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A SIMPLE SYNTHESIS OF 1-(1,3-BUTADIENYL) CARBONATES AND CARBAMATES

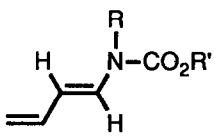
Paul F. De Cusati and R. A. Olofson*

Department of Chemistry, The Pennsylvania State University

University Park, PA 16802, USA

Summary: Crotonaldehyde and its congeners are conveniently and often stereospecifically converted to *trans*-1-(1,3-butadienyl) carbonates and carbamates by treatment first with potassium *tert*-butoxide and then with a chloroformate or carbamyl chloride.

In 1975, Oppolzer[1] reported the synthesis of *trans-N*-(1,3-butadienyl) carbamates **1** by treatment of imines from crotonaldehyde with either $MeS(O)CH_2^-Na^+$ in DMSO or $(Me_3Si)_2N^-Na^+$ in toluene at *ca.* –50 °C followed by acylation with chloroformates. Both Oppolzer[2] and Overman[3] have shown the utility of **1** as a Diels-Alder diene in the regio- and stereospecific total syntheses of several alkaloids and Oppolzer[1] has patented **1** as a monomer in the production of fibers and films. Despite the value of **1** in synthetic and polymer chemistry, the analogous *O*-butadienyl carbamates **2** and carbonates **3** of α,β-unsaturated aldehydes were unknown prior to this work.[4] This also is surprising since butadienyl acetate **4** is a useful synthon[5] and an important commercial monomer. The acetate **4** is as reactive as butadiene and undergoes predominantly 1,4-polymerization to give high-strength, cross-linkable, oil-resistant rubbers which bind tightly to glass, paper, and wood.[6]



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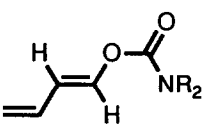

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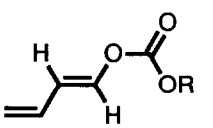

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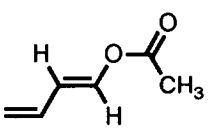

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The absence of **2** and **3** from the literature derives in part because the required analogues of the acetic acid or acetic anhydride used in the main routes to **4**[7] are either unstable or react differently. Also, most chemistry of crotonaldehyde is dominated by its great potency both as an aldol and Michael acceptor.[8] (However, the enolate of the more substituted 2-methyl-2-pentenal has been generated with KH in THF and alkylated in the α-position.[9])

With this background, we are pleased to report that addition of crotonaldehyde to commercial KOtBu in THF at –78 °C affords the enolate which when treated with chloroformates is converted exclusively to the *E*-butadienyl carbonates **3**. Some examples are given in Rxns. **A-D** of the Table. The yield is not sensitive to chloroformate addition time but enolate concentration is important; *e. g.*,

reduction of enolate concentration in **A** from 0.53 to 0.36 *M* lowered the yield of **5E** from 83% to 71%. At enolate concentrations above 0.5 *M*, the mixture after chloroformate addition is difficult to stir. If the enolate is generated at higher temperature, some *Z*-isomer[10] is found: *e.g.*, with **6** at –50 °C, the *E/Z* ratio was 7. However, the enolate once formed can be warmed to –20 °C without loss of stereospecificity. At this temperature, however, the product in **A** (78% corr. yield) was contaminated by 4% $EtOCO_2tBu$. Acylation at 0 °C afforded **5** with *E/Z* = 19 (57% yield).

Even in retrospect, it is surprising that much **3** was obtained. For the reaction to work, the enolate must be formed very rapidly and crotonaldehyde (**18E**) must be a much stronger acid than HOtBu.[11] Otherwise aldol and Michael condensations would prevail. Although a potassium enolate should react with $ClCO_2R$ at oxygen, another reaction-defeating complication remains. The enolate must compete with excess KOtBu and with the HOtBu by-product for $ClCO_2R$. Reaction of $ClCO_2R$ with HOtBu gives HCl which would destroy the enolate. Finally any t-butyl carbonate formed in this competition should (and does) codistill with **3**, a product of similar polarity and molecular weight.

