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Letters

Reaction of TPP-azodicarboxylate zwitterions and aryl aldehydes: unprecedented synthesis of acyl carbamates

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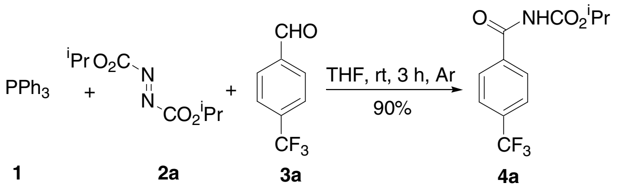
Abstract—An efficient synthesis of acyl carbamates from aryl aldehydes by the reaction of triphenylphosphine and dialkyl azoesters is described.

The formation of a zwitterion by the reaction of triphenylphosphine (TPP) and azoesters has been known for a long time[1] and the critical role of this species in the Mitsunobu reaction is well established.[2] Other synthetically useful reactions of this zwitterion commonly called the Huisgen zwitterion, include preparation of vinyl hydrazine dicarboxylates from ketones,[3] oxadiazolines from α-ketoesters,[4] and protected hydrazones from salicylaldehydes.[5] Recent studies on the chemistry of this zwitterion have uncovered a number of interesting reactions, which include the formation of a monohydrazone from benzil via an unprecedented rearrangement,[6] formation of novel pyrazolopyridazines from dienones,[7] spirooxadiazolines from isatins,[8] and pyrazoles from allenes.[9] In this context, and in view of the general interest in the chemistry of zwitterions,[10] we undertook an investigation of the reactivity of this zwitterion toward aldehydes. Our results describing the unprecedented, direct transformation of aryl aldehydes[4] to acyl carbamates form the subject matter of this Letter. It is noteworthy that acyl carbamates are important due to their pesticidal activity.[11,12]

Acyl carbamate groups also find application as protecting groups in organic synthesis.[13] Although a number of methods are available in the literature for the synthesis of acyl carbamates,[14,15] all of them involve multistep processes; to the best of our knowledge no direct conversion of an aldehyde to an acyl carbamate has been reported.

Our studies commenced with an experiment in which a solution of 4-trifluoromethylbenzaldehyde **3a** and diisopropyl azodicarboxylate (DIAD) **2a** in anhydrous THF was allowed to react with a stoichiometric quantity of triphenylphosphine at room temperature under an argon atmosphere. Work-up followed by column chromatography afforded a white crystalline solid in 90% yield which was characterized as the acyl carbamate **4a** (Scheme 1).[16]

The structure of the product was assigned on the basis of spectroscopic analysis and further confirmation was achieved unambiguously using single crystal X-ray analysis (Fig. 1).[17]



Scheme 1.

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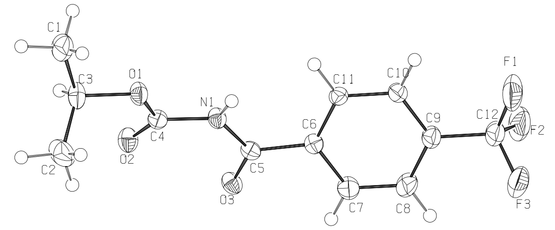
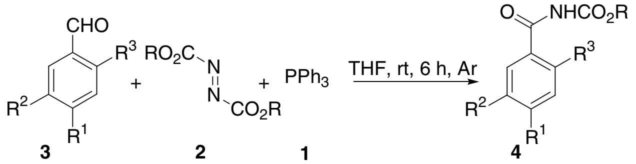


Figure 1. ORTEP diagram for compound **4a**.

