Acyloins as Acyl-Anion Equivalents. The Synthesis of Ketones and Acyloxiranes

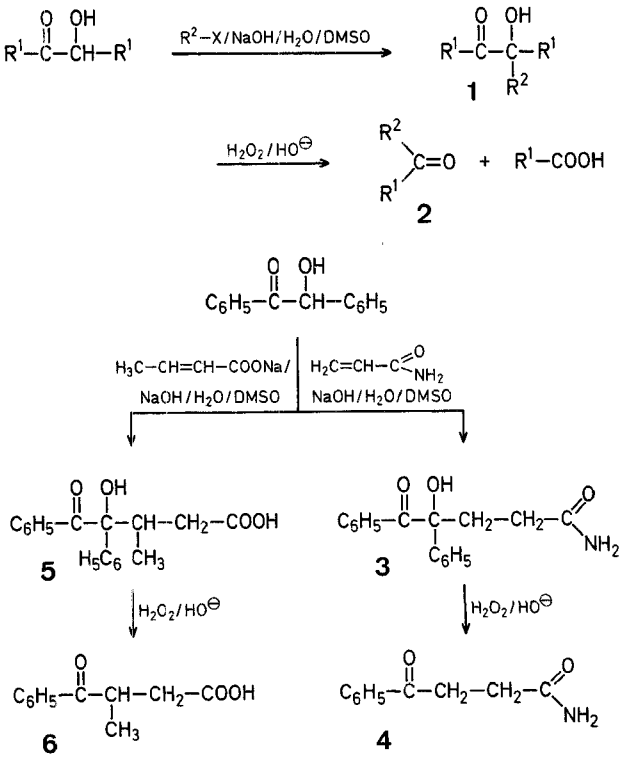
Tapio HASE

Department of Chemistry, Helsinki University of Technology, 02150 Espoo, Finland

In 1975, a report[1] appeared on the use of benzoin as a benzoyl anion equivalent, the method consisting of α-alkylation, borohydride reduction to the diol, and periodate cleavage. The range of applicability was indicated by reactions of benzoin with allylic and benzylic halides.

It is now pointed out that

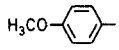
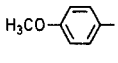
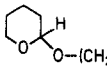
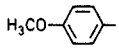
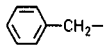
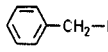
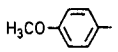
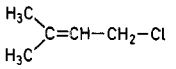
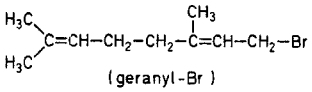
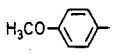
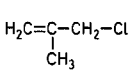
- acyloins in general may be used[2];
- primary and secondary alkyl iodides are effective nucleophiles[3], in addition to allylic and benzylic bromides or chlorides;
- certain Michael acceptors also react with acyloin anions;
- the overall reaction can be streamlined to involve only two steps if use is made of the direct alkaline peroxide oxidation of benzoins[4] **(1)**.



1 **2** **5** **3** **6** **4**

0039-7881/80/0132-0036 $ 03.00

Table 1. New α-Alkylacyloins

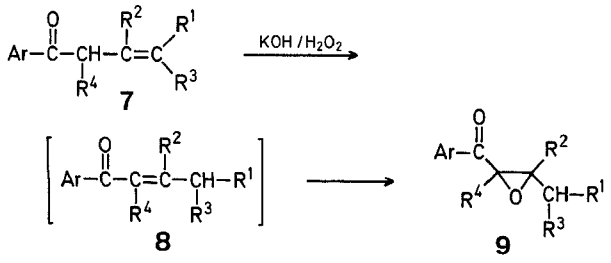
Product	R^1	R^2-X	Yield [%]	m.p. or b.p./torr	Molecular formula[a]	^{1}H-N.M.R.[b] ($CDCl_3$) δ [ppm]
1a		$H_2C=CH-(CH_2)_3-J$	76	33–34°C	$C_{19}H_{20}O_2$ (280.3)	1.30 (m, 2H); 1.95 (t, 2H); 2.22 (t, 2H); 4.93 (m, 2H); 5.56 (m, 1H)
1b		n-C_5H_{11}-J	79	89–91°C	$C_{21}H_{26}O_4$ (342.4)	2.11 (m, 2H); 7.06 (AB-q, 4H); 7.33 (AB-q, 4H)
1c			50	–[c]	$C_{24}H_{30}O_6$ (414.5)	3.59 (m, 2H); 4.52 (m, 1H); 2 AB-q's as in **1b**
1d			88	119°C	$C_{23}H_{22}O_4$ (362.4)	3.64 (s, 2H); 2 AB-q's as in **1b**
1e		$C_2H_5OOC-(CH_2)_3-J$	61	115–116°C	$C_{20}H_{22}O_4$ (326.4)	1.06 (t, 3H); 1.58 (m, 2H); 2.09 (m, 4H); 4.00 (q, 2H)
1f	C_2H_5		64	117–120°C/1	$C_{13}H_{18}O_2$	1.81 (t, 3H); 1.91 (t, 3H); 1.71, 1,74, 2.40, 2.42 (each q, 1H); 2.95 (s, 2H)
1g	C_2H_5	$H_2C=CH-CH_2-Br$	62	58–62°C/1.5	$C_9H_{16}O_2$ (156.2)	2.80 (m, 2H); 4.99 (m, 2H); 5.60 (m, 1H)
1h			80	55–58°C	$C_{21}H_{24}O_4$ (340.4)	1.42, 1.58, 3.62, 3.64 (each s, 3H); 3.00 (br d, 2H); 5.08 (br t, 1H)
1i		 (geranyl-Br)	66	oil	$C_{24}H_{28}O_2$ (348.5)	3.01 (m, 2H); 5.08 (m, 2H)
1j			67	145°C	$C_{20}H_{20}O_2$ (292.4)	3.80 (m, 1H); 5.60 (m, 2H)
1k			81	46°C	$C_{20}H_{22}O_4$ (326.4)	1.58 (br s, 3H); 3.04 (br s, 2H); 4.81 (m, 2H)
3			55	148°C	$C_{17}H_{15}NO_2$ (265.3)	2.29 (m, 4H)
5			61	–[c]	$C_{18}H_{18}O_4$ (298.3)	0.70 (d, 3H); 1.95 (m, 1H); 2.52 (m, 2H)

