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Communications

Simple One-Step Preparations of Vinylic Carbonates from Aldehydes

R. A. Olofson,* Vu Anh Dang, David S. Morrison, and Paul F. De Cusati

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

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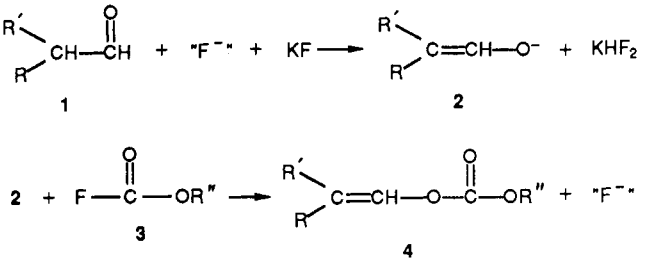
Summary: Enolizable aldehydes are easily converted to 1-alkenyl carbonates by treatment with chloro- or fluoroformates and KF plus an 18-crown-6 catalyst or by reaction with fluoroformates and KF in DMSO with no added catalyst.

Sir: Because ketones are readily deprotonated to their enolates under many preparatively useful conditions, a literature search of the selective chemistry of ketone enolates produces a magnificent wealth of information. The converse is true for aldehydes. In efforts to deprotonate aldehydes, the enolate generated promptly undergoes an aldol or Michael condensation with more aldehyde. The powerful acceptor properties of aldehydes dominate their chemistry. Even trialkylsilyl enol ethers often fail as useful aldehyde enolate precursors. Acetaldehyde enolate normally is made by the RLi-induced ring scission of THF, an elegant and complex but not economical reaction.[1] In another consequence of this dichotomy in reactivity, extensive lists of ketone pK_a's exist, but similar data for aldehydes (expected to be more acidic) are lacking. In this paper, we introduce a simple reaction that provides new insight into the solution C–H acidities of aldehydes and that also affords useful products.

When aldehydes **1** are treated with KF in the presence of an 18-crown-6 catalyst, the enolates **2** are generated and can be trapped efficiently as formed with fluoroformates **3** to give vinylic carbonates **4**. The HF created in the deprotonation step is scavenged by another KF to give KHF_2. Since chloroformates are rapidly converted to fluoroformates by halide exchange[2] under the experimental conditions, commercial chloroformates may be substituted for **3** when desired. However, in the reaction of **3**, only 1 equiv of KF is needed while the chloroformate route requires 2 equiv ($2KF \rightarrow KCl + KHF_2$).



Some results are presented in Table I. In MeCN, the process is best with 1.5–2 equiv of anhydrous KF (for **3**) and 7–10 mol % 18-C-6 (vs **3**). Reactions of acetaldehyde were performed with excess aldehyde in an apparatus topped by a dry ice condenser to prevent loss of the reagent (also used with low boiling point **3**). Reactions were stopped when no **3** remained (IR). Workup consisted of dilution with CH_2Cl_2, extraction with water, and distillation (gave better yields for less volatile or water soluble products; e.g., **4a,c,f**).

The carbonates **4** (with R = R′ = H) have been accessible hitherto only via the costly vinyl chloroformate.[3] However, they have been polymerized to materials which combine attractive properties of polycarbonate and polyvinyl systems.[4] In Table I, the good yields of **4d** and **4e** are notable because they (and $H_2C{=}CHOCO_2CD_3$) have been proposed as useful monomers in fiber optics appli-

(1) Bates, R. B.; Kroposki, L. M.; Potter, D. E. *J. Org. Chem.* **1972**, *37*, 560.

(2) Cuomo, J.; Olofson, R. A. *J. Org. Chem.* **1979**, *44*, 1016.

(3) Lee, L. H. *J. Org. Chem.* **1965**, *30*, 3943. Olofson, R. A.; Bauman, B. A.; Wancowicz, D. J. *Ibid.* **1978**, *43*, 752. Lecolier, S.; Malfroot, T.; Piteau, M.; Senet, J.-P. Eur. Pat. 2973, 1979; *Chem. Abstr.* **1980**, *92*, 6698e and references therein.

