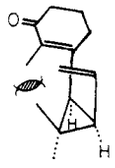
4 Hz. Since it is well known[7] that coupling constants associated with *cis*-vicinal protons on cyclopropane systems are larger than those related to trans protons, the stereochemical assignments appeared to be secure.

In spite of the fact that the copper-bearing carbon atom of the cis cuprate **4** appears to be quite hindered, this reagent reacted smoothly with the iodo enones **13**[8] and **1**[8] to afford the substitution products **14** and **17**, respectively (see Scheme II). Although the former product **14** could be isolated in nearly pure form if reaction workup was carried out at or below room temperature, this compound rearranged slowly (to **15**) upon standing. When a solution of **14** in hexane (bp 69 °C) was refluxed for ~4 h, **15** could be obtained in nearly quantitative yield. If either **14** or **15** was briefly heated (110 °C, neat) and then distilled under reduced pressure, the conjugated ketone **16** was obtained in >90% yield.

In marked contrast to **14**, the structurally similar compound **17** was extraordinarily resistant to Cope rearrangement. In fact, it was found that in this case, there was a competition between rearrangement and "simple" epimerization. For example, when a solution of **17** in *o*-dichlorobenzene (bp 179 °C) was refluxed for 3 h, there was obtained, in high yield, a mixture of two products **18** and **19** (ratio 0.8:1, respectively). In refluxing *o*-xylene (bp 144 °C), ~48 h was required for complete disappearance of **17**, and the two products **18** and **19** were obtained in a ratio of 2.7:1. Under both sets of conditions, the trans isomer **19** was stable.

The Cope rearrangement of *cis*-divinylcyclopropane systems has been proposed[9] to proceed via a boatlike transition state in which the vinyl groups are folded back over the three-membered ring. Molecular models clearly show that if such a geometric arrangement is to be achieved in the case of **17**, there is introduced a severe steric interaction between the vinyl methyl group and the *cis*-methyl group on the cyclopropane ring (cf. **17a**). This type of interaction is not involved in the rearrangement of **2** and **14** and it is thus possible to rationalize, in a qualitative way, the striking difference in reactivity of **17** vs. **2** and **14**.[10]



17a

Treatment of the iodo enones **13** and **1** with the trans cuprate reagent **5** gave excellent yields of the substitution products **20** and **19**, respectively. Cope rearrangement of the former under conditions outlined in Scheme II afforded the annelation product **16** as the only isolable product (59% yield). Similar treatment of **19**, however, resulted mainly in a homo-[1,5]-sigmatropic hydrogen shift[11] to afford the trienone **21**. In this case, the annelation product **18** was formed in only minor amounts (ratio of **18**/**21** = 1:4).

Acknowledgment. Financial support from the National Research Council of Canada and a N.R.C.C. Postgraduate Scholarship (to H.E.M.) are gratefully acknowledged.

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(4) All compounds reported herein exhibited spectral data in full accord with the assigned structures. New compounds gave satisfactory elemental analysis and/or molecular weight determinations (high-resolution mass spectrometry).
(5) The product obtained from the Zn–HOAc reduction of **8** contained **9** and **12** in a ratio of approximately 20:1, respectively. Reduction of **8** with tri-*n*-butyltin hydride gave **9** and **12** in a ratio of about 3.7:1.
(6) In this conversion, the isomeric monobromide could not be detected in the crude product.
(7) Cf. D. H. Williams and I. Fleming, "Spectroscopic Methods in Organic Chemistry", McGraw-Hill, London, 1973, p 107.
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Received April 10, 1978

New Methods and Reagents in Organic Synthesis. 3.[1] Diethyl Phosphorocyanidate: A New Reagent for C-Acylation

Summary: Diethyl phosphorocyanidate [DEPC, $(EtO)_2P(O)CN$], in combination with triethylamine, has been proved a new efficient reagent for the direct C-acylation of active methylene compounds with carboxylic acids.