[a] The microanalyses were in good agreement with the calculated values: C, ± 0.23; H, ± 0.20.
[b] Diagnostic data only.
[c] Mixture of diastereomers.

The improved scope of the method is illustrated by the examples in Tables 1 and 2.

Alkylation products from aliphatic acyloins react very slowly with alkaline hydrogen peroxide. Furthermore, these compounds, like α-alkylbenzoins, are not cleaved by periodate or lead(IV) acetate. It is therefore necessary to resort to the three-step procedure[1], i.e., to include a borohydride reduction step, in order to obtain aliphatic ketones by glycol cleavage.

The oxidation products of α-allylated acyloins are 2-alkenyl ketones (**7**). It was anticipated that these compounds, in the presence of base and excess peroxide, would be in equilibrium with the isomeric 1-alkenyl ketones (**8**) which might be trapped by epoxidation. Thus, a general route to Darzens-type acyloxiranes (**9**) would be available.



7 8 9

Acyloxiranes (**9**) are useful starting materials for further syntheses, e.g., of alkynals[6,7], furan derivatives[8], and α-alkyl-β-ketols[9].

The results obtained with some simple allyl halides (Table 3) show that certain α-allylbenzoins may in fact be converted into aroyloxiranes **9** in one step. Again, the cleavage of α-allylated aliphatic acyloins with alkaline peroxide is impractical. Therefore, aroyloxiranes only are directly available. Also, the β,γ→α,β-isomeration is apparently unfavoured in cases where the α,β-double bond is less substituted than that in the β,γ-position. Thus, the epoxide substitution pattern **9**, $R^4=H$, $R^1=$alkyl, $R^2=$alkyl, is not accessible, the reaction products being β,γ-unsaturated ketones (Table 2, products **2j** and **2k**).

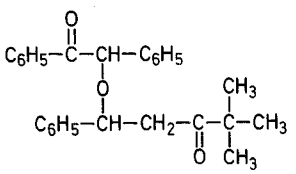
Acyloin anions have been reported[5] to add, via C C bond formation and in modest yields, to certain Michael substrates. We found that acrylamide and sodium crotonate do react to yield the expected product (see Table 1) whereas