With tiglic aldehyde (MeCH=CMeCHO, **19E**) and 2-chlorocrotonaldehyde (**20Z**, same stereo., priority rule change), carbonate formation remained stereospecific in the same sense (Me *trans* to CHO) and the isoprenyl **9E**[10] and chloroprenyl carbonates **10Z,11Z** were obtained. However with senecioaldehyde (**21**), stereochemical discrimination was lost (**13E/Z** = 1.1 in Rxn. **l**) Polymerization during distillation caused the low yield of **10Z** (avoided by chromatographic isolation for **11Z**).

The reaction stereochemistry can be explained. Both **18E** and **19E** exist >90% in planar s-*trans* W-conformations at 25 °C.[12] For **18E**, the calcd. ΔE for the s-*trans* to s-*cis* rotation is 1.8 kcal/mol and $\Delta H^{\dagger}$ is 7.4 kcal/mol (3.2 and 6.8 for **19**).[12] Thus, deprotonation of **18E** or **19E** at low temperature should provide the stereochemically more rigid enolates in the same W-conformation. Acylation of such enolates would yield solely *E*-carbonates (*Z* for **20Z**). In **21**, calculations indicate that the s-*trans* conformation is distorted from planarity, ΔE is only 1.4 kcal/mol, and $\Delta H^{\dagger}$ is 2 kcal/mol less *vs* **18E**.[12] Thus, **21** should react less stereoselectively as is found. By this reasoning, the results would be reversed with mesityl oxide (**22**)[13]. There the s-*cis* isomer is 1.7 kcal/mol more stable than s-*trans* and $\Delta H^{\dagger}$ is *ca.* 4 kcal/mol[12] so the major product should have the *Z*-stereochemistry. Indeed, in **L** and **M**, only **16Z** and **17Z** are found. Any special stability of a U-enolate[14] from alternative deprotonation of the *cis*-methyl in **21** and **22** would increase the amount of *Z*-products in accord with the data.

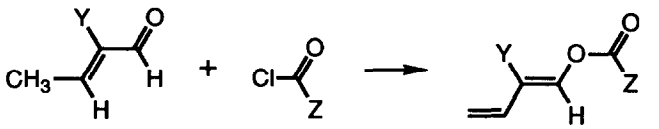
The new methodology also has been extended to the preparation of the previously unknown *O*-butadienyl carbamates **2**. When $ClC(=O)NEt_2$ was added to crotonaldehyde enolate (**18E** + KOtBu in THF) at -78 °C, carbamate **12E** (*no Z*) was obtained in 75% yield. With **21** as expected, this stereochemical discrimination was lost (E/Z = 1.1 for **14** and **15**) In the carbamate forming reactions, the products were contaminated by 10-12% of *O*-*t*-butyl *N,N*-dialkylcarbamate (inert diluent in later chemistry). Thus, carbamyl chlorides are less selective than chloroformates. They also are much less reactive (process occurs *only* after removal of cold bath). To find one reagent both less reactive and less selective than another is rare. Here, the dichotomy is resolved by including the precedented ion pair $[R_2N^+{=}C{=}O\ Cl^-]$ as a competive acylating agent.

A study of some chemistry of these new products is presented in the following paper.

Acknowledgment. We are grateful to Drs. J.-P. Senet and G. P. Wooden for useful discussions and contributions. We also thank SNPE of France for the funds used to perform this research.