Sir: Recent publications from our laboratory have revealed that diethyl phosphorocyanidate [DEPC, $(EtO)_2P(O)CN$], in combination with triethylamine, may be used for (i) N-acylation (peptide bond formation),[2-5] (ii) S-acylation (thiol ester formation),[6] and (iii) O-acylation (esterification)[3] (eq 1–3).

$$RCO_2H \xrightarrow[Et_3N]{(EtO)_2P(O)CN} \begin{cases} \xrightarrow{R'NHR''} RCONR'R'' & (1) \\ \xrightarrow{R'SH} RCOSR' & (2) \\ \xrightarrow{R'OH} RCO_2R' & (3) \end{cases}$$

We now wish to report that DEPC, together with triethylamine, may be efficiently used for the direct C-acylation of active methylene compounds with carboxylic acids as follows (eq 4).

$$RCO_2H + CH_2\begin{<}{X}{Y} \xrightarrow[Et_3N]{(EtO)_2P(O)CN} RCOCH\begin{<}{X}{Y} \qquad (4)$$

X and/or Y: electron-withdrawing group

In the usual base-catalyzed C-acylation of active methylene compounds,[7] carboxylic acids should first be converted to their activated derivatives such as acyl chlorides, acyl cyanides,[8,9] acyl azides,[10,11] mixed anhydrides,[12] carboxylic esters, and so on. Very few methods are concerned with the C-acylation by the direct use of carboxylic acids without prior isolation of active intermediates. Using DEPC in the presence of triethylamine, however, the direct C-acylation[13] of active methylene compounds with carboxylic acids easily occurs in a single operation under exceptionally mild conditions.

The preferred procedure is as follows. To a mixture of the carboxylic acid (1.2 equiv) and the active methylene compound (1 equiv) in dimethylformamide is added DEPC (1.2 equiv), followed by the addition of triethylamine (3.2 equiv). The mixture is stirred with ice cooling for 2 h, and then at room temperature for 20 h. After evaporation of the solvent, the residue is dissolved in benzene–ethyl acetate (1:1) and worked up with acid (10% aqueous H_2SO_4) and alkali (5% aqueous $NaHCO_3$). The crude product is purified by silica gel column chromatography and/or recrystallization. When the acylated product is an oil, it is characterized as its copper salt.

The reactions are best carried out in dimethylformamide solution, though hexane, toluene, diethyl ether, or tetrahydrofuran may be used. We preferably used triethylamine as a base, but *N,N,N',N'*-tetramethylethylenediamine 1,5-

0022-3263/78/1943-3631$01.00/0

Table I

$RCO_2H + CH_2(X)(Y) \xrightarrow[\text{in DMF}]{(EtO)_2P(O)CN,\ Et_3N^a} RCOCH(X)(Y)$

R	X	Y	yield,[b] %	mp,[c] °C
Ph	CN	CO_2Et	93.4 (83)[d]	39.5–40[d]
Ph	NO_2	H	85.5 (73)[e]	106–108[e]
Ph	CN	CN	92.8 (88)[f]	129[f]
			(87)[g]	
Ph	CO_2Et	CO_2Et	96.8[h]	(183–184)[j]
			(68–75)[i]	
Ph	NC	Tos	80.7 (65)[k]	139–141[k]
$Ph(CH_2)_2$	CN	CO_2Et	98.4	(209–211)
n-C_5H_{11}	CN	CO_2Et	97.2	(101–102)
$CH_3CO(CH_2)_2$	CN	CO_2Et	93.4	(168–170)
$CH_3CO(CH_2)_2$	CN	CO_2Bu^t	quant	(163–164)
$CH_3C(CH_2)_2$ (O O)	CO_2Et	CO_2Et	58.1[l]	(134–136)
$PhCH_2CH(NHCOOCH_2Ph)$-	CN	CO_2Et	87.8	146–148[m]
$CH_3CH(OH)CH(NHCOOCH_2Ph)$-	CN	CO_2Et	63.8	128–130[n]

