposes on standing. Can be stored for weeks at –18 °C.

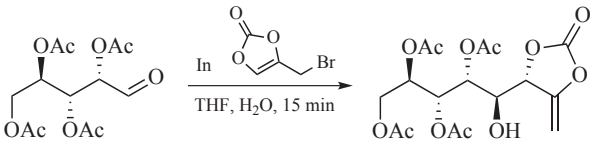
Metal-promoted Allylation of Carbonyl Compounds. Allylation of carbonyl compounds from allyl bromide derivatives is a very important method of C–C bond formation. While the reaction can be promoted by a number of metals (Mg, Ti, Zn, Ga, In, Sn, or Cr)[4–12] as well as by B, Si,[6,7,12] the most popular is the indium-promoted reaction, which can be effected in aqueous medium.[8,10,13,14] As the allyl group can be transformed into various structural units, this reaction has found wide synthetic applications. Furthermore, allyl reagents can be modified to include halogen,[15–18] sulfur,[19] and 2-oxy[20–23] and 3-oxy[24–31]-substituted allylmetallics. 4-(Bromomethyl)-1,3-dioxol-2-one is a reagent that allows a diastereoselective introduction of highly oxygenated allylic moiety into carbonyl compounds.[32] In the presence of indium, it reacts with a series of aromatic aldehydes to give allylated products in excellent yields (eq 3).[1] Allylations are diastereoselective, with a predominance of the *anti*-isomer (>6:1).



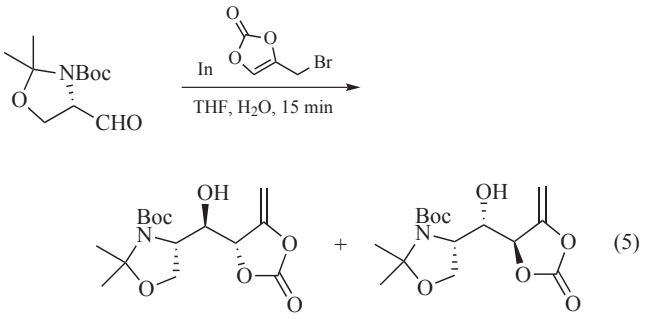
(3)

Ar = Ph–, *o*-MeO–C_6H_4–, *p*-MeO–C_6H_4–, indol-3-yl, 2-furyl–, thiophene-2-yl–

Aliphatic aldehydes are also good substrates for the reaction. Although the reaction still proceeds with *anti*-selectivity, with chiral aldehydes, it is difficult to estimate the influence of stereogenic center at the α-position. Thus, the reaction with arabinose peracetate proceeds with excellent level of asymmetric induction (eq 4), while Garner's aldehyde affords an equimolar mixture of 3,4-*anti*-products (eq 5).

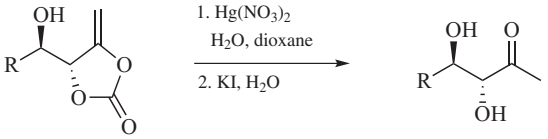


(4)



(5)

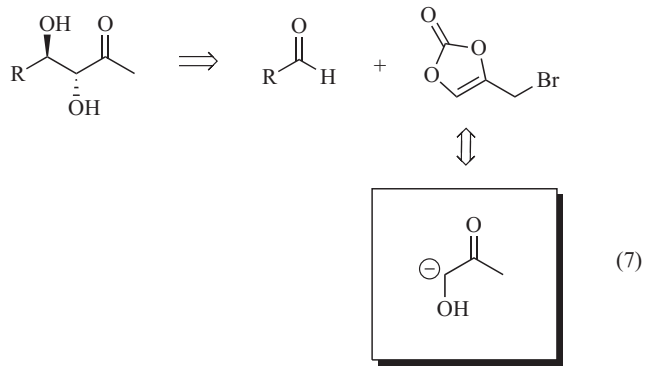
The reaction products are aldols in a latent form. They can be deprotected in the reaction with mercuric acetate to give dihydroxyketones with retention of configuration (eq 6). As such, the reagent can be considered as a synthetic equivalent of a 1-hydroxyacetone enolate (eq 7).



