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THE SYNTHESIS OF MIXED CARBONATES FROM ALCOHOLS, DIALKYL AZODICARBOXYLATE AND TRIS(DIMETHYLAMINO)-PHOSPHINE

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Abstract—A mild method for the synthesis of mixed carbonates from alcohols, dialkyl azodicarboxylate and tris(dimethylamino)-phosphine is described. The yields of carbonates are in the range 22–88%.

The interaction of a trivalent phosphorus compound **1** with dialkyl azodicarboxylate **2** creates a very reactive species[1,2] which undergoes reaction with a variety of substrates such as alcohols,[3] carboxylic acids,[4] thioureas,[5] sulphur trioxide,[2] hexafluoroacetone,[2] etc. Particular attention has been paid to the reaction of **1** and **2** with alcohols and imides leading to substituted imides.[6] This is undoubtedly a valuable method for converting alcohols into amines.† For example:

$$\underset{\mathbf{3}}{R{-}OH} + Ph_3P + \underset{\mathbf{4}}{EtO_2C-N=N-CO_2Et} + HN(CO)_2C_6H_4 \rightarrow$$

$$\rightarrow \underset{\mathbf{5}}{R{-}N(CO)_2C_6H_4} + Ph_3PO + EtO_2C{-}NH{-}NH{-}CO_2Et \qquad (1)$$

In the majority of the above mentioned reactions[2-6] triphenylphosphine **3** was used as the P^{III} component of the reacting system. When in the "amination" reaction (Eq. 1) **3** was replaced by a trialkylphosphine, the general course of the reaction remained unchanged, however, the yields of N-substituted phthalimides **5** were affected. Thus, in the case of 2-octanol the yield of N-(2-octyl)-phthalimide dropped to 50% when tri - n - butylphosphine was used,[8] compared to 82% yield achieved with Ph_3P.[6]

The course of the reaction (Eq. 1) was, however, completely changed when tris(dimethylamino)phosphine **6** was used as the phosphoroorganic substrate. In a smooth reaction, proceeding at room temperature, mixed carbonates, R^1OCOOR^2 **7**, were obtained in moderate to good yields. The formation of N-substituted phthalimides was not observed. Therefore, in repetition of experiments the addition of phthalimide was omitted without affecting the rate of the reaction. Our investigation started with monosaccharide derivatives containing "isolated" hydroxyl groups,[9] and was soon extended to a number of other alcohols. The results are collected in Table 1. The formation of side-products was observed in four cases (Table entries Nos. 1,2,6 and 7). These compounds were identified as derivatives of 1,2 - dicarbalkoxyhydrazine by spectroscopic and analytical data.[16]

We formulated the reaction equation for the mixed carbonate synthesis as follows:

$$\underset{\mathbf{2}}{R^1{-}OH + R^2O_2C{-}N=N{-}CO_2R^2} \xrightarrow{(Me_2N)_3P} \underset{\mathbf{7}}{R^1O{-}CO{-}OR^2} + N_2 + HCO_2R^2 \qquad (2)$$

This was based on the following observations:

(a) After mixing all substrates together, vigorous evolution of gas was observed. Gas chromatography of this gas indicated 72% nitrogen, 23% carbon monoxide and 5% carbon dioxide.

(b) Gas chromatography of the reaction mixture (when benzyl alcohol and diethyl azodicarboxylate **4** were used) showed the presence of ethyl formate, tris(dimethylamino)phosphine **6** and benzyl ethylcarbonate. Hexamethyl phosphoric acid triamide was not found.

(c) One mole of tris(dimethylamino) - phosphine **6** was capable of converting four molar equivalents of benzyl alcohol and **4** into benzylethyl carbonate. While the first portions of reactants reacted very quickly, the reaction with further amounts of substrates slowed down appreciably.‡

We assume that the first step in the reaction (Eq. 2) is the formation of a betaine[1,2] **8** which neutralizes its negative charge with a proton from the R^1OH molecule:

$$R^2O_2C{-}N{=}N{-}CO_2R^2 + (Me_2N)_3P \longrightarrow R^2O_2C{-}\underset{\displaystyle (Me_2N)_3P^{(+)}}{\underset{|}{N}}{-}\overset{(-)}{N}{-}CO_2R^2 \xrightarrow{+\,R^1OH} R^2O_2C{-}\underset{\displaystyle (Me_2N)_3P^{(+)}}{\underset{|}{N}}{-}NH{-}CO_2R^2 \quad R^1O^{(-)}$$

