give a liquid, bp 43° (10 mm). Analysis by glc, ir, and ^{19}F nmr indicated that two compounds were present in about equal amounts. One product was **3**. The other product (probably **5**) showed an ir band at 5.73 μ for C=N and two septets of equal intensity in the ^{19}F nmr spectrum. Attempts to isolate this second product were unsuccessful, for it apparently decomposes easily to hexafluoroacetone and hexafluoroacetone cyanohydrin.

Conversion of 3 to 2,2,5,5-Tetrakis(trifluoromethyl)-4-oxazolidinone (4) by Sodium Hydride.—A solution of 8.5 g of **3** in 10 ml of ethylene glycol dimethyl ether was added to a slurry of 1 g of sodium hydride in mineral oil (50%) in 15 ml of ethylene glycol dimethyl ether. The mixture was then warmed to 50° and the resulting solution was poured into ice and acidified with hydrochloric acid. The oil that formed was extracted with methylene chloride, dried, and distilled to give 3.2 g (38%) of **4**, bp 89° (20 mm), mp 104–106° (after recrystallization from benzene), identified by comparison with an authentic sample.[2]

Registry No.—**1**, 38868-31-4; **1** nitro derivative, 38868-32-5; **2**, 22038-16-0; **3**, 38868-34-7; **3** methyl ether derivative, 38868-35-8; **4**, 7730-28-1; **6**, 677-77-0; hexafluoroacetone, 684-16-2; hydrogen cyanide, 74-90-8.

Synthetic Reactions by Complex Catalsts. XXIX. Esterification of Carboxylic Acid with Alkyl Halide by Means of Copper(I)–Isonitrile Complex

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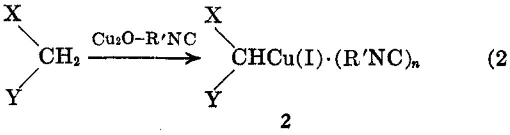
Received September 26, 1972

In a preliminary paper,[1] we have reported that carboxylic acid is readily esterified with alkyl halide in the presence of Cu_2O–isonitrile complex. A reaction scheme was presented in which Cu(I) carboxylate–isonitrile complex (**1**) was first generated from Cu_2O–isonitrile complex and carboxylic acid, and then **1** reacted with alkyl halide to produce the corresponding carboxylic ester (Scheme I).

Scheme I

$$\mathrm{RCO_2H} \xrightarrow{\mathrm{Cu_2O{-}R'NC}} \underset{\mathbf{1}}{\mathrm{RCO_2Cu(I)\cdot(R'NC)_{\mathit{n}}}} \xrightarrow{\mathrm{R''X}} \mathrm{RCO_2R'' + Cu(I)X\cdot(R'NC)_{\mathit{n}}} \quad (1)$$

In the present paper, we wish to report the isolation of Cu(I) carboxylate–isonitrile complex (**1**) as a key intermediate in the above reaction and the stereochemistry of the reaction. It is of interest to note that **1** in Scheme I constitutes a counterpart of organocopper(I)–isonitrile complex (**2**) derived from the reaction of acidic carbon acid such as acetylacetone and malonate with the Cu_2O–isonitrile complex.[2,3]



$$\mathrm{(X)(Y)CH_2} \xrightarrow{\mathrm{Cu_2O{-}R'NC}} \underset{\mathbf{2}}{\mathrm{(X)(Y)CHCu(I)\cdot(R'NC)_{\mathit{n}}}} \quad (2)$$

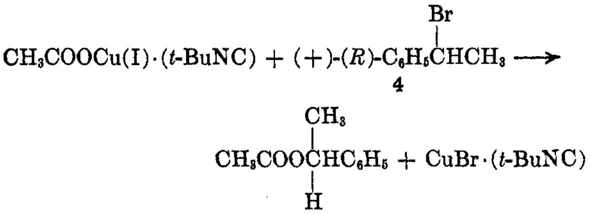
Isolation of Cu(I) Carboxylate–Isonitrile Complex.—On heating, Cu_2O was dissolved in acetic acid in the presence of *tert*-butyl isocyanide under nitrogen. From the reaction mixture, Cu(I) acetate-*t*-BuNC complex (**3**) was isolated. **3** is a white, crystalline

$$\underset{\mathbf{3}}{\mathrm{CH_3COOCu(I)\cdot(\mathit{t}\text{-}BuNC)}}$$

solid, which is soluble in acetonitrile and hot benzene, and air sensitive. **3** could be purified by recrystallization from hot benzene under nitrogen. In the presence of an additional amount of *t*-BuNC, **3** is readily soluble in benzene even at room temperature. The elemental analysis, nmr, and ir were in accord with the structure of **3** (see Experimental Section). By a similar way, Cu(I) benzoate-*t*-BuNC complex was prepared.

