Reformatsky Reaction on α-Oxoketene *S*,*S*-Acetals: Synthesis of Novel Polarized Vinylketene *S*,*S*-Acetals and Dimethyl 2-Aryl(methyl)-propene-1,3-dicarboxylates[1]

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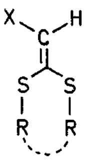
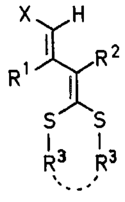
Synthetic applications of polarized ketene *S*,*S*-acetals **1** for the construction of a variety of heterocyclic systems[2] as well as their utility as versatile reagents for 1,3-carbonyl transposition[3,4] have been established. On the other hand, the corresponding polarized vinylketene *S*,*S*-acetals **2** are not known, although a number of simple vinylketene *S*,*S*-acetals **3** are described in the literature. These are shown to be useful isoprenoid synthons with reactivity umpolung[5] and diene components[6] in Diels-Alder reactions. In the present paper we describe the synthesis of novel polarized vinylketene *S*,*S*-acetals **9a–g** (push-pull dienes) by the Reformatsky reaction of ethyl bromoacetate on α-oxoketene *S*,*S*-acetals **5a–g**, followed by subsequent iodine-catalyzed dehydration of the resulting carbinol acetals **7**. The synthesis of novel dimethyl 2-aryl-1,3-propenedicarboxylates **8a–d** and the corresponding 2-methyl derivative[7] **8e** by methanolysis of intermediate carbinol acetals **7** in the presence of boron trifluoride etherate is also described.

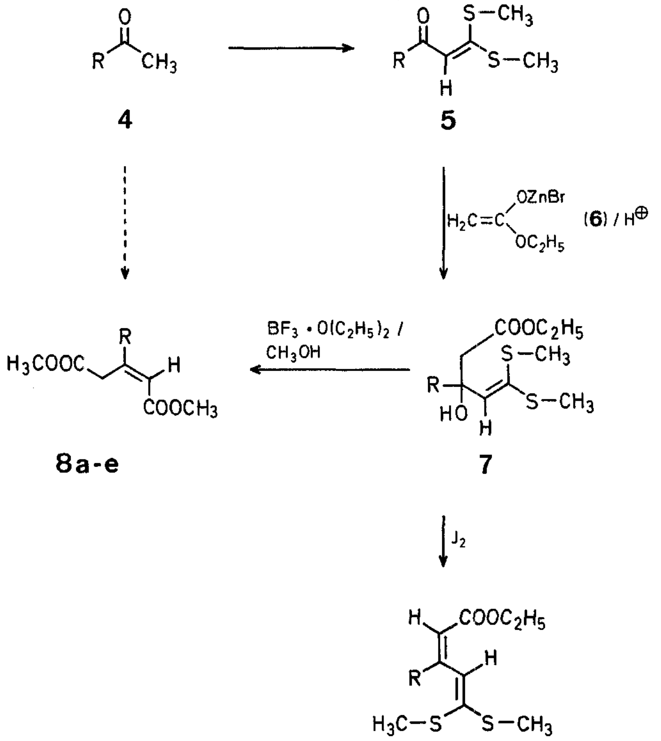


1,2 X = electron-withdrawing group, e.g. R–CO–, C_2H_5OOC–, O_2N–, NC–, etc.



3 X = H
R^1, R^2 = H, CH_3, C_6H_5

When the oxoketene *S*,*S*-acetal **5a** was reacted with zinc bromoacetate (**6**) in refluxing ether/benzene, work-up of the reaction mixture afforded **7a** in nearly quantitative yield. When the crude **7a** was subjected to dehydration in the presence of iodine the diene **9a** wa s obtained in 70% yield. The dienes **9b–g** were similarly obtained from the respective dithioacetals **5b–g** in 45–68% overall yields via the carbinol intermediates **7b–g** (Scheme A).