(4) Boivin, S.; Chettouf, A.; Hemery, P.; Boileau, S. *Polym. Bull.* **1983**, *9*, 114. Meunier, G.; Hemery, P.; Boileau, S.; Senet, J.-P.; Cheradame, H. *Polymer* **1982**, *23*, 849. Meunier, G.; Boivin, S.; Hemery, P.; Boileau, S.; Senet, J.-P. *Ibid.* **1982**, *23*, 861. Boileau, S.; Kassir, F.; Boivin, S.; Cheradame, H.; Wooden, G. P.; Olofson, R. A. *Ibid.* **1985**, *26*, 443.

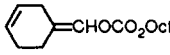
0022-3263/90/1955-0001$02.50/0

Table I. 18-Crown-6-Catalyzed Syntheses of 1-Alkenyl Carbonates from RCHO, XCO_2R', and KF

no.	1-alkenyl carbonate product	X =	RCHO/ XCO_2R'/KF	18-C-6,[a] mol %	solvent	temp, °C/ time, h	yield,[b] %	bp (press.)[c]
4a	$Me_2C{=}CHOCO_2CH_2CMe_3$	Cl	0.9/1/5	19[d]	MeCN	70/1 d[e]	85 (8)	75–78 (3)
4b$_1$	$H_2C{=}CHOCO_2Et$	F	1.5/1/2	7	$PhNO_2$	55/7	83	43–45 (45)
4b$_2$	$H_2C{=}CHOCO_2Et$	Cl	1.5/1/2	7	MeCN	55/11	76 (4)	43–45 (45)
4b$_3$	$H_2C{=}CHOCO_2Et$	Cl	5/1/4	18[d]	PhCN	57/19	56 (7)[f]	
4b$_4$	$H_2C{=}CHOCO_2Et$	F	2/1/2	12	none	60/1d	35 (35)	–
4c	$H_2C{=}CHOCO_2CMe_3$	F	1.7/1/4	12	MeCN	55/15	89	56–58 (30)
4d	$H_2C{=}CHOCO_2Me$	F	2/1/3	10	MeCN	35/36	62 (11)	38–41 (42)
4e	$H_2C{=}CHOCO_2CH_2CF_3$	F	1.2/1/2	7	MeCN	55/16	76 (12)	40–42 (22)
4f$_1$	$H_2C{=}CHOCO_2CH_2(C_6H_5)$	F	2/1/2	10	MeCN	70/3.5	89	112–115 (4)
4g	$H_2C{=}CHOCO_2CH_2CH{=}CH_2$	Cl	1.5/1/5	13	MeCN	70/4	74 (10)	32–34 (2.5)

[a] Versus haloformate. [b] Corrected yield of distilled product (est. yield of 1-fluoroalkyl carbonate side product; easily identified by NMR signal at 6.3–6.5 δ with J_{HCF} = 52–60 Hz). [c] In °C (mm). [d] Early experiment; less 18-C-6 and KF needed. [e] Days = d. [f] NMR yield.

Table II. Synthesis of 1-Alkenyl Carbonates from Aldehydes, Fluoroformates, and KF in DMSO

no.	1-alkenyl carbonate product	ratio RCHO/FCO_2R'/KF	temp, °C/ time, h	yield,[a] %	bp (press.)[b]
4b$_5$	$H_2C{=}CHOCO_2Et$	1.5/1/2	55/20	73	43–45 (45)
4f$_2$	$H_2C{=}CHOCO_2CH_2(C_6H_5)$	2/1/1	70/15	87	112–115 (4)
4h	$H_2C{=}CHOCO_2CH_2CMe_3$	1.5/1/2.8	60/18	72	40–43 (3)
4i	$H_2C{=}CHOCO_2CHMe_2$	1.8/1/2.3	80/20	86	64–66 (70)
4j	$H_2C{=}CHOCO_2$-(1-Admantyl)	1.8/1/2.5	80/1 d[c]	84	mp 37–38[d]
4k	$[H_2C{=}CHOCO_2(CH_2)_3]_2$	1.5/1/1.5[e]	80/1 d	92	130–132 (0.5)
4l	$(H_2C{=}CHOCO_2CH_2CH_2)_2O$	1.5/1/2[e]	90/8	80[f]	123–130 (0.7)
4m	$Me_2C{=}CHOCO_2Et$	1.4/1/2	90/1 d	74	45–47 (16)
4n		1/1/3	90/12	80	110–113 (0.5)
4o	$MeCH{=}CHOCO_2Et$	1.5/1/2.2	70/1 d	71[g]	54–56 (40)
4p	$MeCH{=}CHOCO_2C(Me){=}CH_2$	1.1/1/2	65/1 d	82[h]	40–42 (3)
4q	$Me_2C{=}CHOC(=O)(C_6H_5)$	1.4/1/2.4	60/1 d	80	76–78 (0.6)