Table 2. Ketones from Acyloins

Product	R^1	R^2	Yield [%]	m.p. or b.p./torr found	m.p. or b.p./torr reported	Molecular formula[a]	I.R. ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
2a		$H_2C{=}CH{-}(CH_2)_3{-}$	91	91–92°C/21	88.5°C/16 [19]		–[b]	–[b]
2b	H_3CO–	n-C_5H_{11}	90	72–74°C/1.6	77–78°C/3 [14]		–[c]	–[c]
2c	H_3CO–		88	36–37°C	38°C [10]		1680 (KBr)	0.95 (m, 3H); 2.91 (t, 2H); 3.90 (s, 3H)
2d	H_3CO–	$-CH_2-$	61	45°C		$C_{16}H_{22}O_4$ (278.3)	1680 (KBr)	2.02 (qn, 2H); 3.04 (t, 2H); 4.58 (m, 1H)
2e		$C_2H_5OOC{-}(CH_2)_3{-}$	89	74–75°C	75°C [10]		1675 (KBr)	3.84 (s, 3H); 4.22 (s, 2H); 7.27 (s, 5H); 7.45 (AB-q, 4H)
2f	C_2H_5		51	161–163°C/1.9	178–180°C/10 [15]		1630, 1680 (KBr)	2.02 (m, 2H); 2.42 (m, 2H); 3.01 (t, 2H); 7.46 (m, 3H); 7.98 (m, 2H)
2g	C_2H_5	$H_2C{=}CH{-}CH_2{-}$	91	89–91°C/2.0	102°C/15 [16]		–[b]	–[b]
2h	H_3CO–		77[d]	88–90°C/1.8	227°C/760 [17]		1710 (film)	1.10 (t, 3H); 2.36 (q, 2H); 3.78 (s, 2H); 7.29 (s, 5H)
2i		geranyl	65[d]	125–126°C/760	126–128°C/760 [18]		1710 (film)	1.11 (t, 3H); 2.30 (q, 2H); 3.25 (m, 2H); 5.01 (m, 2H); 5.49 (m, 1H)
2l		CH_3	92	73–76°C/1.3		$C_{13}H_{16}O_2$ (204.3)	1685 (film)	1.71 (br s, 6H); 3.55 (br d, 2H); 5.47 (br t, 1H); 6.88 (d, 2H); 7.91 (d, 2H)
2m		i-C_3H_7	90	117–120°C/1.4		$C_{17}H_{22}O$ (242.3)	1690 (film)	1.75 (m, 9H); 2.03 (m, 4H); 3.74 (d, 2H); 5.06 (m, 1H); 5.58 (t, 1H)
4			89	125°C	125°C [11]		1630, 1680 (KBr)	2.71 (t, 2H); 3.44 (t, 2H); 5.72 (br s, 2H); 7.51 (m, 3H) 7.99 (m, 2H)
6			92	59°C	59–60°C [12]		1685, 1715 (KBr)	1.18 (d, 3H); 2.60 (q, 1H); 2.78 (q, 1H); 3.91 (sx, 1H); 7.32 (m, 3H); 8.00 (m, 2H)

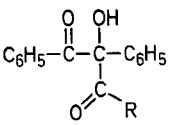
[a] The microanalyses were in good agreement with the calculated values: C, ± 0.16; H, ± 0.19.
[b] Identified by direct comparison with authentic material.
[c] Spectrum in accord with published spectrum[14].
[d] Two-step reaction: 1. $NaBH_4$, 2. JO_4^-.

α,β-unsaturated ketones (2-cyclohexenone, styryl t-butyl ketone) give complex mixtures where products from O-alkylation (e.g., **10**) predominate. The Michael products (**3, 5**) are readily oxidized to the 1,4-dicarbonyl compounds (**4, 6**).



10

Several other electrophiles also quench the reaction of acyloin α-anions. Thus, the α-acylbenzoins **11** were obtained in ~90% yield (under anhydrous conditions; anion generation with lithium diisopropylamide in tetrahydrofuran) from acyl chlorides but it was not possible to control their oxidation so as to give α-diketones.

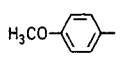


11

For the α-alkylation of acyloins and alkaline peroxide cleavage of the products, the original directions[3,4] were followed. A convenient means of monitoring the alkylation reaction is provided by the fading of the intense green or blue colour of the initially generated α-anion. The oxidation procedure to give compounds **2, 4, 6,** or **9** is given below for **9b** and is the same in all other cases. The reaction is best monitored by T.L.C.

α-(3-Cyclohexenyl)-benzoin (1j):
A solution of benzoin (1.06 g, 5 mmol) in dimethyl sulfoxide (100 ml) is treated with a solution of sodium hydroxide (0.21 g, 5.25 mmol) in water (10 ml) at ambient temperature with stirring, fol-

Table 3. Arolyloxiranes from α-Allylbenzoins

Product	Ar	R^1	R^2	R^3	R^4	Yield [%]	m.p. or b.p./torr	Molecular formula[a] or m.p. reported	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
9a		H	H	H	H	79[b, c]	62°C	62.5–63°C [13]	1.58 (d, 3H); 3.18 (d of q, 1H); 4.00 (d, J = 1.5 Hz, 1H)
9b		H	H	$-(CH_2)_4-$		61	125–128°C/ 2.0	$C_{13}H_{14}O_2$ (202.2)	3.21 (br s, 1H)
9c		H	H		H	64[c, d]	57–58°C	$C_{16}H_{14}O_2$ (238.3)	3.07 (d, 2H); 3.44 (d of t, 1H); 4.00 (d, J = 1.5 Hz, 1H)
9d		H	CH_3	H	H	82	100–103°C/ 1.2	$C_{12}H_{14}O_3$ (206.2)	1.01, 1.45, 3.70 (each s. 3H); 3.91 (s, 1H)

[a] The microanalyses were in good agreement with the calculated values: C, ± 0.15; H, ± 0.09.
[b] From α-allylbenzoin[3].
[c] *trans* only (by T.L.C. and N.M.R.).
[d] From α-cinnamylbenzoin[3].

lowed by the addition of 3-bromocyclohexene (neat; 0.81 g, 5.03 mmol). After the green colour has faded to yellow (10 min), the solution is poured into 10% aqueous sodium chloride (250 ml) and the mixture extracted twice with ether. The combined extracts are washed twice with water, dried, filtered, and evaporated. The product is recrystallized from ethanol; yield: 0.98 g (67%); m.p. 145°C.