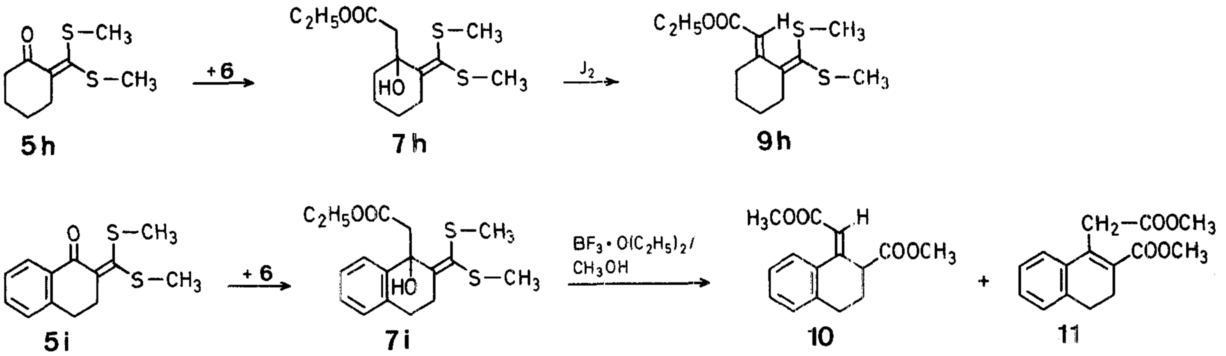
Scheme A

In a separate reaction **7a** was subjected to methanolysis in the presence of boron trifluoride etherate and the corresponding dimethyl 2-phenyl-1,3-propenedicarboxylate **9a** was isolated in 65% yield. Methanolysis of **7b–e** afforded the diesters **8b–e** in 50–70% overall yields (Scheme **A**).

Reformatsky reaction on cyclic oxoketene *S,S*-acetals did not give the consistent results. Thus the expected cyclic diene **9h** was formed (40%) when the dithioacetal **5h**, derived from cyclohexanone was reacted with zinc bromoacetate **(6)** (Scheme **B**). However subsequent methanolysis of the carbinol acetal **7h** afforded a complex isomeric mixture of diesters from which none of the pure product could be isolated.

On the other hand, attempted preparation of the corresponding diene from **7i** under identical conditions afforded only a complex reaction mixture, while on methanolysis it yielded a mixture of diesters **10** and **11** (3:2) in good yields, which were separated by column chromatography (Scheme **B**).

The oxoketene *S,S*-acetals are thus shown to be useful intermediates for the synthesis of novel push-pull dienes. The overall transformation **4** → **5** → **7** → **8** could be considered as simultaneous 1,3-carbonyl transposition of ketones **4** at car-



Scheme **B**

Table 1. 1,1-Bis[methylthio]-3-aryl(alkyl)-4-ethoxycarbonyl-1,3-butadienes **9** prepared