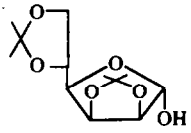
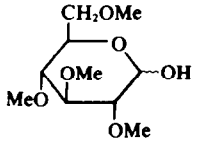
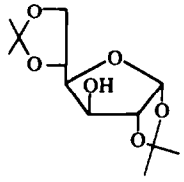
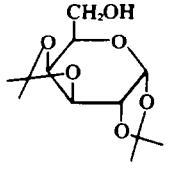
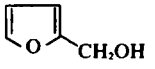
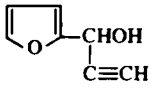
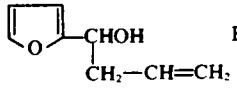
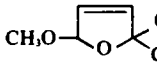
9

†Free amines can be obtained from N-substituted imides by a conversion reaction with primary aliphatic amines.[7]

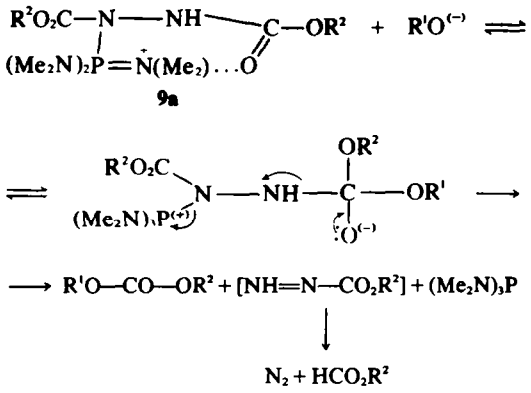
‡After addition of the fourth molar equivalent of benzyl alcohol and diethyl azodicarboxylate it was necessary to keep the solution overnight to complete the reaction.

The positive charge of **9** in its mesomeric form **9a** can be partially compensated by interaction with the π-electrons of the carbonyl group, which increases the electrophilicity of the carbonyl carbon atom. Further reaction with the R^1O anion at the carbon atom and subsequent electron

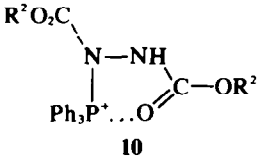
Table 1. Mixed carbonate R^1O–CO–OR^2

	Substrate R^1–OH	R^2	Yield%	b.p. (m.p.)	[α] 16 D (c 1,EtOH)	Calcd. C	Calcd. H	Found C	Found H
		Et[a]	40	130°/10^{-3} mm	+68·0°	54·2	7·3	54·3	7·4
	—"—	Bu[b]	45	135°/10^{-3} mm	+61·0°	56·7	7·8	56·9	7·9
		Et(β)[c]	16	120°/10^{-3} mm	−7·9°	50·6	7·9	50·5	7·7
		Et(α)[c]	62	120°/10^{-3} mm	+109·0°	50·6	7·9	50·5	7·8
4		Et	77	(78–79°)[d]	−33·9°	54·2	7·3	54·1	7·6
5	—"—	Bu	72	130°/10^{-3} mm[e]	−31·2°	56·7	7·8	56·6	7·9
6		Et[f,g]	65	(83–84°)	−44·6°	54·2	7·3	54·1	7·5
7	—"—	Bu[h]	65	130°/10^{-3} mm	−40·0°	56·7	7·8	56·9	8·0
8	$C_6H_5CH_2OH$	Et	75	130°/10 mm[i]	—	66·7	6·7	66·5	6·7
9	$(C_6H_5)_2CHOH$	Et	88	160°/10 mm[j]	—	75·0	6·3	75·0	6·3
10	$(C_6H_5)CH_3CHOH$	Et	84	135°/10 mm[k]	—	68·0	7·3	67·6	7·0
11		Et	71	125°/15 mm[l]	—	56·5	5·9	56·4	5·9
12		Et	35	160°/10 mm	—	61·9	5·2	61·9	5·5
13		Et	30	80°/10^{-1} mm	—	62·8	6·7	62·9	6·6
14		Et(cis)[n]	35	170°/10 mm	—	51·7	6·9	51·7	6·9
		Et(trans)[n]	9	170°/10 mm	—	51·7	6·9	51·7	7·1
15	$C_6H_5CH_2CH_2CH_2OH$	Et	25	105°/10^{-1} mm[o]	—	69·2	7·7	69·5	7·6
16	$C_{14}H_{29}OH$	Et	22	130°/5·10^{-2} mm	—	71·3	12·0	71·3	11·8

