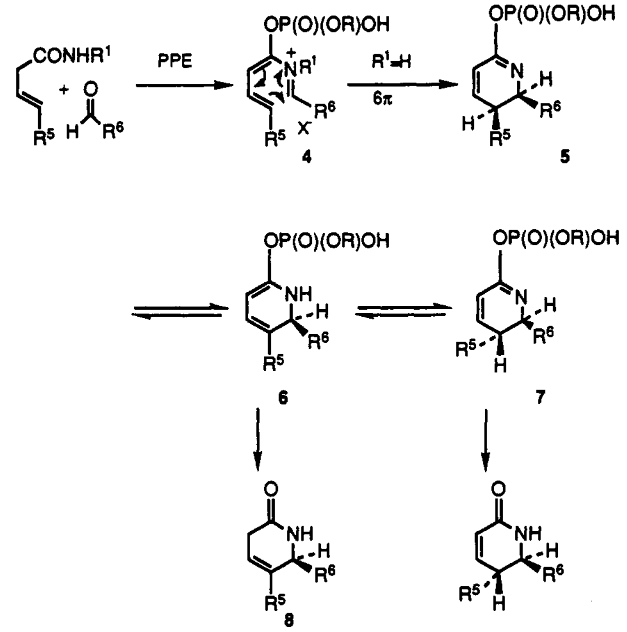
Scheme II



catalysts or stabilizing or activating groups.

Condensation of a variety of 3-alkenamides with aldehydes in PPE[21] affords a general route to substituted 5,6-dihydro-2(1*H*)-pyridinones whose stereochemistry can be rationalized by assuming that (*i*) *such cyclizations do not always proceed solely, or at all, through N-acyliminium species; in certain cases, enol phosphate intermediates are involved,* (*ii*) *the formation of a cis-5,6-disubstituted-5,6-dihydro-2(1H)-pyridinone ring is the result of a thermal 6π electrocyclic disrotatory ring-closure,*[22,23] and (*iii*) *trans-5,6-disubstituted-5,6-dihydro-2-(1H)-pyridinone rings are formed from the cis-isomers* (*or their reaction intermediates*) *by processes which involve a combination of enol phosphate intermediates and equilibration to the trans isomers* (*as for entries* **1c**, **1d**, **1e**, *and* **1g**) *either by prototropic shifts or by [1,5]sigmatropic rearrangement of hydrogen.*[23] An uninvestigated possibility is that for amide **1f** (Table I), the 5,6-cis-substituents do not isomerize because the blocking *N*-methyl group precludes the possibility of a [1,5] hydrogen shift. In addition to **1f**, the formation of a β-hydroxy amide (a single diastereoisomer) is consistent with an acid-catalyzed aldol condensation of an enol phosphate intermediate with benzaldehyde. A Prins reaction[18] to account, for example, for the deconjugated amide **8a** cannot be rigorously excluded; however, β-protonation of intermediate **6** appears more plausible.

2,2-Dimethyl-3-pentenamide failed to react with benzaldehyde in PPE at 40 °C, presumably because enolization cannot occur. PPE evidently favors the formation of enol phosphates, and hence δ-lactams via 6π ring closure, unless steric factors prevent coplanarity of the substituents. Thus, condensation of (*E*)-*N*-benzyl-3-pentenamide with benzaldehyde in PPE (35 °C, 24 h) gave exclusively the *N*-benzyl derivative (52%) of the indano-fused γ-lactam previously obtained from a condensation in PPA.[17] A medium of PPA or $MeSO_3H-P_2O_5$ generally favors the formation of the γ-lactam, presumably via *N*-acyliminium cations. However, where this mode would proceed via a primary carbocation, the alternative ring closure operates to give a δ-lactam, e.g, **1a**. Thus, the size of the lactam ring can be controlled exclusively by selection of the acidic medium. In no case studied here was a mixture of γ- and δ-lactams isolated.

In summary, efficient, highly stereocontrolled one-pot syntheses of substituted unsaturated δ-lactams by the condensation of 3-alkenamides with aldehydes in media of phosphoric acids or esters, principally PPE, have been demonstrated. Condensations proceed under mild conditions and can be effected in multigram quantities; activating or stabilizing groups are not required. The reaction medium can critically determine whether a γ-lactam[17] or a δ-lactam is formed. Pathways and synthetic applications are under investigation.