3 reacted with alkyl halide even at room temperature to give the corresponding acetate. In the reaction of **3** with phenethyl bromide and chloride, phenethyl acetate was obtained in the yields of 88 and 12%, respectively. For the purpose of comparison, Cu(I) acetate prepared by Calvin's procedure[4,5] was also treated with alkyl halide. The results are summarized in Table I. Here it is seen that the isonitrile ligand enhances the reactivity of Cu(I) carboxylate toward alkyl halide.

Reaction of Cu(I) Acetate-*t*-BuNC Complex with (+)-(*R*)-Phenethyl Bromide.—The stereochemical course of the reaction of Cu(I) carboxylate-*t*-BuNC with alkyl halide was examined using an optically active halide, (+)-(*R*)-phenethyl bromide (**4**), having $[\alpha]^{25}\mathrm{D}$ +58.6°. The optical purity of **4** employed in the present study was 45%.[6]



$$\mathrm{CH_3COOCu(I)\cdot(\mathit{t}\text{-}BuNC)} + (+)\text{-}(R)\text{-}\underset{\mathbf{4}}{\mathrm{C_6H_5\overset{Br}{C}HCH_3}} \longrightarrow \mathrm{CH_3COO\underset{H}{\overset{CH_3}{C}}HC_6H_5 + CuBr\cdot(\mathit{t}\text{-}BuNC)} \quad (3)$$

$[\alpha]^{25}\mathrm{D}$ −41.6° (*c* 6.27, cyclohexane)

The reaction proceeded quantitatively (Table I). The product was purified by preparative glpc, which showed an optical rotation of $[\alpha]^{25}\mathrm{D}$ −41.6° (Table I). The optical purity was calculated at 33% on the basis of the known rotation of optically pure phenethyl acetate.[7] As the authentic ester, (−)-(*S*)-phenethyl acetate was prepared by the reaction of (−)-(*S*)-phenethyl alcohol with acetic anhydride in pyridine, which was known to proceed with the retention of configuration.[7] It has been established that the bromination of alcohol using PBr_3 proceeds with the inversion of

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[1] T. Saegusa and I. Murase, *Syn. Commun.*, **2**, 1 (1972).

[2] T. Saegusa, Y. Ito, and S. Tomita, *J. Amer. Chem. Soc.*, **93**, 5656 (1971).

[3] T. Saegusa, Y. Ito, S. Tomita, and H. Kinoshita, *Bull. Chem. Soc. Jap.*, **45**, 496 (1972).

[4] M. Calvin, *J. Amer. Chem. Soc.*, **61**, 2230 (1939).

[5] T. Cohen and A. H. Lewin, *J. Amer. Chem. Soc.*, **88**, 4521 (1966).

[6] C. L. Arcus and G. V. Boyd, *J. Chem. Soc.*, 1580 (1951).

[7] R. Huisgen and C. Rüchardt, *Justus Liebigs Ann. Chem.*, **601**, 31 (1956).

TABLE I

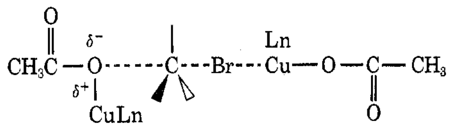
REACTION OF COPPER(I) ACETATE WITH PHENETHYL HALIDES

Copper acetates[f] (mmol)	Halides[f] (mmol)	Temp, °C	Time, hr	Product	
				Yield, %	Optical activity $[\alpha]^{22}\mathrm{D}$
$CH_3COOCu(I)$ (4.1) (598-54-9)	(±)-Phenethyl bromide (5)[b] (38661-81-3)	45	3	93	
$CH_3COOCu(I)$ (4.1)	(±)-Phenethyl bromide (2.4)[b]	r.t.[d]	2	52	
3 (8) (38641-29-1)	(±)-Phenethyl bromide (5)[a,c]	r.t.[d]	2	88	
3 (8)	(±)-Phenethyl chloride (5)[a,c] (38661-82-4)	r.t.[d]	2.5	12	
3 (8)	(±)-Phenethyl chloride (5)[a,c]	50	1	56	
$(CH_3COO)_2Cu(II)$ (5) (142-71-2)	(±)-Phenethyl bromide (5)[b]	45	3	Trace	
$CH_3COOCu(I)$ (3)	(+)-(*R*)-Phenethyl bromide (2.2)[b] (1459-14-9)	50	3	>90	−0.3° (*c* 6.62, cyclohexane)[e]
3 (4)	(+)-(*R*)-Phenethyl bromide (2.4)[b]	45	2	>90	−41.6° (*c* 6.27, cyclohexane)[e]