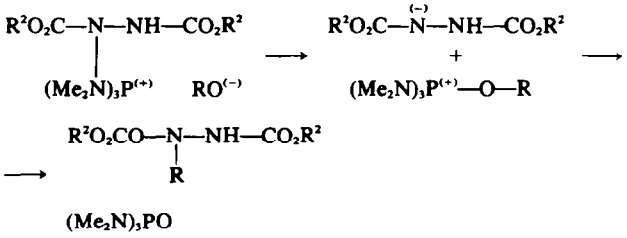
[a] The yield of the second product, (2,3,5,6 - di - 0 - isopropylidene - α - D - mannofuranosyl) - 1,2 - dicarbethoxyhydrazine, was 51%.
[b] Yield of (2,3:5,6 - di - 0 - isopropylidene - α - D - mannofuranosyl)-1,2 - dicarbobutoxyhydrazine 35%
[c] Anomers.
[d] Lit.[10] m.p. 73°, $[\alpha]_D$ − 38° ($CHCl_3$).
[e] Lit.[10] m.p. 37–38°, $[\alpha]_D$ − 35° ($CHCl_3$).
[f] Yield of 6 - (1,2 - dicarbethoxyhydrazino) - 6 - deoxy - 1,2:3,4 - di - 0 - isopropylidene - α - D - galactopyranose 5%.
[g] A sample of 6 - 0 - ethoxycarbonyl - 1,2:3,4 - di - 0 - isopropylidene - α - D - galactopyranose prepared from the substrate and ethyl chloroformate in pyridine was identical (IR, NMR, m.m.p.) with that obtained here.
[h] Yield of 6 - (1,2 - dicarbobutoxyhydrazino) - 6 - deoxy - 1,2:3,4 - di - 0 - isopropylidene - α - D-galactopyranose 5%.
[i] Lit.[11] b.p. 122–124°/20 mm.
[j] M.p. 47–48°, lit.[12] m.p. 52°.
[k] Lit.[13] b.p. 72°/0·5 mm.
[l] Lit.[14] b.p. 66°/0·6 mm.
[m] Mixture of cis and trans isomers.
[n] Cis configuration was ascribed to the isomer exhibiting, in the NMR spectrum, an H-5 signal at δ 5·58 and trans to that showing H-5 at δ 5·85.[15]
[o] Lit.[14] b.p. 130°/2 mm.



shifts lead to a carbonate molecule and other products. We think that intramolecular transfer of the positive charge in the phosphonium ion **10** is also responsible for the formation of small amounts of mixed carbonates which were observed in "amination" reactions (Eq. 1).[17] Apparently, a five-membered quasi-ring **10** is sterically less favourable than the six-membered one.



The formation of substituted 1,2-dicarboxyhydraxines as by-products can be accounted for by the following reaction sequence (cf. also ref. 3):



The classical method for the preparation of mixed carbonates utilizes the reaction of alkyl chloroformates with alcohols in the presence of bases.[18] The reactions described in this paper represent a new method of carbonate synthesis, which can be competitive with the chloroformate method especially in those cases when neutral reaction conditions are required. Also, the results presented here extend the knowledge of the reactivity of the R_3P-dialkyl azodicarboxylate system.

EXPERIMENTAL

M.ps and b.ps are uncorrected. Optical rotations were measured with a Perkin-Elmer Model 141 automatic polarimeter at 25°. IR spectra were recorded with a Unicam SP-200 spectrophotometer (film or KBr discs). All carbonates showed a strong carbonyl absorption between 1745 and 1760 cm^{-1} (cf. 1740 – 1760 cm^{-1}).[19] NMR spectra were recorded on a Varian HA-60/IL (60 MHz) and Jeol JMN-4 H-100 (100 MHz) spectrometers. The NMR spectra of carbonates showed all signals of the parent compounds, with the –CH–OCOOR proton signal shifted *ca.* 1 ppm downfield compared with the starting alcohol, signals of the EtO or BuO groups were also present. TLC was performed with Silica gel G, Merck, and column chromatography with Silica gel for chromatography, Merck. Derivatives of monosaccharides were obtained according to methods described.[20] 1(2-Furyl) - prop - 2 - yn - 1 - ol and 1(2-furyl) - but - 3 - en - 1 - ol were prepared from furfural and acetylene[21] and allylmagnesium bromide,[22] respectively. 2,5-Dimethoxy-2,5-dihydrofurfuryl alcohol was prepared from furfuryl alcohol by the reaction with bromine in methanol.[23] Other alcohols were of commercial origin, purified before use.