(6)

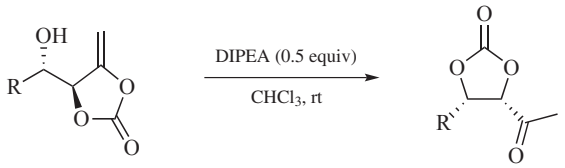
R = *n*-C_6H_{13}–, Ph–, *p*-MeO-C_6H_4– benzo[d][1,3]dioxole-5-yl–

49–75%
dr = 73–100%



(7)

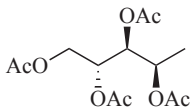
Alternatively, the initial enol carbonate-type products can be transformed under very mild conditions into another protected form of the aldol, namely, saturated cyclic carbonates of *anti*-α,β-dihydroxyketones (eq 8).



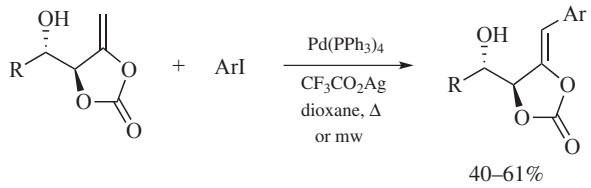
(8)

53–90%

R = *n*-C_6H_{11}–, MeCH:CH–, PhCH:CH–, Ph–, *p*-MeO-C_6H_4–

p-Cl-C_6H_4–, benzo[d][1,3]dioxole-5-yl– 

Enol carbonates also undergo Heck reaction to give arylated products (eq 9).[33] This transformation expands the synthetic applicability of the reagent, as a tactical combination of reactions: allylation/Heck reaction, makes 4-(bromomethyl)-1,3-dioxol-2-one a synthetic equivalent not only of 1-hydroxyacetone enolate but also of variously substituted hydroxymethyl benzyl ketones (eq 10).

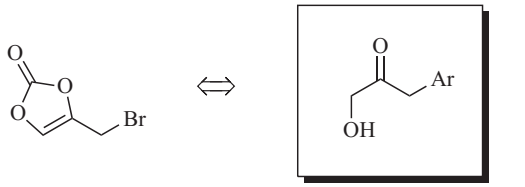


(9)

40–61%

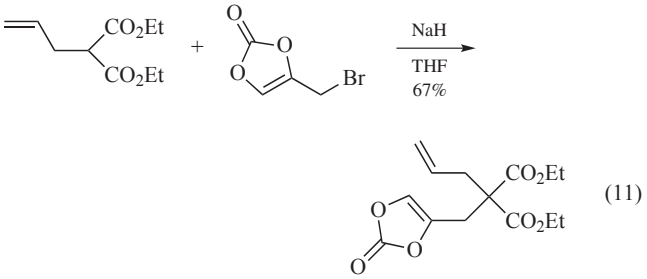
R = *n*-C_3H_7–, Ph–, benzo[d][1,3]dioxole-5-yl–, *p*-Cl-C_6H_4–, thiophene-2-yl–

Ar = Ph–, *p*-MeO-C_6H_4–, *o*-MeO_2C–C_6H_4–, *p*-MeO_2C-C_6H_4–

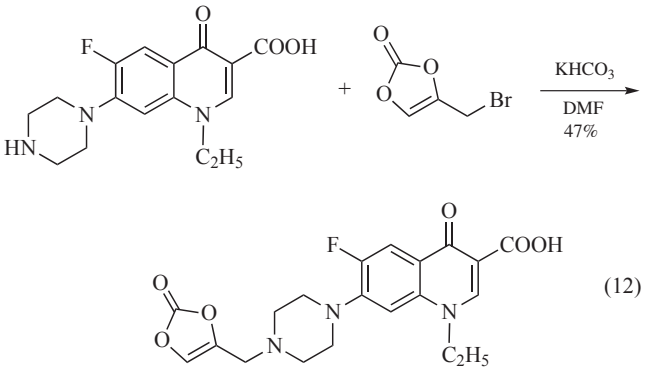


(10)

Alkylation of Enolates and Other Anionic Species. 4-(Bromomethyl)-1,3-dioxol-2-one reacts with enolates to furnish the allylated products. The new C–C bond is formed at the less substituted end, that is, without allylic transposition (eq 11).[34] Also, 4-(bromomethyl)-1,3-dioxol-2-one reacts with heteroatom nucleophiles such as *N*,[2] *O*,[35] and *S*[36] This is employed in synthesis of antimicrobial drug *N*-(2-oxo-1,3-dioxol-4-yl)methyl norfloxacin (eq 12).[36]



(11)



(12)

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