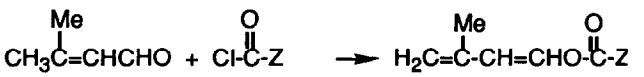
TABLE. ALKYL DIENYL CARBONATES AND CARBAMATES FROM REACTION OF:

I. Crotonaldehydes with KOtBu and Choroformates or Carbamoyl Chlorides.



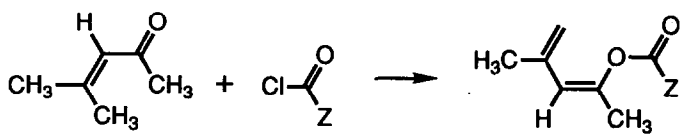
Rxn.	Y =	Z =	Product	Yield	Bp at pressure	IR(C=O)[a]
A	H	-O-Ethyl	**5E**	83%	42 °C at 3 mm	1760 cm^{-1}
B	H	-O-Neopentyl	**6E**	81%	45-47 °C at 0.4 mm	1765
C	H	-O-Allyl	**7E**	58%	55 °C at 0.8 mm	1750
D	H	-O-CH_2CCl_3	**8E**	68%	99 °C at 0.7 mm	1770
E	Me	-O-Ethyl	**9E**	78%[b]	48-51 °C at 0.6 mm	1760
F	Cl	-O-Ethyl	**10Z**	32%	58-61 °C at 1.5 mm	1780
G	Cl	-O-Neopentyl	**11Z**	55%	Flash chrom (hexane)	1765
H	H	-N-$(Ethyl)_2$	**12E**	75%[c]	74-84 °C at 1 mm	1715

II. Senecioaldehyde with KOtBu and Chloroformates or Carbamoyl Chlorides.



Rxn.	Z =	Product	E:Z ratio	Yield	Bp at pressure	IR(C=O)[a]
I	-O-Ethyl	**13E,Z**	1.1/1	74%	46-57 °C at 4 mm	1760 cm^{-1}
J	-N-$(Methyl)_2$	**14E,Z**	1.1/1	62%[d]	62-70 °C at 0.8 mm	1720
K	-N-$(Ethyl)_2$	**15E,Z**	1.1/1	62%[e]	63-73 °C at 0.4 mm	1720

III. Mesityl Oxide with KOtBu and Chloroformates.



Rxn.	Z =	Product	Yield	Bp at pressure	IR(C=O)[a]
L	-O-Ethyl	**16Z**	63%	Flash chrom (hex/CH_2Cl_2)	1760 cm^{-1}
M	-O-CH(Cl)CH_3	**17Z**	87%	70 °C at 2 mm	1770

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[a]Spectra taken in CCl_4. [b]Yield corr. for presence of 3% $(EtO)_2C=O$. [c]Yield corr. for presence of 10% Et_2NCO_2tBu. [d]Yield corr. for presence of 12% Me_2NCO_2tBu. [e]Yield corr. for presence of 12% Et_2NCO_2tBu.

***E*-1-(1,3-Butadienyl) Ethyl Carbonate (5E).** Crotonaldehyde (dried, distilled) (8.70 g, 0.12 mol) in dried THF (20 mL) was dripped (40 min) into a stirred, -78 °C solution of KOtBu (Aldrich) (15.7 g, 0.14 mol) in 200 mL THF under N_2. Once the yellow enolate was formed, $ClCO_2Et$ (16.2 g, 0.15 mol) in THF (15 ml) was dripped into the mixture, causing it to become red and viscous. Removal of the cold bath after adding half the $ClCO_2Et$ facilitated stirring. When the mixture reached room temperature, it was quenched with ice and extracted with ether (3 x 50 mL). The extracts were washed with brine (50 mL), dried (Na_2SO_4), and distilled to obtain pure **5E** as a clear liquid; bp 42 °C at 3 mm, 14.6 g (83% yield); IR (CCl_4) 1760 (s), 1670 (m), 1250 (s) cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 7.20 (d, 1 H, J = 12 Hz), 6.6-5.8 (m, 2 H), 5.4-4.9 (m, 2 H), 4.25 (q, 2 H, J = 7 Hz), 1.25 (3 H, J = 7 Hz; ^{13}C NMR ($CDCl_3$) 152.0 (s, C=O), 140.0 (d, C^3), 131.0 (d, C^1), 116.4 (t, C^4), 115.3 (d, C^2), 64.1 (t, CH_2) 13.5 (q, CH_3) ppm; high res. MS 142.0635 (M^+ at 142.0630, 30%), 70 (100%), 60 (63%).