1 - 0 - *Ethoxycarbonyl* - 2,3:5,6 - *di* - 0 - *isopropylidene* - α - D - *mannofuranose and* N - (2,3:5,6 - *di* - 0 - *isopropylidine* - α - D - *mannofuranosyl*) - 1,2 - *dicarbethoxyhydrazine.* A solution of 2,3:5,6 - di - 0 - isopropylidene - D - mannofuranose (520 mg, 2 mmol) and tris(dimethylamino)phosphine (**6**, 326 mg, 2 mmol) in 10 ml of tetrahydrofuran was treated with 0·44 g (2·2 mmol) of diethyl azodicarboxylate **4**, and left overnight at room temperature. The solvent was evaporated under reduced pressure, and the residue chromatographed over a silica gel column with a mixture of benzene and ether (9:1 v/v) affording 266 mg (40·1%) of the title carbonate and 425 mg (51%) of the hydrazino compound.

1 - 0 - *Butoxycarbonyl* - 2,3:5,6 - *di* - 0 - *isopropylidene* - α - D *mannofuranose and* N(2,3:5,6 - *di* - 0 - *isopropylidene* - α - D - *mannofuranosyl*) - 1,2 - *dicarbobutoxyhydrazine* were obtained in an analogous preparation in which **4** was replaced by dibutyl azodicarboxylate.

To all products α anomeric configuration was assigned on the basis of the H-1 NMR signal being a singlet in all four cases (β anomers of alkyl 2,3:5,6- di - 0 - isopropylidene - D - mannofuranosides exhibit H-1 as a doublet with $J_{12} \approx 3{\cdot}5$–$4{\cdot}0$ Hz).

1 - 0 - *Ethoxycarbonyl* - 2,3,4,6 - *tetra* - 0 - *methyl* - α *and* β - *glucopyranosides.* A solution of 2,3,4,6 - tetra - 0 - methyl - D - glucopyranose (236 mg, 1 mmol) and **6** (163 mg, 1 mmol) in 5 ml THF was treated with 0·22 g (1·1 mol) of **4** at room temperature, and left overnight. After evaporation of the solvent, products were isolated by column chromatography using a mixture of petroleum ether and ethyl acetate (8:2 v/v) for elution. β Anomeric carbonate (48 mg, 15·5%) was eluted first, followed by the α anomer (190 mg, 61·8%). The anomeric configuration was ascribed on the basis of the H-1 NMR signal: δ 6·28, $J_{12} = 3{\cdot}4$ Hz for the α and δ 5·40, $J_{12} = 7{\cdot}6$ Hz for the β anomer.

3 - 0 - *Ethoxycarbonyl- and* 3 - 0 - *butoxycarbonyl* - 1,2:5,6 - *di* - 0 - *isopropylidene* - α - D - *glucofuranoses*, 6 - 0 - *ethoxycarbonyl* - *and* 6 - 0 - *butoxycarbonyl* - 1,2:3,4 - *di* - 0 - *isopropylidene* - α - D - *galactopyranoses* were obtained analogously from equimolar amounts of 1,2:5,6 - di - 0 - isopropylidene - α - D - glucofuranose or 1,2:3,4 - di - 0 - isopropylidene - α - D - galactopyranose, $P(NMe_2)_3$ and diethyl or dibutyl azodicarboxylate. In the case of galacto compounds 5% of the corresponding 1,2-dicarbalkoxyhydrazino derivatives were isolated by chromatography (see Table 1).

Ethoxycarbonyl derivatives of alcohols (Table, entries Nos. 8–16) were prepared as follows. To the solution of the alcohol (1 mmol) and **6** (1 mmol) in 5 ml of THF, 1·1 mmol of diethyl azodicarboxylate was added and the mixture was left overnight at room temperature. The product was isolated by distillation. In the case of ethyl (2,5 - dimethoxy - 2,5 - dihydrofurfuryl) carbonate cis and trans isomers were separated on a silica gel column with a mixture of petroleum ether and ethyl acetate (9:1 v/v).

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