ion pair alkylations. One of us (L. L.) would like to thank the Undergraduate Research Fund as administered by the State University of New York at Buffalo Student Association for a grant in support of this work. The National Science Foundation provided financial aid in the purchase of the nmr spectrometer used in this research.

Registry No.—Methyl acetoacetate, 105-45-3; benzyl chloride, 100-44-7; 3-carbomethoxy-4-phenylbutanone, 3666-82-8; 4-phenyl-2-butanone, 2550-26-7; allyl bromide, 106-95-6; 4-carbomethoxy-1-hexen-5-one, 3897-04-9; allyl chloride, 107-05-1; dimethylallyl chloride, 503-60-6; 3-carbomethoxy-6-methyl-5-hepten-2-one, 20962-72-5; geranyl bromide, 5389-87-7; 3-carbomethoxy-6,10-dimethyl-5,9-undecadien-2-one, 51933-45-0; geranyl acetone, 3796-70-1.

References and Notes

(1) C. M. Starks, *J. Amer. Chem. Soc.*, **93**, 195 (1971).
(2) J. Solondar, *Tetrahedron Lett.*, 287 (1971); J. Dockx, *Synthesis*, 441 (1973), and references cited therein.
(3) "Alaquat 336," General Mills Chemical Co. catalyst tricaprylmethylammonium chloride, Minneapolis, Minn. 55435.
(4) (a) W. J. le Noble and H. F. Morris, *J. Org. Chem.*, **34**, 1969 (1969); (b) A. L. Kurz, I. P. Beletskaya, A. Macias, and O. A. Reutov, *Tetrahedron Lett.*, 3679 (1968); 3037 (1971).
(5) (a) G. Brieger and W. M. Pelletier, *Tetrahedron Lett.*, 3555 (1965); (b) W. J. le Noble and J. E. Puerta, *ibid.*, 1087 (1966); (c) N. Kornblum, R. Seltzer, and P. Haberfield, *J. Amer. Chem. Soc.*, **85**, 1148 (1963); (d) N. Kornblum and A. P. DeLurie, *ibid.*, **81**, 2705 (1959); (e) N. Kornblum, P. J. Berrigan, and W. J. le Noble, *ibid.*, **85**, 1141 (1963).
(6) Reaction products were examined by ir, nmr, and gc. The β-alkoxy-α,β-unsaturated ester absorptions at 1685 and 1630 cm^{-1} were missing. There were no nmr absorptions at τ 4.8–5.15 characteristic of vinyl protons. Gc analysis showed only one major peak (99% by intergration) which corresponds to monoalkylated methyl benzylacetoacetate. This product was hydrolyzed, decarboxylated, and shown to consist of only 4-phenyl-2-butanone. See Experimental Section.
(7) D. Picker and A. W. Herriott, First Fall Organic Conference, Cape Cod, Mass., Oct , 1973; *Tetrahedron Lett.*, 4521 (1972).
(8) R. M. Coates and J. E. Shaw, *J. Org. Chem.*, **35**, 2601 (1970).
(9) R. C. Fuson, "Reactions of Organic Compounds," Wiley, New York, N. Y., 1962.
(10) H. D. Durst and E. Leete, *J. Label. Compounds*, **7**, 52 (1971).
(11) (a) H. D. Zook, T. J. Russo, E. F. Ferrand, and D. S. Stotz, *J. Org. Chem.*, **33**, 2222 (1968); (b) H. E. Zaugg, B. W. Horrom, and S. Borgwardt, *J. Amer. Chem. Soc.*, **82**, 2895 (1960); H. E. Zaugg, *ibid.*, **82**, 2903 (1960); **83**, 837 (1961).
(12) Zaugg, *et al.*,[11b] reports using nonpolar solvents, such as benzene, in a malonic ester type alkylation. In this case the solution, although visually homogeneous, was determined to be a colloidal suspension. The molecular weight of these colloidal particles was calculated to be at least 10,000. Thus, the solubility of alkali metal salts in hydrocarbon solvents is relatively low. Although we performed the benzyl chloride alkylations using the phase transfer catalyst in several nonpolar solvents, we only checked the reactivity of the methyl acetoacetate anion without added catalyst in two solvent systems, benzene and hexene. In both cases substantial enhancement of product formation was observed using the phase transfer procedure (25 *vs.* 85% using benzene; <5 *vs.* 40% using hexane as a solvent). We presume that the same trend will be followed with the other solvents.
(13) C. Roux and F. Katzanevas, *Can. J. Chem.*, **47**, 4455 (1969).
(14) E. W. Collington and A. I. Meyers, *J. Org. Chem.*, **36**, 3044 (1971); E. I. Snyder, *ibid.*, **37**, 1466 (1972); C. W. Spangler, *et al.*, *ibid.*, **36**, 1695 (1971).

