Pergamon

Tetrahedron Letters 41 (2000) 7517–7520

TETRAHEDRON
LETTERS

New synthesis of α-acyl imines by radical-mediated group-transfer imidoylation of acyl tellurides with isonitriles

Shigeru Yamago,* Hiroshi Miyazoe, Takashi Sawazaki, Ryuta Goto and Jun-ichi Yoshida*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

Received 27 June 2000; revised 21 July 2000; accepted 24 July 2000

Abstract

Acyl radicals generated from either acyl tellurides or alkyl tellurides and carbon monoxide react with isonitriles to give α-acyl-substituted imidoyl tellurides in good to excellent yield. Hydrolysis of the product under oxidative conditions provides the corresponding α-acyl amides. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: radicals and radical reactions; carbonylation; isocyanides; imidic acids and derivatives.

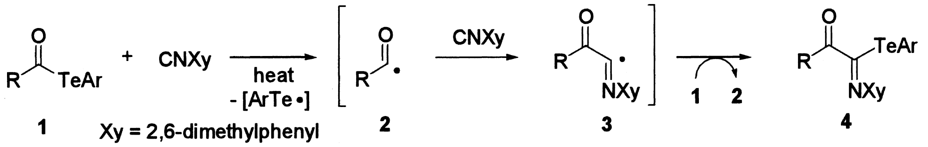
The synthesis of α-acyl carbonyl compounds, e.g. α-acyl ketones, esters and amides, has attracted considerable interest because these compounds not only serve as versatile building blocks in organic synthesis, but also exhibit broad biological activity.[1] Although direct introduction of C1 carbonyl synthons to organic molecules is an attractive approach, only a few examples have been reported so far in electrophilic reactions of isonitriles[2] or metal-mediated double carbonylations and imidoylations.[3,4] The attractive possibility of using a radical-mediated process[5] was problematic as carbonylation of acyl radicals by carbon monoxide (CO) does not proceed even under extremely high CO pressure.[6] Until Ryu and Kim found recently that sulfonyl oximes could serve as excellent C1 acceptors for acyl radicals,[7] the synthetic utility of such radical methodology was unknown. We have already shown that isonitriles are better C1 carbonyl synthons than carbon monoxide in reacting with stabilized radicals, such as α-alkoxy radicals.[8] These results prompted us to investigate the reaction of acyl radicals with isonitriles. We chose acyl tellurides as the acyl radical precursors, because Crich in his pioneering work had shown that they are excellent acyl radical precursors,[9,10] and found that isonitriles are excellent acceptors for acyl radicals. We report here a new synthesis of α-acyl imines by thermal radical reaction of the acyl tellurides **1** and isonitriles to give the α-acyl-substituted imidoyl tellurides **4**,

---

* Corresponding authors. Fax: +81-75-753-5911; e-mail: yamago@sbchem.kyoto-u.ac.jp

PII: S0040-4039(00)01287-9

which are hydrolyzed to the α-acyl amides in good yield (Eq. (1)). We also observed the trapping of isonitriles with in situ generated acyl radicals from alkyl radicals and CO. These results clearly show that isonitriles serve as efficient C1 units for radical-mediated 1,2-dicarbonyl syntheses.



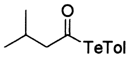
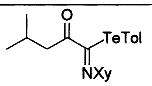
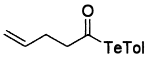
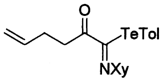
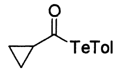
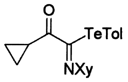
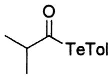
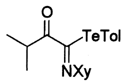
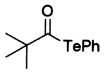
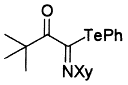
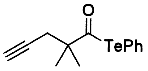
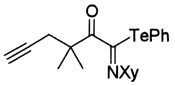
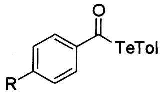
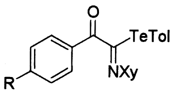
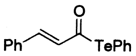
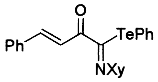
(1)

The feasibility of the present imidoylation reaction of acyl radicals was first examined using *p*-methylphenyl 3-methyltellurobutyrate (**1a**); the reaction took place smoothly under ambient thermal conditions. Thus, a 0.6 M C_6D_6 solution of **1a** and 2,6-dimethylphenylisonitrile (2.0 equiv.) was heated at 100°C for 6 h, and the imidoylated product **4a** was formed in 87% yield (Table 1, entry 1). While the decarbonylation of acyl radicals potentially competes with the coupling reaction, no such products were detected. Although photo-irradiation has been reported to accelerate the radical generation from acyl tellurides, irradiation using simple UV lamps (6 W×6) or a high pressure Hg lamp (250 W) resulted in lower yield (74 and 41% yield, respectively). Since the consumption of **1a** was accelerated by UV irradiation, the observed result was presumably due to the instability of the product under UV irradiation. The reaction could also be carried out in various solvents, e.g. hexane, EtCN, EtOH and H_2O, and the desired product was obtained in good to excellent yield in all cases. The observed insensitivity of the reaction to solvent is consistent with a radical chain mechanism, which involves the generation of the acyl radical **2** from **1**, the reaction of **2** with the isonitrile to form **3** and the subsequent group-transfer reaction of **3** with **1** (Eq. (1)). While the reaction in H_2O gave the best results, we chose the aromatic solvent for the reaction because of the high solubility of the substrates.