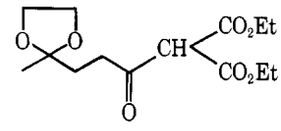
[a] Unless otherwise stated, the reactions were carried out as described in the text. [b] Yields by the reported procedures are in parentheses. [c] Melting points of copper salts are in parentheses. [d] Benzoyl cyanide was used: lit.[8] mp 41 °C. [e] Benzoyl cyanide was used: lit.[9] mp 105–106 °C. [f] Benzoyl cyanide was used: lit.[8] mp 129–130 °C. [g] Benzazide was used.[10] [h] Sodium hydride was used in place of triethylamine. [i] The mixed anhydride from benzoic acid and ethyl chlorocarbonate was used.[12] [j] Lit. mp 182 °C: D. S. Tarbell and J. A. Price, *J. Org. Chem.*, **22**, 245 (1957). [k] Benzoyl chloride was used. The isolated product was 5-phenyl-4-tosyloxazole. Lit. mp 142–143 °C: A. M. van Leusen, B. F. Hoogenboom, and H. Siderius, *Tetrahedron Lett.*, 2369 (1972). [l] Sodium hydride (2 equiv) and 1,5-diazabicyclo[5.4.0]undec-5-ene (2 equiv) were used in place of triethylamine. [m] $[\alpha]^{23}_D$ +37.1° (*c* 0.9, benzene). [n] $[\alpha]^{23}_D$ +38.2° (*c* 0.99, chloroform).

diazabicyclo[5.4.0]undec-5-ene, sodium hydride, or potassium carbonate can be used with similar efficiency. Three equivalents of the base are indispensable, because 2 equiv are used for the activation of both the carboxylic acid and the active methylene compound and 1 equiv for the salt formation of the acylated product.

The scope of the new C-acylation procedure is shown in Table I.[14] Benzoic acid efficiently coupled with various active methylene compounds, e.g., ethyl cyanoacetate, nitromethane, malononitrile, diethyl malonate, and tosylmethyl isocyanide. In the case of benzoylation of diethyl malonate, the use of sodium hydride in place of triethylamine gave a better result. Compared with the known method using activated forms of benzoic acid, the present method is more convenient to perform and gives benzoylated products in much higher yields under mild reaction conditions, as shown in Table I.

3-Phenylpropionic acid and hexanoic acid caused no trouble to couple with ethyl cyanoacetate. Levulinic acid which contains γ-keto function smoothly reacted with cyanoacetates to give the corresponding C-acylated products in excellent yields. The ethylene ketal derivative of levulinic acid also coupled with diethyl malonate to yield the C-acylated product **1**, which was easily converted to the 1,4-diketone[15] **2** by the successive treatment with (i) allyl iodide in the presence of tetra-*n*-butylammonium hydroxide,[16] (ii) sodium chloride in hot wet dimethyl sulfoxide,[17] and (iii) methanolic hydrogen chloride.

Another interesting example of the C-acylation is the coupling of ethyl cyanoacetate with two N-protected derivatives



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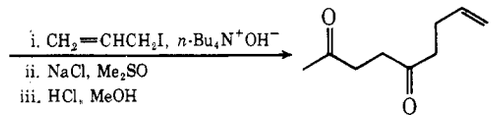

2

of α-amino acids, i.e., *N*-benzyloxycarbonyl-L-phenylalanine and -L-threonine, since the optical activities of the starting acids were retained in the products.

This direct C-acylation procedure in a single operation using DEPC appears to be quite general, may be used for many substrates containing various functions, and offers advantages over many existing methods.

Acknowledgment. We wish to thank Emeritus Professor S. Yamada and Professor K. Koga of University of Tokyo for their interests and discussions.

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Received April 18, 1978

Thallium in Organic Synthesis. 52. Oxidations of 3-(Alkoxyaryl)propionic Acids by Thallium(III) Trifluoroacetate: Synthesis of Dihydrocoumarins, Spirocyclohexadienone Lactones, and *p*-Benzoquinones[1,2]

Summary: Dihydrocoumarins, spirocyclohexadienone lactones, and *p*-benzoquinones are formed via intramolecular capture of radical cation intermediates generated from 3-(alkoxyaryl)propionic acids by oxidation with TTFA.

Sir: The products obtained from the reactions of aromatic compounds with thallium(III) trifluoroacetate (TTFA) depend on the oxidation potentials of the aromatic substrates. Arylthallium bis(trifluoro)acetates, the products of overall

0022-3263/78/1943-3632$01.00/0