Acknowledgment. We thank the Science and Engineering Research Council and SmithKline Beecham for a CASE award (to U.G.).

Registry No. **1a**, 142422-26-2; **1b**, 142422-27-3; **1c**, 142422-28-4; **1d**, 142422-29-5; **1e**, 142422-30-8; **1f**, 142422-31-9; **1g**, 142422-32-0; **8a**, 142422-33-1; PhCHO, 100-52-7; *p*-$MeOC_6H_4CHO$, 123-11-5; *p*-$O_2NC_6H_4CHO$, 555-16-8; $H_2C{=}CHCH_2CONH_2$, 28446-58-4; $H_2C{=}CHCH_2CONHCH_2Ph$, 85390-58-5; (*E*)-$H_3CCH{=}CHCH_2CONH_2$, 133099-99-7; (*E*)-$H_3CCH{=}CHCH_2CONHMe$, 142422-34-2; (*E*)-$H_3CCH_2CH{=}CHCH_2CONH_2$, 133128-00-4; (*E*)-$H_3CCH{=}C(CH_3)CH_2CONH_2$, 142422-35-3.

Supplementary Material Available: Procedures and characterization data for **1a–g** and **8a** (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[21] PPA was purchased from BDH Chemicals Ltd., Poole. For a review on PPA see: Rowlands, D. A. In *Synthetic Methods*; Pizey, J. S., Ed.; Wiley: New York, 1985; Vol. 6. p 156. For some uses of PPE in synthesis, see: (a) Kanaoaka, Y.; Ban, Y.; Mayashita, K.; Iria, K.; Yonemitsu, O. *Chem. Pharm. Bull.* **1966**, *14*, 934. (b) Kanaoka, Y.; Sato, E.; Yonemitsu, O.; Ban, Y. *Tetrahedron Lett.* **1964**, *35*, 2419. PPE was prepared as described by Cava, M. P.; Lakshmikantham; Mitchell, M. J. *J. Org. Chem.* **1969**, *34*, 2665.

[22] An (*E*)-configuration about the C=N bond has also been assumed. The thermal ring closure might also proceed through an intermediate containing an uncharged nitrogen atom in the case of $R^1 = H$ in Scheme II. The precise constitution of enol phosphate intermediates is not currently known.

[23] (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970, pp 114–140. (b) Spangler, C. W. *Chem. Rev.* **1976**, *76*, 187. (c) Mironov, V. A.; Fedorovich, A. D.; Akhrem, A. A. *Russ. Chem. Rev.* **1981**, *50*, 666.

Synthesis of 1,4-Diketones by Palladium-Catalyzed Reductive Coupling of Acid Chlorides with (*E*)-1,2-Bis(tri-*n*-butylstannyl)ethene or β-Stannyl Enones

Marta Pérez, Ana M. Castaño, and Antonio M. Echavarren*[1]

Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain

Received June 1, 1992

Summary: The palladium-catalyzed coupling of acid chlorides with (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene or β-stannyl enones gives butane-1,4-diones directly by reduction of the intermediate enedicarbonyl derivative by

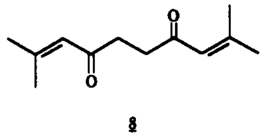
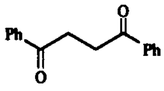
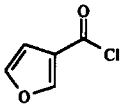
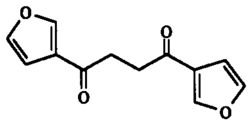
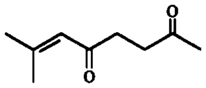
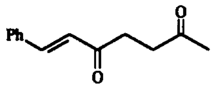
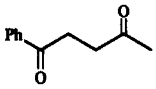
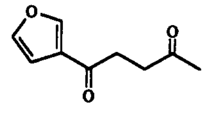
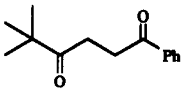
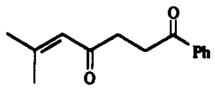
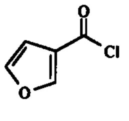
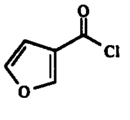
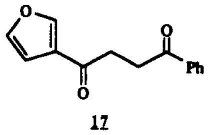
a palladium hydride derived from n-Bu_3SnCl.