Synthetic Reactions by Complex Catalysts. XXXVI. A New Synthesis of Cyclopentanecarboxylates. Cyclization of 1,3-Diiodopropane with α,β-Unsaturated Esters by a Copper–Isonitrile Complex

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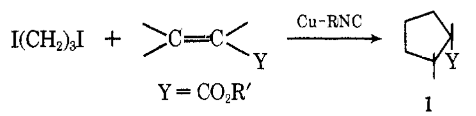
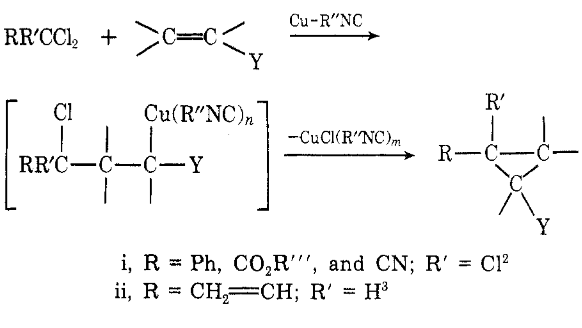
The present paper describes a new synthetic method for cyclopentanecarboxylates (1) by the reaction of 1,3-diiodopropane with an α,β-unsaturated ester in the presence of copper and isonitrile (RNC) (Table I). This reaction was



1

(1)

found in the course of exploratory studies on the synthetic reactions caused by Cu–RNC mixture. Previously we have found[1] that an aliphatic halide reacts with metallic copper in the presence of RNC to form the corresponding organocopper–isonitrile complex, which then adds to α,β-unsaturated carbonyl and nitrile compounds in the manner of a conjugate addition. Moreover, an organocopper–isonitrile complex bearing a halogen atom in the same molecule readily undergoes cyclization by the intramolecular elimination of copper halide–isonitrile complex. The following cyclopropane syntheses, for example, have been based upon this interesting reactivity of organocopper–isonitrile complex.



(2)

i, R = Ph, CO_2R''', and CN; R' = Cl[2]
ii, R = CH_2=CH; R' = H[3]

The reaction described in the present paper (eq 1) affords a five-membered ring. For this reaction the transient formation of a 3-iodopropylcopper–isonitrile complex may be proposed, which is followed by the subsequent addition to an α,β-unsaturated carbo ester and the final cyclization through the intramolecular elimination of the copper halide–isonitrile complex.

Results and Discussion

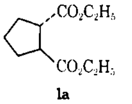
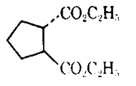
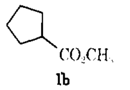
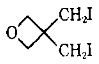
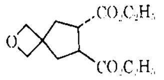
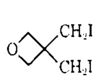
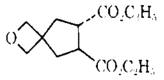
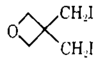
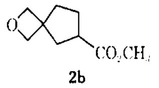
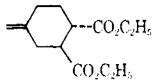
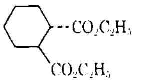
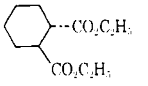
On heating a mixture of 1,3-diiodopropane, diethyl fumarate, cyclohexyl isocyanide, and metallic copper in refluxing toluene under nitrogen, *trans*-1,2-dicarbethoxycyclopentane was produced in a high yield and high selectivity. Also the reaction of 1,3-diiodopropane with diethyl maleate by an identical procedure gave the same product. Since it has been found by us that maleate is readily isomerized to fumarate by the Cu–RNC system,[1] and that cyclopropane-, cyclopentane-, and cyclohexane-*cis*-1,2-dicarboxylates are isomerized to the corresponding trans isomers, respectively, under the present reaction conditions, it is conceivable that diethyl maleate is converted to diethyl fumarate prior to the cyclization reaction and/or that *cis*-1,2-dicarbethoxycyclopentane once formed is converted to *trans*-1,2-dicarbethoxycyclopentane.