Product	R	Yield [%][a]	m.p. [°C]	Molecular Formula[b]	I.R. (KBr) ν[cm^{-1}]	^{1}H-N.M.R. (CCl$_4$/TMS) δ[ppm]	MS m/e(M$^+$)
9a	C_6H_5	70	36–37°	$C_{15}H_{18}O_2S_2$ (294.4)	1695, 1595	1.25 (s, 3H, $OCH_2C\underline{H}_3$); 2.0 (s, 3H, SCH_3); 2.42 (s, 3H, SCH_3); 4.15 (q, 2H, $OC\underline{H}_2CH_3$); 5.83 (s, 1$H_{olefinic}$); 7.23 (s, 1$H_{olefinic}$); 7.30 (s, 5H_{arom})	294
9b	$4\text{-}H_3C{-}C_6H_4$	68	39–40°	$C_{16}H_{20}O_2S_2$ (308.5)	1700, 1595	1.45 (t, 3H, $OCH_2C\underline{H}_3$); 2.20 (s, 3H, SCH_3); 2.52 (s, 3H, SCH_3); 2.63 (s, 3H, SCH_3); 4.30 (q, 2H, $OC\underline{H}_2CH_3$); 6.0 (s, 1$H_{olefinic}$); 7.20–7.40 (m, 4H_{arom} + 1$H_{olefinic}$)	308
9c	$4\text{-}Cl{-}C_6H_4$	55	70°	$C_{15}H_{17}ClO_2S_2$ (328.9)	1700, 1595	1.30 (t, 3H, $OCH_2C\underline{H}_3$); 2.05 (s, 3H, SCH_3); 2.48 (s, 3H, SCH_3); 4.15 (q, 2H, $OC\underline{H}_2CH_3$); 5.82 (s, 1$H_{olefinic}$); 7.28 (s, 1$H_{olefinic}$); 7.32 (s, 4H_{arom})	328
9d	$4\text{-}Br{-}C_6H_4$	62	65–66°	$C_{15}H_{17}BrO_2S_2$ (373.3)	1700, 1595	1.32 (t, 3H, $OCH_2C\underline{H}_3$); 2.12 (s, 3H, SCH_3); 2.50 (s, 3H, SCH_3); 4.18 (q, 2H, $OC\underline{H}_2CH_3$); 5.82 (s, 1$H_{olefinic}$); 7.20–7.60 (m, 4H_{arom} + 1$H_{olefinic}$)	373
9e	$4\text{-}H_3CO{-}C_6H_4$	60	oil	$C_{16}H_{20}O_3S_2$ (324.5)	1700, 1600[c]	1.22 (t, 3H, $OCH_2C\underline{H}_3$); 2.0 (s, 3H, SCH_3); 2.40 (s, 3H, SCH_3); 3.70 (s, 3H, OCH_3); 4.10 (q, 2H, $OC\underline{H}_2CH_3$); 5.75 (s, 1$H_{olefinic}$); 6.60–7.40 (m, 4H_{arom} + 1$H_{olefinic}$)	324
9f	2-naphthyl	50	76–77°	$C_{19}H_{20}O_2S_2$ (344.5)	1705, 1650, 1600	1.32 (t, 3H, $OCH_2C\underline{H}_3$); 2.03 (s, 3H, SCH_3); 2.50 (s, 3H, SCH_3); 4.20 (q, 2H, $OC\underline{H}_2CH_3$); 6.03 (s, 1$H_{olefinic}$); 7.35–7.95 (m, 7H_{arom} + 1$H_{olefinic}$)	344
9g	CH_3	45	oil	$C_{10}H_{16}O_2S_2$ (232.4)	1710, 1660, 1595[c]	1.20–1.50 (2t, 3H, $OCH_2C\underline{H}_3$); 2.20–2.50 (m, 9H, two $SC\underline{H}_3$ + $C\underline{H}_3$); 3.90–4.30 (2q, 2H, $OC\underline{H}_2CH_3$); 5.30, 5.48 (2s, 1$H_{olefinic}$); 5.80, 6.10 (2s, 1$H_{olefinic}$)[d]	232
9h	–	40	oil	$C_{13}H_{20}O_2S_2$ (272.4)	1710, 1660, 1615	1.2 (t, 3H, $OCH_2C\underline{H}_3$); 1.3–2.0 [m, 8H, $-(CH_2)_4-$]; 4.0 (q, 2H, $OC\underline{H}_2CH_3$); 7.2 (s, 1$H_{vinylic}$)	–

[a] Yield of pure, isolated product.

[b] Satisfactory microanalyses obtained: C ±0.30, H ±0.27.

[c] Neat.

[d] Isomeric mixture.

Table 2. Dimethyl-2-Aryl(alkyl)-propene-1,3-dicarboxylate **8** and Diesters **10** and **11** prepared

Product	R	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr	Molecular Formula[b]	I.R. (Nujol) ν[cm^{-1}]	^{1}H-N.M.R. (CCl_4/TMS) δ[ppm]	M.S. m/e(M^+)
8a	C_6H_5	65	semi-solid	$C_{13}H_{14}O_4$ (234.3)	1750, 1710, 1630	3.65 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 4.15 (s, 2H, CH_2); 6.20 (s, 1H$_{vinylic}$); 7.30–7.50 (m, 5H$_{arom}$)	234
8b	4-H_3C—C_6H_4	70	38–39°	$C_{14}H_{16}O_4$ (248.3)	1745, 1720, 1630	2.32 (s, 3H, CH_3); 3.60 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 4.10 (s, 3H, CH_2); 6.18 (s, 1H$_{vinylic}$); 7.0–7.40 (q, 4H$_{arom}$)	248
8c	4-Cl—C_6H_4	55	48–49°	$C_{13}H_{13}ClO_4$ (268.7)	1750, 1715, 1630	3.65 (s, 3H, OCH_3); 3.72 (s, 3H, OCH_3); 4.12 (s, 3H, CH_2); 6.20 (s, 1H$_{vinylic}$); 7.35 (s, 4H$_{arom}$)	268
8d	4-H_3CO—C_6H_4	63	semi-solid	$C_{14}H_{16}O_5$ (264.3)	1745, 1720, 1635	3.62 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 3.78 (s, 3H, OCH_3); 4.20 (s, 3H, CH_2); 6.23 (s, 1H$_{vinylic}$); 6.88, 7.42 (2d, 4H$_{arom}$)	264
8e	CH_3	50	60–70°/1.5	–[c]	1755–1720 (br), 1660, 1630[d]	1.95, 2.20 (2d, J = 2 Hz, 3H, CH_3); 3.10, 3.20 (2s, 2H, CH_2); 3.70–3.95 [m, 6H, $(OCH_3)_2$]; 6.95, 7.05 (m, 1H$_{vinylic}$)[e]	–
10	–	30	viscous oil	$C_{15}H_{16}O_4$ (260.3)	1740, 1690, 1650, 1620	2.1–2.80 (m, 4H$_{methylene}$ + 1H$_{methine}$); 3.30 (s, 3H, OCH_3); 3.55 (s, 3H, OCH_3); 5.80 (s, 1H$_{vinylic}$); 6.90–7.20 (m, 4H$_{arom}$)	–
11	–	20	semi-solid	$C_{15}H_{16}O_4$ (260.3)	1740, 1710, 1620	2.40–2.80 (m, 4H$_{methylene}$); 3.60 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 3.97 (s, 2H, CH_2); 7.0–7.40 (m, 4H$_{arom}$)	–