The synthetic scope of the reaction has been examined with various acyl tellurides, and the results are summarized in Table 1. Acyl tellurides bearing alkyl, aryl, and alkenyl carbon residues are found to react with 2,6-dimethylphenylisonitrile to give the desired products in good to excellent yields under moderate thermal conditions (entries 1–10). In the reaction of acyl tellurides bearing secondary and tertiary alkyl carbon residues, decarbonylation of CO from the acyl radicals was found to be a serious side reaction (entries 4 and 5). However, we found that the decarbonylation reaction could be avoided by carrying out the reaction under CO pressure (50 atm), because the application of high CO pressure retards the decarbonylation reaction.[5] It is noteworthy that decarbonylation did not take place in the cyclopropyl-substituted acyl telluride (entry 3). This is probably because cyclopropyl radicals, which possess sp^3 radical character, are less stable than the conformationally unrestrained secondary alkyl radicals,[11] since the rate of the decarbonylation becomes faster when the decarbonylated radical becomes more stable.[12] The acyl tellurides bearing olefin and acetylene moieties also afforded the simple imidoylated products without undergoing intramolecular radical cyclization from the imidoyl radical intermediates (entries 2 and 6).[13] The decarbonylation reaction of the aryl- and alkenyl-substituted acyl tellurides did not take place at all, and the desired coupling reaction proceeded in good yield (entries 7–10).

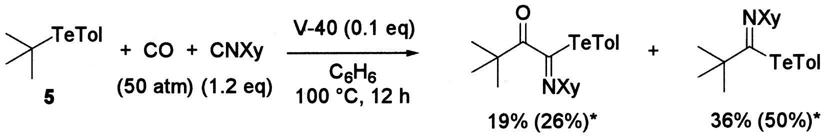
We next examined the imidoylation of acyl radicals generated in situ from alkyl radicals and CO. Thus, *t*-butyl *p*-tolyl telluride (**5**) and 2,6-dimethylphenylisonitrile in C_6H_6 were heated at 100°C under 50 atm of CO pressure in the presence of the radical initiator V-40 [1,1′-azobis(cy

Table 1
Imidoylation reaction of acyl telluride with 2,6-dimethylphenylisonitrile

Entry	Substrate	Solvent	Time (h)	Product	Yield (%)
1		hexane	12		83^{b}
		C_6D_6	12		87
		CD_3CN	12		73^{b}
		EtOH	12		80^{b}
		H_2O	12		87
2		C_6D_6	7		78
3		C_6D_6	19		73^{c}
4		C_6D_6	12		26^{d}
		C_6H_6	12		$87^{e,f}$
5		C_6D_6	12		0^{g}
		C_6H_6	12		$73^{e,h}$
6		C_6H_6	12		61^{e}
7					
	R = Cl	C_6D_6	6		52
8	R = H	C_6D_6	6		48
9	R = OMe	C_6D_6	6		50
10		C_6D_6	6		52

[a] Reaction conditions: a 0.6 M solution of the acyl telluride and 2,6-dimethylphenylisonitrile (2.0 eq) was heated at 100 °C. [b] Determined by ^{1}H NMR. [c] The reaction was carried out at 100-120 °C. [d] *i*-Propyl tolyl telluride formed in 22% yield. [e] The reaction was carried out under CO pressure (50 atm). [f] *i*-Propyl tolyl telluride formed in 5% yield. [g] *t*-Butyl tolyl telluride formed in 78% yield. [h] *t*-Butyl tolyl telluride formed in 7% yield.

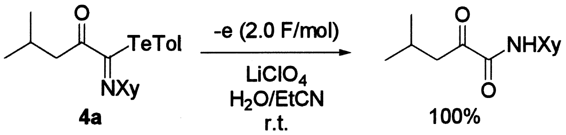
clohexane-1-carbonitrile)]. The desired product formed in 19% yield (26% yield based on conversion) together with the imidoylated product of *t*-butyl tolyl telluride in 36% yield (Eq. (2)).



(2)

*Yield based on the converted **5**.