1,4-Diketones are important intermediates for the synthesis of cyclopentenones and heterocyclic compounds such as furans, pyrroles, thiophenes, and pyridazines.[2-4] Their syntheses have been carried out by a variety of methods,[2-4,5] including the benzoin condensation between aldehydes and Michael acceptors catalyzed by cyanide or thiazolium salts.[4,6,7]

The acylation of organostannanes by acid chlorides in the presence of palladium catalyst gives ketones in a general way.[8,9] The corresponding reaction with alkenyl stannanes yields α,β-unsaturated ketones in moderate to good yields.[10,11] On the other hand, couplings of organic electrophiles with (E)-1,2-bis(tri-n-butylstannyl)ethene (1)[12] can yield either the mono-[13] or the dicoupled[14] derivative depending on the reaction conditions. In this paper we report the development of a new method for the synthesis of butane-1,4-diones by reaction of acid chlorides with (E)-1,2-bis(tri-n-butylstannyl)ethene (1) catalyzed by palladium complexes. This synthetic method can also be applied to the preparation of unsymmetrical derivatives by using β-stannyl enones in the coupling process (Scheme I). In this context, stannane 1 behaves as a synthetic equivalent for the ethane 1,2-dianion.[15]

The reaction of benzoyl chloride and 3-furoyl chloride with stannane 1 (1 equiv) in the presence of $Pd(PPh_3)_4$ catalyst in 1,4-dioxane under reflux for 1–2 h yielded β-stannyl enones 3 (27% yield) and 4 (35% yield), respectively. Stannane 2 was better prepared by acetylation of 1 (acetyl chloride, $AlCl_3$) by a known procedure.[16] When the coupling reaction of benzoyl chloride and 1 (0.5 equiv) was performed for 2–3 h, 5 was obtained in 25–32% yield. Similarly, reaction of stannane 3 with acetyl chloride gave 6 (86%), and stannane 2 reacted with 3-furoyl chloride to give 7 (93%). Surprisingly, longer reaction times led to butane-1,4-dione derivatives resulting from a reduction of doubly conjugated olefin (Table I). This reduction allows for the preparation, in a single step, of both symmetrical

Table I. Palladium-Catalyzed Coupling of Acid Chlorides with Stannanes[a]

entry	acid chloride	stannane	product	yield (%)
1	$Me_2C=CHCOCl$	1	 8	63
2	PhCOCl	1	 9	50
3		1	 10	55
4	$Me_2C=CHCOCl$	2	 11	86
5	PhCH=CHCOCl	2	 12	52
6	PhCOCl	2	 13	70
7	MeCOCl	3	9	47
8	MeCOCl	4	 14	100
9	$(Me_3)CCOCl$	3	 15	87
10	$Me_2C=CHCOCl$	3	 16	97
11		2	14	70
12		3	 17	64

[a] See ref 17 for reaction conditions.

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(1) Present address: Departamento de Química, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain.

(2) Ellison, R. A. *Synthesis* **1973**, 397.

(3) Ho, T.-L. *Polarity Control for Synthesis*; Wiley: New York, 1991; Chapter 7.

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(5) For recent references, see: (a) Lu, X.; Ji, J.; Ma, D.; Shen, W. *J. Org. Chem.* **1991**, *56*, 5774. (b) Motoyoshiya, J.; Hongo, Y.; Tanaka, H.; Hayashi, S. *Synth. Commun.* **1991**, *21*, 997. (c) Freeman, F.; Kim, D. S. H. L.; Rodriguez, E. *J. Org. Chem.* **1992**, *57*, 1722.

(6) Hassner, A.; Rai, K. M. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, Chapter 2.4.

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(10) For recent lead references, see: (a) Crisp, G. T.; Bubner, T. P. *Synth. Commun.* **1990**, *20*, 1665. (b) Baldwin, J. E.; Adlington, R. M.; Ramcharitar, S. H. *J. Chem. Soc., Chem. Commun.* **1991**, 940. (c) Verlhac, J.-P.; Pereyre, M.; Shin, H. A. *Organometallics* **1991**, *10*, 3007.

(11) For related reactions, see: (a) Balas, L.; Jousseaume, B.; Shin, H.; Verlhac, J.-P.; Wallian, F. *Organometallics* **1991**, *10*, 366. (b) Kobayashi, T.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1985**, *26*, 3463.