[a] The reaction was carried out in the presence of *tert*-butyl isocyanide (4 mmol). [b] Benzene (5 ml) was used as solvent. [c] Benzene (10 ml) was used as solvent. [d] r.t. = 18–20°. [e] Optical purity can be calculated on the optically pure phenethyl acetate[7] having $[\alpha]^{21}\mathrm{D}$ −124.5 (*c* 3, benzene). [f] Registry numbers are in parentheses below compound.

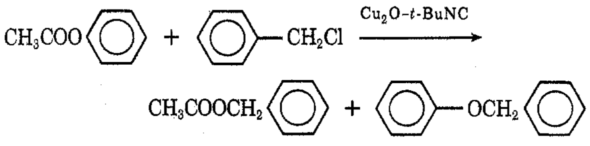
configuration.[8,9] From these facts, it is concluded that the reaction (3) proceeds with a predominant stereochemistry of ~75% inversion of configuration. Next, Cu(I) acetate[4,5] having no isonitrile ligand was subjected to the reaction with optically active (+)-(*R*)-phenethyl bromide ($[\alpha]^{25}\mathrm{D}$ +58.6°) under the designated conditions in Table I. In this case, the product, phenethyl acetate, has a very small rotation of $[\alpha]^{25}\mathrm{D}$ −0.3°, indicating that this reaction proceeds with racemization. Here, it has become clear that the employment of isonitrile ligand in the reaction of Cu(I) carboxylate with alkyl halide greatly influences the stereochemistry of the reaction. Recently, Lewin[10] reported that the reaction of copper(I) carboxylate with alkyl halide in refluxing pyridine afforded ester with inversion. This is not inconsistent with our results, because pyridine as well as isonitrile are strongly coordinated ligands on copper. Perhaps the simplest mechanistic rationale of predominant inversion in reaction 3 is indicated in Scheme II. It may be supposed that the isonitrile ligand increases the nucleophilicity of carboxylate anion to cause a SN2 displacement.

SCHEME II



Ln = ligand isonitrile

In the course of our study, we found that the Cu_2O–isonitrile complex induced the ester interchange reaction between ester and alkyl halide, being accompanied with the formation of ether as formulated by eq 4. For example, a mixture of phenyl acetate and benzyl chloride was heated in benzene at 80° for 12 hr in the presence of Cu_2O-*t*-BuNC. The products were benzyl acetate and benzyl phenyl ether (eq 4). By glpc analysis, no other species, except for the starting two compounds, was detected in the reaction mixture.



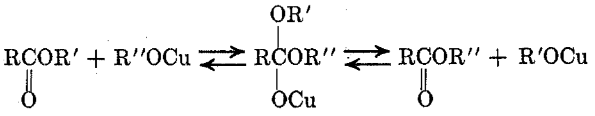
(4)

Other examples of the ester interchange reaction (*i.e.*, phenyl acetate–*n*-butyl bromide and benzyl benzoate–*n*-butyl bromide) are shown in Table II. The two alkyl groups of the product ether are derived from alkyl halide and ester.

From the material balance, one oxygen atom of Cu_2O is to be transferred to one of the products. The following (Scheme III) may be assumed. The reaction is initiated by the reaction of alkyl halide and Cu_2O to form Cu(I) alkoxide (eq 5). Then Cu(I) alkoxide may act as the key intermediate in the following manner. The isonitrile ligand is being omitted in this equation. The transient formation of Cu(I) alkoxide has been supported by a reference experiment in which a mixture of benzyl chloride (20 mmol), Cu_2O (10 mmol), and *t*-BuNC (20 mmol) at 80° for 12 hr produced benzyl ether in a yield of 51% on the basis of benzyl chloride. In this reaction, the transient formation of Cu(I) benzylate (**5**) will be assumed (eq 8).

