REACTION OF DICYCLOHEXYLCARBODIIMIDE WITH CARBOXYMETHYLTRIPHENYLPHOSPHONIUM CHLORIDE

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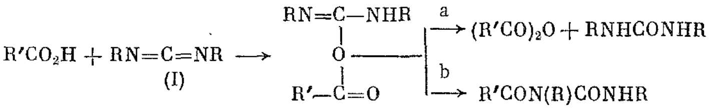
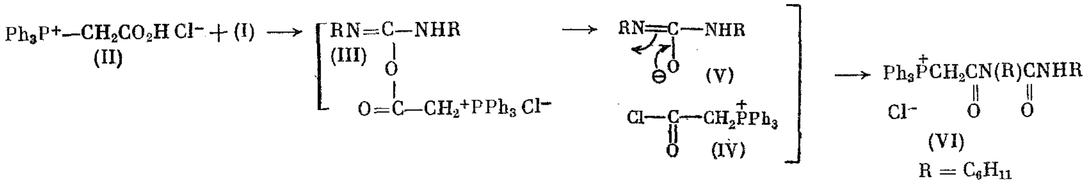
Dicyclohexylcarbodiimide (DCC) (I) reacts with carboxylic acids to give: a) acid anhydrides (main direction), and b) N-acyldialkylureas [1, 2]. The role of the first direction increases with increase in the concentration and ionization constants of the acid [2, 3].



In the present paper it was established that the reaction of (I) with carboxymethyltriphenylphosphonium chloride (II) goes exclusively by path b, despite the substantial strength of acid (II).* In CH_2Cl_2 (20°C), at a reactant concentration of 0.3 mole/liter, the reaction is ended in less than 5 min and acylurea (VI) is formed in quantitative yield. Immediately after mixing the reactants the difficultly soluble acid goes into solution, whose IR spectrum is identical with the spectrum of the end product (VI). The $^{31}P-\{^1H\}$ NMR spectrum has one singlet of the reaction product at 22 ppm. It could be assumed that this direction of the reaction is caused by a lack of acid in the solution due to its poor solubility. However, the same reaction with a double excess of the acid in DMF, in which (II) is completely soluble, leads to the same results: The excess acid remains in solution and gradually decarboxylates to give $Ph_3\overset{+}{P}-MeCl^-$. It is known that acid (II) is decarboxylated instantly by bases [5]. Since this does not occur when (I) and (II) are reacted, the proton and anion of this acid apparently add simultaneously to the carbodiimide.



The absence of the anhydride of acid (II) in the reaction products† must be explained by the rapid rearrangement of the intermediate addition product (III). It could be assumed that in this case the rearrangement rate is especially great due to the presence of a counterion (Cl^-), which is acylated with the intermediate formation of the ion pair of acid chloride (IV) and mesomeric anion (V). The latter is immediately irreversibly acylated at the N. In such case this rearrangement in its mechanism resembles our described O → C rearrangement of O-alkylated [6] and O-acylated phosphorus β-ketoylides [7].

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* It could be expected that acid (II) should be a strong acid due to the inductive effect of the positively charged phosphorus, but its pK_a could not be determined due to the rapid decarboxylation of the salts.

† It could be assumed that the anhydride and dialkylurea are formed initially, and then the latter is acylated. However, it is known that even such an acylating agent as trifluoroacetic anhydride reacts very slowly with a dialkylurea [4].

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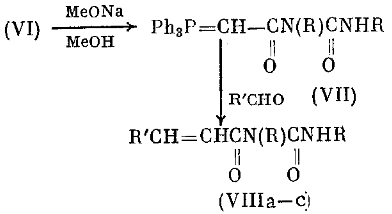
Phosphonium salt (VI) is readily soluble in polar organic solvents, is gradually hydrolyzed by water, and is converted to the stable ylide (VII) when treated with sodium methylate in methanol. The latter reacts smoothly with various aldehydes via the Wittig reaction, which makes it possible to synthesize an acylurea with a conjugated system of C = C − C = O bonds.



R = C_6H_{11}, R′ = CCl_3 (a), Ph (b), Me (c)

EXPERIMENTAL

Absolute solvents were used. The IR spectra were recorded on a UR-20 spectrophotometer in fluorite cells with a layer thickness of 0.1 mm. The $^{31}P-\{^1H\}$ NMR spectra were taken on a Bruker HX-90 instrument (36.43 MHz) using H_3PO_4 as the external standard.

Preparation of (II). To a solution of 5.2 g (20 mmoles) of Ph_3P in dichloroethane was added a solution of 2 g (21 mmoles) of chloroacetic acid. After a week the solvent was distilled from the reaction mixture. The residue crystallized when rubbed with ether. We obtained 4.9 g (70%) of (II), mp 220°C (reprecipitated from DCE solution with ether) (cf. [5]). Infrared spectrum (Nujol, ν, cm^{-1}): 1450 (m, P−Ph), 1740 (s, C = O), 2200-2800 (OH•••H). $^{31}P-\{^1H\}$ NMR spectrum (δ, ppm): 20.1 s (DMF); 20.2 s (CH_2Cl_2).