$C_{20}H_{20}O_2$	calc.	C 82.15	H 6.89
(292.4)	found	82.09	6.79

I.R. (KBr): ν = 3400, 1690 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 1.1–2.1 (m, 6H); 3.00 (s, 1H, exchangeable with D_2O); 3.80 (m, 1H); 5.60 (m, 2H); 7.35 (m, 3H); 7.91 ppm (m, 2H).

1-Benzoylcyclohexene Epoxide (9b):

A solution of α-(3-cyclohexenyl)-benzoin (**1j**; 0.80 g, 2.74 mmol) in methanol (50 ml) is treated with 30% aqueous hydrogen peroxide (0.5 ml, 4.4 mmol) and a solution of potassium hydroxide (0.20 g, 3.6 mmol) in water (5 ml) with stirring at ambient temperature. After 8 h, the solution is concentrated under vacuum, diluted with water, and extracted twice with ether. The combined extracts are washed twice with water, dried, filtered, and evaporated. The product is isolated as an oil by preparative T.L.C. on silica gel using chloroform as eluent; yield: 0.34 g (61%).

$C_{13}H_{14}O_2$	calc.	C 77.20	H 6.98
(202.2)	found	77.11	7.07

I.R. (film): ν = 1670 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): δ = 1.1–2.15 (m, 8H); 3.21 (br s, 1H); 7.43 (m, 3H); 7.98 ppm (m, 2H).

Received: March 21, 1979
(Revised form: June 11, 1979)

[1] Y. Ueno, M. Okawara, *Synthesis* **1975**, 268.
[2] J. H. van de Sande, K. R. Kopecky, *Can. J. Chem.* **47**, 163 (1969).
[3] For a thorough study of the α-alkylation of benzoins, see H. G. Heine, *Justus Liebigs Ann. Chem.* **735**, 56 (1970).
[4] Y. Ogata, Y. Sawaki, M. Shiroyama, *J. Org. Chem.* **42**, 4061 (1977).
[5] J. Cologne, P. Brison, *Bull. Soc. Chim. Fr.* **1962**, 96, 175.
[6] G. A. MacAlpine, J. Warkentin, *Can. J. Chem.* **56**, 308 (1978).
[7] O. Felix et al., *Helv. Chim. Acta* **55**, 1276 (1972).
[8] S. I. Pennanen, *Tetrahedron Lett.* **1977**, 2631.
[9] E. J. Corey, L. S. Melvin, M. F. Haslanger, *Tetrahedron Lett.* **1975**, 3117.
[10] K. Nakazawa, S. Matsuura, K. Kusuda, *Yakugaku Zasshi* **74**, 495 (1954); *C. A.* **49**, 8182 (1955).
[11] A. N. Kost, T. A. Shchegoleva, L. G. Yudin, *Zh. Obshch. Khim.* **25**, 2464 (1955); *C. A.* **50**, 9410 (1956).
[12] L. Higginbotham, A. Lapworth, C. Simpson, *J. Chem. Soc.* **1924**, 2339.
[13] I. G. Tishchenko, L. S. Stanishevskii, *Vestsi Akad. Navuk B. SSR, Ser. Khim. Navuk* **1967**, 132; *C. A.* **68**, 59220 (1968).
[14] A. Padwa, D. Eastman, *J. Am. Chem. Soc.* **91**, 462 (1969).
[15] M. Y. Lure, I. S. Trubnikov, N. P. Shusherina, R. Y. Levina, *Zh. Obshch. Khim.* **28**, 1351 (1958); *C. A.* **52**, 20138 (1958).
[16] B. E. Hudson, C. R. Hauser, *J. Am. Chem. Soc.* **63**, 3163 (1941).
[17] E. B. Ludlam, *J. Chem. Soc.* **81**, 1189 (1902).
[18] I. N. Nazarov, I. I. Zaretskaya, *Zh. Obshch. Khim.* **27**, 624 (1957); *C. A.* **51**, 16317 (1957).
[19] C. R. Noller, R. Adams, *J. Am. Chem. Soc.* **46**, 1889 (1924).

0039-7881/80/0132-0039 $ 03.00