[a] Yield of pure, isolated product.

[b] Satisfactory microanalyses obtained: C ±0.33, H ±0.28.

[c] Ref.[7], b.p. 68–69°C/2 torr (*cis*), 65–66°C/0.7 torr (*trans*).

[d] Neat.

[e] Mixture of isomers.

bonyl as well as α-carbon atom[8]. Further synthetic transformations based on these novel dienes **9** and diesters **8** leading to a variety of nitrogen and oxygen heterocycles are in progress.

1,1-Bis[methylthio]-3-aryl(alkyl)-4-ethoxycarbonyl-1,3-butadienes 8a–h; General Procedure:

A suspension of activated zinc (0.08 mol), ethyl bromoacetate (0.04 mol) and a few crystals of iodine in dry ether (40 ml) is refluxed for 0.5 h with stirring. A solution of the respective α-oxoketene *S,S*-acetal **5** (0.02 mol) in benzene (40 ml) is added dropwise with refluxing during 1 h and the mixture is further refluxed for 3 h with stirring. The mixture is further refluxed for 3 h with stirring. The mixture (A) is then poured over ice-cooled 20% sulphuric acid (100 ml), the organic layer is separated, the aqueous layer extracted with benzene (2 × 50 ml), and the combined extracts washed with water (2 × 100 ml), dried with sodium sulphate and concentrated first on water bath, then under vacuum, to give the crude carbinols **7**. To a solution of **7** in benzene (30 ml), a few crystals of iodine are added and the solution is refluxed for 0.5–1 h (monitored by T.L.C.). The residue after removal of benzene is passed through silica gel column. Elution with ethyl acetate/hexane (1 : 19) yields the dienes **8a–h** (Table 1).

Alternatively, the dienes **8** could also be obtained in nearly similar yields by concentrating the mixture (A) to ~ 40 ml at 70–80 °C and further refluxing for 4–5 h after addition of a few crystals of iodine. The reaction mixture, after the work-up as described above, gives a residue, which are column chromatographed over silica gel. Elution with ethyl acetate/hexane (1 : 19) afforded the pure dienes **8** (Table 1).

Dimethyl 2-Aryl(alkyl)-propene-1,3-dicarboxylates 8a–e, 10 and 11; General Procedure:

The crude carbinol **7** obtained from the Reformatsky reaction (from 0.02 mol of **5**, 0.08 mol of zinc and 0.04 mol of ethyl bromoacetate as described above) is dissolved in dry methanol (20 ml) and a solution of boron trifluoride etherate (5 ml) in methanol (20 ml) added. The combined mixture is refluxed with stirring for 15–20 h (monitored by T.L.C.) and neutralized after cooling with saturated sodium hydrogen carbonate solution (~ 20 ml), extracted with dichloromethane (3 × 50 ml), washed with water (2 × 50 ml), dried with sodium sulphate, and concentrated to give crude diesters **8**, which are purified by passing through silica gel column. Elution with ethyl acetate/hexane (1 : 9) afforded pure diesters **8a–e** (Table 2).

In case of oxoketene *S,S*-acetal **5i**, elution with hexane gives first the diester **10** as a viscous liquid. Further elution with hexane/ethyl acetate (19 : 1) affords the diester **11** as a viscous liquid, which slowly solidifies on keeping (Table 2).

A.R. and A.D. thank C.S.I.R., New Delhi for post-doctoral Research Associateship and Junior Research Fellowship, respectively.

Received: Juli 9, 1984

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