Similarly, the reaction of 1,3-diiodopropane with methyl acrylate afforded cyclopentanecarboxylic acid methyl ester in 58% yield. Use of electron-deficient olefins other than fumarate, maleate, and acrylate in the present reaction, however, gave rise to decreased yields and selectivities of the corresponding cyclopentane derivatives.

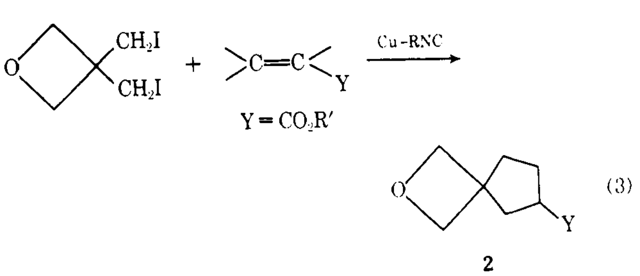
3,3-Bis(iodomethyl)oxetane can be used in place of 1,3-diiodopropane. The product is the corresponding oxaspirane carboxylate (**2**). Cyclization of tetraiodoneopentane with fumarate gave **3** instead of the spirocyclononanetetracarboxylate. Compound **3** is supposed to be produced through intermediate **4**.[4]

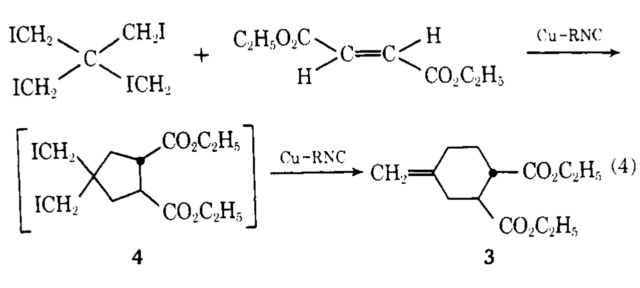
Employment of iodides in the present reaction is essen-

Table I
Reaction of Diiodopropane with the Cu(0)-Isonitrile Complex in the Presence of α,β-Unsaturated Esters

Halide (registry no.)	Olefin (registry no.)	Conditions	Product (%)[a, b]		Registry no.
$I(CH_2)_3I$ (627-31-6)	*trans*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$ (623-91-6)	110°, 13 hr	 1a	(90)[c]	30689-38-4
$I(CH_2)_3I$	*cis*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$ (141-05-9)	110°, 13 hr	 1a	(89)[c]	
$I(CH_2)_3I$	$CH_2{=}CHCO_2CH_3$ (96-33-3)	80°, 12 hr	 1b	(58)[d]	4630-80-2
 (2402-82-6)	*trans*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$	110°, 14 hr	 2a	(46)[c,e]	52239-59-5
	*cis*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$	110°, 14 hr	 2a	(23)[c,e]	
	$CH_2{=}CHCO_2CH_3$	80°, 15 hr	 2b	(66)[d]	52239-60-8
$(ICH_2)_4C$ (1522-88-9)	*trans*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$	110°, 12 hr	 3	(50)[c]	52239-61-9
$I(CH_2)_4I$ (628-21-7)	*trans*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$	110°, 15 hr	 7	(37)[c]	17357-22-3
$I(CH_2)_4I$	*cis*-$C_2H_5O_2CCH{=}CHCO_2C_2H_5$	110°, 13 hr	 7	(55)[c]	

[a] All new compounds in the table gave satisfactory elemental analyses. [b] The yields of products are not necessarily optimum, since only one or two experiments have been done for each combination. [c] Cyclohexyl isocyanide was used. [d] *tert*-Butyl isocyanide was used. [e] Stereochemistry of **2a** has not been definitely determined. However, the trans configuration was deduced from the following reasons: either diethyl fumarate or maleate react with 3,3-bis(iodomethyl)oxetane to yield the same product, and *cis*-1,2-dicarbethoxycyclopentane is readily isomerized to the trans isomer under the present reaction conditions.





tial. 1,3-Dichloro- and 1,3-dibromopropane gave the cyclopentane products only in low yields.