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(13) Haack, R. A.; Penning, T. D.; Djuric, S. W.; Dziuba, J. A. *Tetrahedron Lett.* **1988**, *29*, 2783.

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(15) (a) For the preparation of 1,2-dilithioethane, see: Eikema Hommes, N. J. R.; Bickelhaupt, F.; Klumpp, G. W. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1083. (b) For a review on di-Grignard compounds, see: Bickelhaupt, F. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 990.

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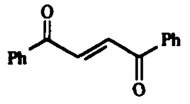

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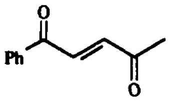
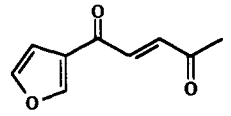


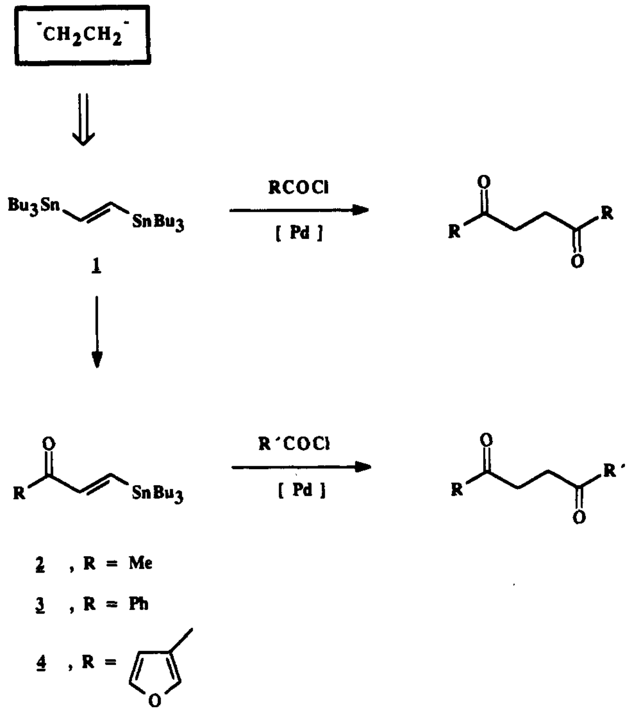
6



7

(entries 1–3) and unsymmetrical 1,4-diketones (entries 4–12) by coupling of acid chlorides with distannane 1 or β-stannyl enones 2–4. The couplings proceed in moderate to excellent yields with a variety of acid chlorides in the presence of $Pd(PPh_3)_4$ in 1,4-dioxane under reflux for 23–30 h.[17] Noteworthy, α,β-unsaturated acid chlorides (entries 1, 4, 5, and 10) yielded α,β-unsaturated-1,4-diketones in which the olefin conjugated with a single carbonyl group is not reduced under the reaction conditions.[18] This reaction was applied to the synthesis of the naturally occurring ipomeanine (14)[19] (Table I, entries 8 and 11) in a single step from readily available starting materials.

Scheme I



Noteworthy, 1,4-diphenyl-2-butene-1,4-dione (5) could be reduced to 9 by n-Bu_3SnCl, the byproduct of the coupling reaction, in the presence of several palladium catalysts (refluxing dioxane).[20] Hence, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$, $(PhCH_2)Pd(PPh_3)_2Cl$, $Pd(dppf)Cl_2$, $Pd(MeCN)_2Cl_2$, $Pd_2(dba)_4$ + PPh_3 (2–4 equiv), and $Pd_2(dba)_4$ + PCy_3 (2 equiv)[21] gave similar results, while $Pd_2(dba)_4$, $Ni(PPh_3)_2Cl_2$, and $Ni(CO)_2(PPh_3)_2$ were ineffective. When the reduction of 5 to 9 was performed with n-Bu_3SnCl (1–2 equiv) and $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ as the catalysts in $CDCl_3$ at 90 °C (sealed tube), a mixture of 1- and 2-butenes (cis and trans isomers)[22] and n-Bu_2SnCl_2 were also observed by ^1H and ^{13}C NMR.[23] Furthermore, almost clean conversion of n-Bu_3SnCl to n-Bu_2SnCl_2 and butenes was also observed in $CDCl_3$ at 90 °C ($Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ as the catalysts).[23a,c] These experiments indicate that n-Bu_3SnCl reacts with the palladium catalyst to give a n-butylpalladium intermediate, which undergoes β-hydride elimination to yield 1-butene and a palladium hydride. Accordingly, no reduction of 5 with Me_3SnCl was observed under the same reaction conditions. Further studies on the mechanism of this process as well as application to the synthesis of unsymmetrically substituted pyrrolidines are in progress.