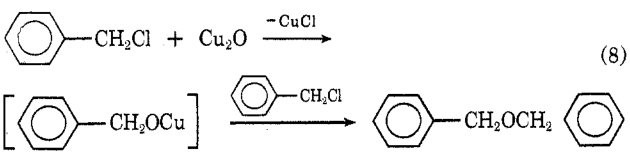
SCHEME III

$$R''X + Cu_2O \longrightarrow R''OCu + CuX \qquad (5)$$



$$\mathrm{R}\underset{\underset{\displaystyle\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OR'} + \mathrm{R''OCu} \rightleftarrows \mathrm{R}\overset{\overset{\displaystyle\mathrm{OR'}}{|}}{\underset{\underset{\displaystyle\mathrm{OCu}}{|}}{\mathrm{C}}}\mathrm{OR''} \rightleftarrows \mathrm{R}\underset{\underset{\displaystyle\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OR''} + \mathrm{R'OCu} \qquad (6)$$

$$R'OCu + R''X \longrightarrow R'OR'' + CuX \qquad (7)$$



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(8)

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[8] W. Gerrard, *J. Chem. Soc.*, 848 (1945).

[9] D. G. Goodwin and H. R. Hudson, *J. Chem. Soc. B*, 1333 (1968).

[10] A. H. Lewin and N. L. Goldberg, *Tetrahedron Lett.*, 491 (1972).

TABLE II

REACTION OF ESTER WITH ALKYL HALIDE[a]

Ester[d] (mmol)	Halide[d] (mmol)	Cu_2O, mmol	t-BuNC, mmol	Time, hr	Product yield,[b] %
CH_3COOPh (10) (122-79-2)	$PhCH_2Cl$ (10) (100-44-7)	5	20	12	CH_3COOCH_2Ph 43[c] $PhOCH_2Ph$ 45[c]
CH_3COOPh (10)	*n*-BuBr (40) (109-65-9)	10	20	5	CH_3COO-*n*-Bu 40 PhO-*n*-Bu 41
$PhCOOCH_2Ph$ (10) (120-51-4)	*n*-BuBr (50)	10	15	8	PhCOO-*n*-Bu 38 $PhCH_2O$-*n*-Bu 36

[a] A mixture of ester with alkyl halide was heated at 80° in 10 ml of benzene under nitrogen. [b] Yield was determined by glpc analysis and calculated on the basis of ester. [c] Calculated on the basis of benzyl chloride. [d] Registry numbers are in parentheses.

In the two reactions of eq 5–7 and 8, a stoichiometric amount of Cu_2O is converted into Cu(I) halide. The formation of Cu(I) alkoxide requires alkyl halide.

Experimental Section

Materials.—Cu_2O and Cu(II) acetate were commercial reagents of analytical grade and were dried under nitrogen prior to use. Cu(I) acetate was prepared under nitrogen according to Calvin's method.[4,5] *tert*-Butyl isocyanide was prepared according to Ugi's procedure.[11] (−)-(*S*)-Phenethyl alcohol, $[\alpha]^{25}\mathrm{D}$ −45.6° (*c* 3.29, cyclohexane) (lit. $[\alpha]^{23}\mathrm{D}$ −45.5°),[12] was prepared according to Kenyon's method,[12] and was converted to (+)-(*R*)-phenethyl bromide, $[\alpha]^{25}\mathrm{D}$ +58.6° (*c* 3.94, cyclohexane) (lit. $[\alpha]^{22}\mathrm{D}$ +130.96°)[8] (optical purity 45%), according to a published method of Gerrard.[8]

Preparation of 1:1 Complex of Cu(I) Acetate–*t*-BuNC (3).—All the reagents were carefully dried and distilled under nitrogen. Under nitrogen, a mixture of acetic acid (34 mmol), Cu_2O (17 mmol), and *t*-BuNC (34 mmol) was heated in 24 ml of benzene at 80° for 2.5 hr. During the reaction, the production of water was observed. After filtration, the filtrate was subjected to evaporation *in vacuo* (10 mm). Then 20 ml of benzene was added and recrystallization was carried out by warming the mixture up to 80°. This procedure was repeated three times. The white residue was dried *in vacuo* (2–3 mm) at 80° for 12 hr (**3**, 1.85 g, 53% on the basis of Cu_2O). **3** was sensitive to air. When **3** was exposed to air in solid state, it turned light blue gradually, and in benzene solution it turned greenish blue immediately. Cu(I) acetate–*t*-BuNC (**3**) had nmr (CD_3CN) τ 8.51 (singlet, CH_3– and *tert*-butyl protons at the same position); ir (KBr) 2169 (C≡N), 1585, 1560 (COO), 1410, 1235, 1210 cm^{-1} (*tert*-butyl group).

Anal. Calcd for $C_7H_{12}NO_2Cu$: C, 40.87; H, 5.88; N, 6.81; Cu, 30.98. Found: C, 40.83; H, 6.13; N, 6.80; Cu, 30.40.