References and Notes

(1) Oppolzer, W.; Frostl, W. *Helv. Chim. Acta* **1975**, *58*, 587; Oppolzer, W. *U. S. Patent 4,065,946* **1977** [*Chem. Abs.* **1977**, *88*,190064m]. A Curtius rearrangement route also has been used to make **1** by: Overman, L. E.; Taylor, G. F.; Petty, C. B.; Jessup, P. J. *J. Org. Chem.* **1978**, *43*, 2164.

(2) Oppolzer, W.; Frostl, W.; *Helv. Chim. Acta* **1975**, *58*, 590; Oppolzer, W.; Frostl, W. Weber, H. *Ibid.* 593.

(3) Overman, L. E.; Taylor, G. F.; Houk, K. N.; Domelsmith, L. N. *J. Am. Chem. Soc.* **1978**, *100*, 3182; Overman, L. E.; Jessup, P. J. *Ibid.* 5179.

(4) The analogous α,β-unsaturated ketone derivatives, especially cyclohexenones, are known.

(5) See syntheses of β-lycorane (Hill, R. K.; Joule, J. A.; Loeffler, L. J. *J. Am. Chem. Soc.* **1962**, *84*, 4951), oryzoxymycin (Shin, C.; Yamaura, M.; Inui, E.; Ishida, Y.; Yoshimura, J. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2618), suragatoxin (Okada, K.; Sakuma, H.; Kondo, M.; Inoue, S. *Chem. Lett.* **1979**, 213), and thienamycin (Johnston, D. B. R.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313).

(6) Gressier, J.-C.; Pinazzi, C. P.; Levesque, G. *Makromol. Chem.* **1975**, *176*, 341; Levesque, G.; Gressier, J.-C. *C. R. Acad. Sci., Ser. C* **1973**, *277*, 555; Japan Synthetic Rubber Co. *Jpn. Kokai JP 82 209,909* **1982** [*Chem. Abs.* **1983**, *99*, 23841h]; copolymers also adhere to metals.

(7) Yoshida, Y.; Shinohara, H.; Hanari, I *Jpn. Kokai 78 90212* **1978** [*Chem. Abs.* **1978**, *89*, 196985e]; Wichterle, O.; Hudlicky, M. *Coll. Czech. Chem. Comm.* **1947**, *12*, 564; Hagemeyer, H. J.; Hull, D. C. *Ind. Eng. Chem.* **1949**, *41*, 2920.

(8) Even *E,Z*-(1-TMS-*O*)-butadiene is obtained in only 50% yield from crotonaldehyde, Et_3N, and TMS-Cl: Fleming, I.; Goldhill, J.; Paterson, I. *Tetrahedron Lett.* **1979**, 3205, 3209.

(9) Groenewegen, P.; Kallenberg, H.; van der Gen, A. *Tetrahedron Lett.* **1978**, 491.

(10) Easily differentiated by J_{vic} in the ^1H NMR spectra: J_{trans} = 11-13 Hz and J_{cis} = 6-7 Hz. Also, C^1H is normally at 7.1-7.2 δ in the *trans* -isomer and at 6.7-6.9 δ in the *cis*-product. This latter result was used to assign stereochemistry when C^1 or C^2 was substituted. Such assignments were confirmed by NOE experiments in **9** and **16**. Several comparison isomer pairs were available.

(11) For data suggesting that even simple aldehydes may be more acidic than previously thought see: Olofson, R. A.; Dang. V. A.; Morrison, D. S.; De Cusati, P. F. *J. Org. Chem.* **1990**, *55*, in press.

(12) Liljefors, T.; Allinger, N. L. J. Am. Chem. Soc. 1976, 98, 2745; for exp. $\Delta H^{\dagger}$'s see refs. therein.

(13) Reaction with KOtBu and then $ClCO_2R$ failed with other α,β unsaturated ketones; e.g., cyclohexenone.

(14) Due to chelation or orbital symmetries: Hoffman, R.; Olofson, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 943.

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