Table 1. Reactions of aldehydes with TPP-azoester zwitterion



3 **2** **1** **4**

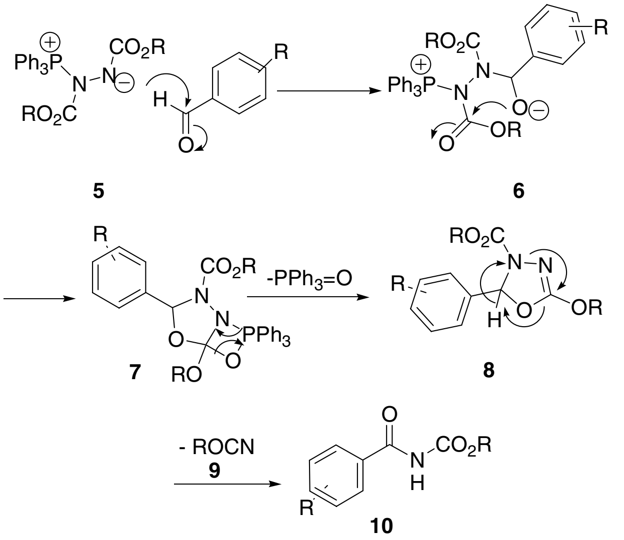
Entry	R	R^1	R^2	R^3	Product	Yield (%)
1	Isopropyl	Cl	Cl	H	**4b**	85
2	Isopropyl	H	NO_2	H	**4c**	76
3	Isopropyl	Br	H	H	**4d**	50 (67)[a]
4	Isopropyl	Cl	H	H	**4e**	78
5	Isopropyl	H	Cl	H	**4f**	75
6	Isopropyl	F	H	H	**4g**	75
7	Isopropyl	F	F	H	**4h**	86
8	Isopropyl	H	H	F	**4i**	37 (83)[a]
9	Isopropyl	H	H	H	**4j**	64
10	Ethyl	CF_3	H	H	**4k**	86
11	Ethyl	Cl	Cl	H	**4l**	74
12	Ethyl	NO_2	H	H	**4m**	73
13	Ethyl	Br	H	H	**4n**	64
14	Ethyl	Cl	H	H	**4o**	71
15	Ethyl	F	H	H	**4p**	75
16	*tert*-Butyl	Cl	Cl	H	**4q**	89

[a] Recovered yield.

The reaction was found to be general with a variety of aromatic aldehydes. The results are summarized in Table 1.

The following mechanistic postulate may be invoked to rationalize the formation of the acyl carbamate from aldehyde. Initially zwitterion **5** generated from the azodicarboxylate and triphenylphosphine adds to the aldehyde carbonyl to form intermediate **7** which then eliminates triphenylphosphine oxide by a well precedented step to form the oxadiazoline derivative **8**. It is conceivable that the oxadiazoline can undergo ring fragmentation and concomitant hydride transfer to deliver the acyl carbamate **10** with the loss of alkyl cyanate. Although we have no direct evidence for this mechanistic pathway, the detection of a peak corresponding to the alkyl cyanate ($m/z = 85.46$, $R = {}^{i}Pr$) **9** in the low resolution mass spectrum of the reaction mixture may validate the proposed mechanism (Scheme 2).

In conclusion, we have developed a novel, direct transformation of aromatic aldehydes to acyl carbamates. It is reasonable to assume that this reaction will be useful in organic synthesis.



Scheme 2.

Acknowledgments

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16. *Typical experimental procedure*: To a solution of 4-trifluoromethylbenzaldehyde **3a** (0.55 mmol) and DIAD (0.66 mmol) in dry THF (3 mL) under an atmosphere of Ar was added triphenylphosphine (216 mg, 0.83 mmol) and the reaction mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure on a rotary evaporator. The residue was subjected to column chromatography on silica gel (100–200 mesh) using 85:15 petroleum ether-ethyl acetate as eluent to afford the corresponding acyl carbamate derivative **4a** as white crystals. Mp: 145–147 °C, IR (KBr) ν_{max}: 3352, 3055, 2985, 1742, 1642, 1477, 1421, 1381, 1323, 1269, 1259, 1172, 1109, 1072, 896, 759, 734, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, rt): δ 8.52 (bs, 1H), 7.49 (d, $J = 7.8$ Hz, 2H), 7.73 (d, $J = 8.2$ Hz, 2H), 5.09–5.02 (m, 1H), 1.30 (d, $J = 6.2$ Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 164.3, 150.6, 136.5, 134.6, 128.3, 125.7, 125.3, 121.6, 70.6, 21.8. HRMS (EI) for $C_{12}H_{12}F_3NO_3$, Calcd (M^+): 275.0769, found: 275.0780.
17. The crystal structure of compound **4a** has been deposited at the Cambridge Crystallographic Data Centre and allocated the reference no. CCDC 642242.