Preparation of 1:1 Complex of Cu(I) Benzoate–*t*-BuNC Complex.—A similar procedure was carried out with benzoic acid. The 1:1 complex was obtained: nmr (CD_3CN) τ ~2.6 (5 H), 8.55 (9 H); ir (KBr) 3060 (phenyl), 2168 (C≡N), ~1600, 1570 cm^{-1} (COO and phenyl).

Reaction of 3 or Cu(I) Acetate with (+)-(*R*)-Phenethyl Bromide. A.—Under nitrogen, **3** (4 mmol) was mixed with *t*-BuNC (2 mmol) in 5 ml of benzene. The solution became clear by the addition of *t*-BuNC. To this mixture, (+)-(*R*)-phenethyl bromide (2.35 mmol) was added dropwise at room temperature. The reaction mixture was stirred for 30 min at room temperature. Then it was elevated up to 45° and allowed to react for 2 hr. After the reaction, 30 ml of *n*-pentane was added to remove CuBr-*t*-BuNC by filtration. The filtrate was condensed at room temperature by evaporation *in vacuo* (10 mm). Analysis by glpc showed that the reaction was quantitative. The product ester was purified by preparative glpc. The specific rotation of the ester was $[\alpha]^{25}\mathrm{D}$ −41.6° (*c* 6.27, cyclohexane), being opposite in sign to the original halide. This sign was the same as that obtained from the reaction of (−) alcohol with acetic acid anhydride.[7]

B.—The reaction of Cu(I) acetate with (+)-(*R*)-phenethyl bromide was carried out at 50° for 3 hr by a similar procedure. Yield of the ester was over 90%. The specific rotation of the product ester was $[\alpha]^{25}\mathrm{D}$ −0.3° and $[\alpha]^{25}_{350}$ −1.5° (*c* 6.62, cyclohexane). By a reference experiment, it was confirmed that the optical active ester obtained in the above reaction (A) was not racemized under the reaction conditions.

Reaction of Ester with Alkyl Halide by Cu_2O–*t*-BuNC.—A typical procedure is as follows. Under nitrogen, a mixture of Cu_2O (5 mmol), phenyl acetate (10 mmol), and *t*-BuNC (20 mmol) in benzene was stirred at 80° for 5 min, and then benzyl chloride (10 mmol) was added dropwise and heated for 12 hr. Then 20 ml of petroleum ether was poured into the cooled reaction mixture. The precipitated CuCl–*t*-BuNC and some unreacted Cu_2O were removed by filtration. The yields of products were determined by glpc analysis of the filtrate. Benzyl acetate and benzyl phenyl ether were obtained in the yield of 42.5 and 44.5%, respectively. Dibenzyl ether was not detected in the reaction mixture. The product structures were determined by comparison of nmr and ir with those of the authentic sample.

Reaction of Benzyl Chloride by Cu_2O–*t*-BuNC.—Under nitrogen, a mixture of benzyl chloride (20 mmol), Cu_2O (10 mmol), and *t*-BuNC (20 mmol) was heated at 80° for 12 hr. *n*-Pentane was added to remove CuCl–*t*-BuNC and the unreacted Cu_2O by filtration. The yield of product was determined by glpc analysis of filtrate. Dibenzyl ether was obtained in a yield of 51% (on the basis of Cu_2O).

Registry No.—Acetic acid, 64-19-7; Cu_2O, 1317-39-1; *t*-BuNC, 7188-38-7; benzoic acid, 65-85-0; Cu(I) benzoate–*tert*-butyl isocyanide complex, 38641-30-4; benzyl ether, 103-50-4.

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[11] I. Ugi and R. Meyer, *Chem. Ber.*, **93**, 239 (1960).

[12] A. J. H. Houssa and J. Kenyon, *J. Chem. Soc.*, 2260 (1930).

Nucleophilic Methanolysis of 1-Acetyltetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane (2-Acetylquadricyclene) and Methyl 1-Tetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane carboxylate (2-Carbomethoxyquadricyclene)

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Received October 24, 1972

Although electrophilic additions to saturated, strained carbocyclic systems are commonplace, the corresponding nucleophilic additions are rare. Thus, such reactions as the alcoholysis of strained carbon linkages are usually feasible only in the presence of electrophilic catalysts (*e.g.*, H^+, Ag^+, etc.). We wish to report, however, that α-carbanion stabilizing substituents, such as the acetyl group, render the quadricyclene skeleton exceedingly reactive toward methanolysis not only under basic conditions but even in neutral solvent.

2-Acetylquadricyclene (**1a**), previously unreported, was prepared in nearly quantitative yield by sensitized