The present cyclization may be explained by a scheme involving an intermediate of 3-iodopropylcopper–isonitrile complex (**5**) which is initially formed by the reaction of diiodopropane with Cu-RNC.[1,2] The addition of **5** to α,β-unsaturated ester gives the second organocopper species (**6**), which in turn undergoes the cyclization by the intramolecular 1,5-elimination of CuI-RNC complex (Scheme I).

Scheme I

$$ICH_2CH_2CH_2I + Cu\text{-}RNC \longrightarrow ICH_2CH_2CH_2Cu(RNC)_n$$

5

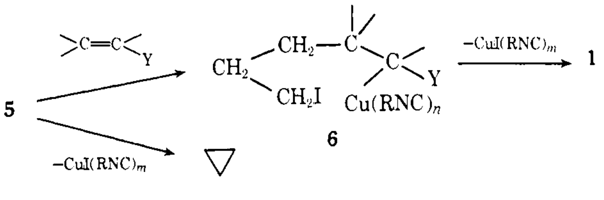


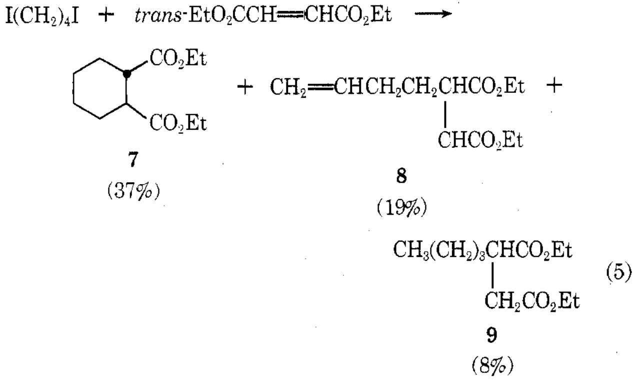
Table II
Characterization of Products[c]

	Ir, cm^{-1} [a]	Nmr, τ [b]	Mass, m/e
1a	1733	5.84 (q, 4 H, J = 7.5 Hz), 6.68–7.06 (m, 2 H), 7.62–8.92 (m, 6 H), 8.74 (t, 6 H, J = 7.5 Hz)	
1b	1735	6.30 (s, 3 H), 6.90–7.50 (m, 1 H), 7.92–8.47 (m, 6 H)	128 (M^+)
2a	1730	5.49 (s, 4 H), 5.90 (q, 4 H, J = 6.5 Hz), 6.62–7.10 (m, 2 H), 7.58–7.90 (m, 4 H), 8.79 (t, 6 H, J = 6.5 Hz)	
2b	1735	5.41 and 5.42 (two s, 4 H), 6.30 (s, 3 H), 6.90–7.50 (m, 1 H), 7.75–8.20 (m, 6 H)	
3	3060, 1732, 1650, 895	5.24 (s, 2 H), 5.84 (q, 4 H, J = 7.0 Hz), 7.10–8.25 (m, 8 H), 8.77 (t, 6 H, J = 7.0 Hz)	240 (M^+)
7	1732, 890	5.87 (q, 4 H, J = 7.0 Hz), 7.25–7.60 (m, 2 H), 7.85–9.00 (m, 8 H), 8.81 (t, 6 H, J = 7.0 Hz)	

[a] Neat. [b] $CDCl_3$ solution with TMS. [c] Satisfactory analytical data were reported for all compounds in the table.

The intermediacy of 3-iodopropylcopper–isonitrile complex **5** is supported by the formation of cyclopropane in the treatment of 1,3-diiodopropane with the Cu–RNC system in the absence of olefin at about 100°. In the presence of an α,β-unsaturated carboester, however, the formation of cyclopropane as a by-product was almost negligible.

The reaction of 1,4-diiodobutane with fumarate by the Cu-RNC system produced acyclic compounds **8** and **9** along with the desired product, *trans*-1,2-cyclohexanedicarboxylate (**7**).