[a] Of distilled product; workup as in Table I by dilution with CH_2Cl_2 and extraction with water before distillation (apparatus for reactions of volatile reagents in text). [b] In °C (mm). [c] Days = d. [d] Crystallized from hexane. [e] Per FC(=O) unit. [f] Plus 3% separable CH_3CHF product. [g] E/Z = 0.3. [h] E/Z = 0.33.

cations.[5] The high yields of **4c**, **4f**, and **4g** are significant in future uses of **4** as synthons[6] because Boc, Cbz, and Alloc groups are important agents for hydroxyl protection (no benzyl or allyl fluoride side product found).

In the transformation **1** → **4**, no aldol (or derived carbonate) from trapping of the enolate **2** with **1** was observed and no problems from the release of a proton from KHF_2 were encountered. Dehydration of an aldol to a crotonaldehyde would give water and deactivate the catalyst. However, one side product was $RR'CHCH(F)OCO_2R''$ (**5**) from acylation of a **1** + F^- adduct with **3**, a process most important when the reaction was done neat (**4b$_4$**). In much projected chemistry of **4** (e.g., polymerization), **5** would be an inert diluent. Also, its formation was averted in a useful variation of our original procedure.

While chloroformates react explosively with DMSO, fluoroformates **3** are stable in this solvent, a result already used to advantage in this laboratory[7] for the carboalkoxylation of polar reactants. Based on this fact and the recognition that DMSO activates F^- as a base/nucleophile,[8] scheme **1** → **4** should be feasible with no costly 18-C-6 catalyst if performed in DMSO with **3**. Thus, when MeCHO (1.5 equiv) was treated with FCO_2Et and KF (2 equiv, *no 18-C-6*) in 4 equiv of DMSO at 55 °C for 20 h, the vinyl carbonate **4b** was isolated in 73% distilled yield (87% NMR yield before workup, 56% yield with 2 equiv of DMSO). While KF is not as activated by DMSO as with 18-C-6/MeCN, no side product **5** was found in the DMSO method. Since only 8 mg of KF dissolves in 100 g of DMSO at 25 °C,[8] any major activation might seem surprising. While CsF reacted faster than KF, the yield of **4b** was only 30% (no reaction with NaF or LiF).

Results for the synthesis of several alkenyl carbonates **4** by the KF/DMSO procedure are in Table II. Primary, secondary, tertiary, benzyl, and alkenyl fluoroformates all work. Acetaldehyde reacts faster than RCH_2CHO, which is more active than R_2CHCHO in accord with steric and CH acidity arguments. With RCH_2CHO, the hindered *Z* stereoisomer is the predominant product (**4p,q**). In an important entry in Table II, diethylene glycol bis-vinyl carbonate (**4m**) is made in 80% yield. The material in most prescription safety glasses is the polymer of the analogous bis-allyl carbonate (CR-39). The carbonate **4m** is known to polymerize much more easily than its allyl congener to a "glass" of similar properties[9] but heretofore has not been accessible at acceptable cost.