Acknowledgment. We are grateful to the DGICYT (Project PB87-0201-C03-02) for support of this research. A.M.C. acknowledges the receipt of a predoctoral fellowship by the Comunidad Autónoma de Madrid.

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[17] General procedure: A mixture of acid chloride (1 mmol), stannane 2–4 (1 mmol) and $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (7 mL) was heated under reflux for 23–30 h (Ar atmosphere). For the double couplings of entries 1–3, 0.5 mmol of 1 and 0.1 mmol of $Pd(PPh_3)_4$ were used. After being cooled to room temperature, the mixture was partitioned between EtOAc and aqueous $NaHCO_3$ (5%). The organic extract was washed with aqueous HCl (1.2 M), dried (Na_2SO_4), and evaporated. The residue was chromatographed to yield the 1,4-diketones. Treatment with aqueous HCl was omitted with the furyl derivatives. All compounds have been fully characterized spectroscopically. Known compounds gave satisfactory physical data. (a) 5: Lutz, R. E. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 248. (b) 6: Mayring, L.; Severin, T. *Chem. Ber.* **1981**, *114*, 3863. (c) 8: ref 4. (d) 9: ref 5c. (e) 10: Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487. (f) 11: ref 4. (g) 12: Stetter, H.; Hilboll, G.; Kuhlmann, H. *Chem. Ber.* **1979**, *112*, 84. (h) 13: ref 5b. (i) 14: ref 19. (j) 15: Schulz, G.; Gruber, P.; Steglich, W. *Chem. Ber.* **1979**, *112*, 3221. (k) 16: ref 17g.

[18] However, small amounts of 7-phenylheptane-2,5-dione were observed in the reaction of cinnamoyl chloride with stannane 2 (Table I, entry 5).

[19] Previous syntheses: (a) Kubota, T. *Tetrahedron* **1958**, *4*, 68. (b) Watanabe, E.; Imai, N.; Inomata, K.; Kinoshita, H.; Kotake, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3225. (c) Dimitriadis, E.; Massy-Westropp, R. A. *Phytochemistry* **1984**, *23*, 1325. (d) Liu, W. H.; Wu, H. J. *J. Chin. Chem. Soc.* **1988**, *35*, 241; *Chem. Abstr.* **1989**, *110*, 94846v.

[20] Similarly, dimethyl acetylenedicarboxylate reacts with n-Bu_3SnCl in the presence of $Pd(PPh_3)_4$ to give a mixture of dimethyl fumarate and dimethyl succinate. Maleic anhydride gave succinic anhydride under these reaction conditions.

[21] dba = dibenzylideneacetone; dppf = 1,1′-bis(diphenylphosphino)ferrocene.

[22] The 1-butene was completely isomerized to a mixture of cis- and trans-2-butenes after 12 h.

[23] (a) No n-$BuSnCl_3$ was detected in these reactions. Cleaner conversion into n-Bu_2SnCl_2 was obtained in the presence of LiCl. (b) $(n$-$Bu_3Sn)_2$ was also observed by GC-MS analysis of the reaction mixture. (c) Additionally, small amounts of uncharacterized materials were also formed in these experiments.

Asymmetric Cyclization via Tandem Conjugate Addition by Using Metal Amide Reagents. Importance of the Folded Orientation of Two Enoate Moieties

Naomi Shida, Tadao Uyehara, and Yoshinori Yamamoto*

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

Received June 8, 1992

Summary: Di-(−)-menthylnona-2,7-diene-1,9-dioate (1) is converted to (−)-menthyl 3(*S*)-(*N*-benzylamino)-2(*S*)-(−)-menthoxycarbonyl)-1(*S*)-cyclohexane-1-acetate (2) with high diastereoselectivity upon treatment with the amide

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