Since various synthetic transformations of the reactive C–Te bond are known,[14] the products **4** would be useful precursors for a variety of 1,2-dicarbonyl compounds and their equivalents. For example, electrochemical oxidation of **4a** in the presence of water afforded the corresponding α-acyl amide in quantitative yield (Eq. (3)). Further synthetic exploration is currently underway.



(3)

References

1. Recent examples: (a) Wasserman, H. H.; Chen, J.-H.; Xia, M. *J. Am. Chem. Soc.* **1999**, *121*, 1401. (b) Wasserman, H. H.; Xia, M.; Petersen, A. K.; Jorgensen, M. R.; Curtis, E. A. *Tetrahedron Lett.* **1999**, *40*, 6163. (c) Singh, R. P.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem.* **1999**, *64*, 2579. (d) Katritzky, A. R.; Oniciu, D. C.; Ghiviriga, I.; Soti, F. *J. Org. Chem.* **1998**, *63*, 2110. (e) Wasserman, H. H.; Petersen, A. *Tetrahedron Lett.* **1997**, *38*, 953. (f) Baldino, C. M.; Casebier, D. S.; Caserta, J.; Slobodkin, G.; Tu, C.; Coffen, D. L. *Synlett* **1997**, 488. (g) Yamamoto, Y.; Kimachi, T.; Kanaoka, Y.; Kato, S.; Bessho, K.; Matsumoto, T.; Kusakabe, T.; Sugiura, Y. *Tetrahedron Lett.* **1996**, *37*, 7801. (h) Slee, D. H.; Laslo, K. L.; Elder, J. H.; Ollmann, I. R.; Gustchina, A.; Kervinen, J.; Zdanov, A.; Wlodawer, A.; Wong, C.-H. *J. Am. Chem. Soc.* **1995**, *117*, 11867. (i) Takahashi, T.; Okano, T.; Harada, T.; Imamura, K.; Yamada, H. *Synlett* **1994**, 121. (j) Wipf, P.; Kim, H. *J. Org. Chem.* **1993**, *58*, 5592. (k) Hagihara, M.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 6357.
2. (a) Ugi, I.; Fetzer, U. *Chem. Ber.* **1961**, *94*, 1116. (b) Capuano, L.; Wamprecht, C.; Hell, W. *Liebigs Ann. Chem.* **1986**, 132. (c) Westling, M.; Smith, R.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 1163.
3. (a) Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 433. (b) Ozawa, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1985**, *107*, 3235. (c) Ozawa, F.; Kawasaki, N.; Okamoto, H.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1987**, *6*, 1640.
4. Murakami, M.; Masuda, H.; Kawano, T.; Nakamura, H.; Ito, Y. *J. Org. Chem.* **1991**, *56*, 1.
5. (a) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177. (b) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050.
6. (a) Brubaker, M. M.; Coffman, D. D.; Hoehn, H. H. *J. Am. Chem. Soc.* **1952**, *74*, 1509. (b) Coffman, D. D.; Pinkney, P. S.; Wall, F. T.; Wood, W. H.; Young, J. S. *J. Am. Chem. Soc.* **1952**, *74*, 3391.
7. Ryu, I.; Kuriyama, H.; Minakata, S.; Komatsu, M.; Yoon, J.-Y.; Kim, S. *J. Am. Chem. Soc.* **1999**, *121*, 12190.
8. (a) Yamago, S.; Miyazoe, H.; Goto, R. Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 2347. (b) Miyazoe, H.; Yamago, S.; Yoshida, J. *Angew. Chem., Int. Ed.* in press.
9. Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991.
10. (a) Chen, C.; Crich, D.; Papadatos, A. *J. Am. Chem. Soc.* **1992**, *114*, 8313. (b) Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937.
11. Walborsky, H. M. *Tetrahedron* **1981**, *37*, 1625.
12. (a) Fischer, H.; Paul, H. *Acc. Chem. Res.* **1987**, *20*, 200. (b) Lunazzi, L.; Ingold, K. U.; Scaiano, J. C. *J. Phys. Chem.* **1983**, *87*, 529. (c) Turro, N. J.; Gould, I. R.; Baretz, B. H. *J. Phys. Chem.* **1983**, *87*, 531. (d) Vollenweider, J.-K.; Paul, H. I. *J. Chem. Kinet.* **1986**, *18*, 791. (e) Tsentalovich, Y. P.; Fischer, H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 729. (f) See also Refs. 3b and 9.
13. The failure of the intramolecular cyclization is probably due to the conformational effects; the imidoyl radical intermediate may prefer to take extended conformations rather than folded ones due to the dipole–dipole repulsion of the carbonyl and the imine moieties.
14. Petragnani, N. *Tellurium in Organic Synthesis* Academic: London, 1994.