In contrast to aldehydes, simple ketones effectively failed to yield vinyl carbonates by this route. Acetone did not react even in 4 days at 130 °C (sealed tube). Acetophenone reacted with $FCO_2CH_2CMe_3$ (**6**), but in only 34% yield after 4 days in refluxing MeCN. In DMSO, **6** reacted with cyclohexanone in 54% yield after *9 days at 90 °C*. However, the more acidic phenylacetone reacted with **6** nearly as fast as acetaldehyde. The respective pK_a's of acetone, acetophenone, cyclohexanone, and phenylacetone in DMSO are 26.5, 24.7, 26.4, and 19.3.[10] Although the

(5) Boutevin, B.; Pietrasanta, Y.; Gigal, G.; Rousseau, A. *Ann. Chim. (Paris)* **1984**, *9*(6), 723.
(6) For example, 4 cycloadds to dichloroketene: Morrison, D. S., unpublished.
(7) Dang, V. A.; Olofson, R. A.; Wolf, P. R.; Piteau, M. D.; Senet, J.-P. G. *J. Org. Chem.*, in press. Dang, V. A.; Olofson, R. A. *J. Org. Chem.*, in press.
(8) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429. Yakobson, G. G.; Akhmetova, N. E. *Synthesis* **1983**, 169.
(9) Strain, R.; Kung, F. U.S. Pat. 2,384,143, 1945; *Chem. Abstr.* **1946**, *40*, 589[5].
(10) Bordwell, F. G. *Pure Appl. Chem.* **1977**, *49*, 963 (scale shifted several pK_a units down in water).

present work measures a value closer to a kinetic acidity than a thermodynamic pK_a, it is surprising that acetaldehyde might be in the acidity range of phenylacetone. However, there is increasing evidence[8,11] that relative C–H acidity rankings determined with classical bases do not hold for "naked fluoride". As seen in the present work, this base can be much stronger than might be expected.

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

(11) Note ease of deprotonating $C_6H_5C{\equiv}CH$ (pK_a 28.8 vs 26.5 for acetone[10]) with F^- (Nakamura, E.; Hashimoto, K.; Kuwajima, I. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 805).

Stereoselective Construction of the Taxinine AB System through a Novel Tandem Aldol–Payne Rearrangement Annulation

Charles S. Swindell* and Bomi P. Patel

Department of Chemistry, Bryn Mawr College, Bryn Mawr, Pennsylvania 19010

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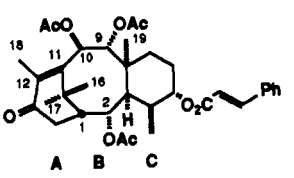
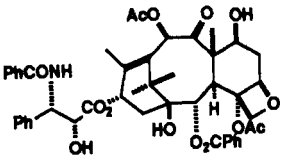
Summary: The construction of the fully functionalized AB portion of taxinine through a series of stereoselective operations on the eight-membered ring including annulation of the A ring through a novel tandem aldolization–Payne rearrangement process is described.

Sir: One view of the synthesis of the taxane diterpenes[1] (e.g. taxinine,[2] **1**, and taxol,[3] **2**) is that it should provide an exercise in the stereocontrolled manipulation of the eight-membered ring. Our A-ring annulation strategy for addressing this challenge has relied on two notions: (1) that the requisite bicyclo[6.4.0] BC intermediates possessing trans ring fusion stereochemistry and (at least) C-9–C-10 unsaturation assume conformations[4] (**3**) appropriate for α stereocontrol at relevant sites; and (2) that the taxane skeleton will tolerate the reversible relocation of C-11–C-12 unsaturation (or its structurally close relative) to C-10–C-11, an idea well founded in Lythgoe's seminal structural work.[5] Herein we report the selective introduction of oxygenation at three taxane B-ring sites culminating in the construction of the taxinine AB substructure (**4**) through a single-operation A-ring annulation process, which triggers elaboration of the B ring.



1



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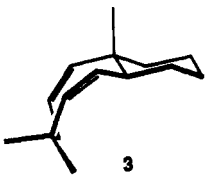

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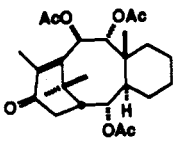