1,3-Dicyclohexylureidocarbonylmethyl)triphenylphosphonium Chloride (VI). To a suspension of 1.3 g (36 mmoles) of salt (II) in CH_2Cl_2 was added 0.85 g (41 mmoles) of DCC in CH_2Cl_2. The solution becomes clear after 5 min. The solvent was removed and the residue was washed with ether to give 2.08 g (99%) of (VI), mp 175-178° (reprecipitated from CH_2Cl_2 with ether). Found: C 69.92; H 6.86; P 5.44; N 4.80%. $C_{33}H_{40}ClN_2O_2P$. Calculated: C 70.39; H 7.16; P 5.50; N 4.97%. IR spectrum (CH_2Cl_2, ν, cm^{-1}); 1450 m (P−Ph), 1540 s (amide II), 1660 s, (NHCON), 1705 s, (C = O), 3150 w (NH). IR spectrum (Nujol, ν, cm^{-1}): 1540, 1655, 1710. NMR spectrum (δ, ppm): 21.54 s (CH_2Cl_2), 21.21 s (DMF).

Reaction of (II) with (I) (2:1). Using a 2:1 ratio of the reactants, in CH_2Cl_2, the absorption bands of product (VI) are observed in the IR spectrum of the filtrate after 5 min. The excess acid remains undissolved and is completely decarboxylated in a day. The IR spectrum has the absorption band of CO_2 at 2370 cm^{-1}, while the PMR spectrum indicates the presence of methyltriphenylphosphonium chloride (IX) in the reaction mixture.

Reaction of DMF, where the acid is completely soluble, gives the same results. Together with the signal of the acylated urea (VI) at 21.14 ppm, 5 min after mixing the reactants (0.0006 and 0.003 M in 2 ml of DMF) the ^{31}P NMR spectrum displays the signal of the starting acid at 20.14 ppm. After 2.5 h this signal decreases nearly in half, with the simultaneous appearance of an equally intense signal of phosphonium salt (IX) at 22.3 ppm.

(1,3-Dicyclohexylureidocarbonylmethylene)triphenylphosphorane (VII). The calculated amount of MeONa was added dropwise to a solution of 1.14 g (2 mmoles) of salt (VI) in MeOH. The methanol was removed completely, and the ylide was extracted from the residue with CH_2Cl_2. After distilling off the solvent the residue was washed with ether and recrystallized from acetone to give 0.57 g (55%) of (VII), mp 157-158°. Found: C 75.09; H 7.45; P 5.86; N 5.20%. $C_{33}H_{39}N_2O_2P$. Calculated: C 75.26; H 7.46; P 5.88; N 5.32%. IR spectrum (CH_2Cl_2, ν, cm^{-1}): 1450 m, (P−Ph), 1520 s, (P = C − C = O), 1665 s$(-NH-CO-\underset{|}{N}-)$, 3070 w (NH). ^{31}P NMR spectrum (δ, ppm): 17.6 s (CH_2Cl_2).

Reaction of Ylide (VII) with Aldehydes. A 20% excess of the freshly distilled aldehyde was added at 20° to a solution of (VII) in CH_2Cl_2. After 14 h the solvent was removed in vacuo from the reaction mixture. The residue was recrystallized twice from MeOH. The yield* and constants of the obtained compounds are given in Table 1.

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* The low yields are explained by the losses incurred during the recrystallizations, which were needed to completely remove the Ph_3PO.

TABLE 1. Unsaturated Compounds $RCH=CHCON(C_6H_{11})CONHC_6H_{11}$

R	Yield, %	mp, °C	Found/calc., %			Empirical formula	Infrared spectrum (CH_2Cl_2, ν, cm^{-1})
			C	H	N		
CCl_3	45	141,5–142	51,39 51,60	6,11 6,37	6,83 7,08	$C_{17}H_{25}Cl_3N_2O_2$	1515 (s, amide II) 1645 (m, C=C) 1670, 1720 (s, –CO–NH–CO–) 3070 (w, NH)
Ph	60	167	74,54 74,54	8,44 8,53	7,88 7,90	$C_{22}H_{30}N_2O_2$	1520 (s, amide II) 1625 (m, C=C) 1665, 1710 (s, –CO–NH–CO–) 3070, 3300 (w, NH)
Me *	31	143–144	69,92 69,83	10,04 9,65	9,64 9,58	$C_{17}H_{28}N_2O_2$	1520 (s, amide II) 1640 (m, C=C) 1675, 1709 (s, –CO–NH–CO–) 3070, 3300 (w, NH)

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* Judging by the TLC of the reaction mixture and the end product, it is possible that one of the geometric isomers is lost after recrystallization from methanol.

CONCLUSIONS

1. Dicyclohexylcarbodiimide reacts with carboxymethyltriphenylphosphonium chloride to give exclusively N-acyl-N,N'-dicyclohexylureas. A mechanism of the rearrangement was proposed.

2. The stable ylide (1,3-dicyclohexylureidocarbonylmethylene)triphenylphosphorane was obtained, from which were synthesized N-acyl-N,N'-dialkylureas with a conjugated system of C=C–C=O bonds.

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