4

Photoproduct **5**[6] (Scheme I) was converted through Rubottom type oxidation[7] to silyloxy ketone **6**, and thence through our five-step fragmentation protocol[6] to enone **7**. Preparation of the dilithio dianion derived from **7** and its alkylation[8] produced **8** with all AB carbons in place and with correct C-1 α stereochemistry. Dehydration of the secondary formamide function in **8** to give a keto isocyanide and its dissolving metal reduction[6] installed concomitantly in **9** the angular methyl substituent and the C-2 α hydroxyl. The facility with which isocyanides suffer reductive cleavage by metal–liquid ammonia reagents is crucial to maintenance of the allylic silyloxy group in this step. Both the reduction of the C-2 carbonyl and the alkylation which precedes it are completely stereoselective within the limits of conventional FT NMR procedures.[9] Further conversion of **9** into **10** seemed to require the initial three-step sequence illustrated; preliminary attempts to hydrolyze directly side chain enol ether containing substances led to their decomposition while intermediate acid treatment closed the methyl acetal ring and provided a useful hydrolytic substrate. Although one-step deprotection of intermediates like **9** should be possible, the relative acid stability of their derived cyclic acetals and the internal protection thereby afforded the C-2 hydroxyl have important implications for the elaboration of taxinine C-ring functionality at the corresponding stage of its synthesis.

Pivotal intermediate **10** could be converted to taxane skeleta of increasing complexity (Scheme II). Its hydro-

(1) For references to taxane structural and synthesis studies through early 1987, see: Swindell, C. S.; Patel, B. P. *Tetrahedron Lett.* **1987**, *28*, 5275. For more recent taxane synthesis reports, see: Benchick-le-Hocine, M.; Do Khac, D.; Fetizon, M.; Hanna, I.; Zeghdoudi, R. *Synth. Commun.* **1987**, *17*, 913. Berkowitz, W. F.; Perumattam, J.; Amarasekara, A. *J. Org. Chem.* **1987**, *52*, 1119. Bonnert, R. V.; Jenkins, P. R. *J. Chem. Soc., Chem. Commun.* **1987**, 1540. Kraus, G. A.; Thomas, P. J.; Hon, Y.-S. *J. Chem. Soc., Chem. Commun.* **1987**, 1849. Lin, J.; Nikaido, M. M.; Clark, G. *J. Org. Chem.* **1987**, *52*, 3745. Denis, J. N.; Greene, A. E.; Guenard, D.; Gueritte-Voegelein, F.; Mangatal, L.; Potier, P. *J. Am. Chem. Soc.* **1988**, *110*, 5917. Funk, R. L.; Daily, W. J.; Parvez, M. *J. Org. Chem.* **1988**, *53*, 4143. Shea, K. J.; Haffner, C. D. *Tetrahedron Lett.* **1988**, *29*, 1367. Holton, R. A.; Juo, R. R.; Kim, H. B.; Williams, A. D.; Harusawa, S.; Lowenthal, R. E.; Yogai, S. *J. Am. Chem. Soc.* **1988**, *110*, 6558. Ohtsuka, Y.; Oishi, T. *Chem. Pharm. Bull.* **1988**, *36*, 4711. Ohtsuka, Y.; Oishi, T. *Chem. Pharm. Bull.* **1988**, *36*, 4722. Winkler, J. D.; Lee, C.-S.; Rubo, L.; Muller, C. L.; Squattrito, P. J. *J. Org. Chem.* **1989**, *54*, 4491. Horiguchi, Y.; Furukawa, T.; Kuwajima, I. *J. Am. Chem. Soc.* **1989**, *111*, 8277.

(2) Dukes, M.; Eyre, D. H.; Harrison, J. W.; Scrowston, R. M.; Lythgoe, B. *J. Chem. Soc. C* **1967**, 448.

(3) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325.

(4) Our initial conclusions regarding the preferred conformation for this hydrocarbon model as reported in an earlier publication (Swindell, C. S.; deSolms, S. J. *Tetrahedron Lett.* **1984**, *25*, 3801.) were led astray by a faulty MM2 calculation. We thank Professor R. Alder, University of Bristol, for pointing this out to us. Since that time, both we and Wender (Wender, P. A.; Ihle, N. C. *Tetrahedron Lett.* **1987**, *28*, 2451) have confirmed that conformations like **3** apply.

(5) Harrison, J. W.; Scrowston, R. M.; Lythgoe, B. *J. Chem. Soc. C* **1966**, 1933.

0022-3263/90/1955-0003$02.50/0