$I(CH_2)_4I$ + *trans*-$EtO_2CCH{=}CHCO_2Et \longrightarrow$

7 (37%)

$$+\ CH_2{=}CHCH_2CH_2\underset{\displaystyle CHCO_2Et}{\underset{|}{C}}HCO_2Et\ +$$

8 (19%)

$$CH_3(CH_2)_3\underset{\displaystyle CH_2CO_2Et}{\underset{|}{C}}HCO_2Et \qquad (5)$$

9 (8%)

Experimental Section

Reagents. Metallic copper was prepared by reducing[5] $CuSO_4$ with zinc powder and dried under nitrogen. *tert*-Butyl and cyclohexyl isocyanide were prepared by Ugi's procedure.[6] Olefins such as fumarate, maleate, and acrylate were commercial reagents and purified by distillation under nitrogen prior to use. Trimethylene diiodide and 3,3-bis(iodomethyl)oxetane were synthesized by the reaction of the corresponding dichloride and NaI in acetone.[7] Pentaerythrityl tetriodide[8] was prepared by iodination of pentaerythrityl tetrabromide, which was synthesized by the reaction of pentaerythritol and PBr_3.[9] Tetramethylene diiodide was prepared by the reaction of tetrahydrofuran with KI, orthophosphoric acid, and phosphoric anhydride.[10]

Reaction of Trimethylene Diiodide with Diethyl Fumarate by the Copper-Isonitrile System. Under nitrogen, 1.48 g (5 mmol) of trimethylene diiodide in 4 ml of toluene was added dropwise with stirring over 30 min, to a preheated mixture of 1.27 g (20 mg-atoms) of metallic copper, 4.40 g (40 mmol) of cyclohexyl isocyanide, 1.72 g (10 mmol) of diethyl fumarate, and 6 ml of toluene at 110°. After the reaction mixture was heated for 12 hr at 110°, it was treated with ether to remove copper iodide–isonitrile complex. The extract was concentrated and distilled *in vacuo*. *trans*-1,2-Diethoxycarbonylcyclopentane was isolated in a yield of 90% by preparative glpc. The structure of the product was confirmed by spectral data and elemental analysis. These data are shown in Table II.

Reaction of Trimethylene Diiodide with Methyl Acrylate by Copper–Isonitrile System. A mixture of 1.48 g (5 mmol) of trimethylene diiodide, 1.72 g (20 mmol) of methyl acrylate, and 4 ml of benzene was added with stirring to a mixture of 1.27 g (20 mg-atoms) of metallic copper, 3.32 g (40 mmol) of *tert*-butyl isocyanide, and 6 ml of benzene at 80°. After the reaction mixture was heated for an additional 12 hr at 80°, the mixture was extracted with ether. The extract was concentrated and analyzed by glpc. Methyl cyclopentanecarboxylate was isolated in a yield of 58%. Reactions of 3,3-bis(iodomethyl)oxetane and tetramethylene diiodide with olefins by the copper–isonitrile system were carried out by similar ways.

Reaction of Pentaerythrityl Tetriodide with Diethyl Fumarate by the Copper–Isonitrile System. A mixture of 2.30 g (4 mmol) of pentaerythrityl tetriodide, 1.72 g (10 mmol) of diethyl fumarate, 1.27 g (20 mg-atoms) of metallic copper, 4.40 g (40 mmol) of cyclohexyl isocyanide, and 20 ml of toluene was stirred at 110° for 12 hr. The reaction mixture was extracted with ether. The extract was concentrated and distilled *in vacuo*. 3,4-*trans*-Diethoxycarbonylmethylenecyclohexane was isolated in a yield of 50%.

Registry No.—Copper, 7440-50-8; cyclohexyl isocyanide, 931-53-3; *tert*-butyl isocyanide, 7188-38-7.

References and Notes

(1) (a) T. Saegusa, Y. Ito, and S. Tomita, *J. Amer. Chem. Soc.*, **93**, 5656 (1971); (b) T. Saegusa, K. Yonezawa, I. Murase, T. Konoike, S. Tomita, and Y. Ito, *J. Org. Chem.*, **38**, 2319 (1973).
(2) T. Saegusa, K. Yonezawa, and Y. Ito, *Syn. Commun.*, **2**, 431 (1972).
(3) Y. Ito, K. Yonezawa, and T. Saegusa, *J. Org. Chem.*, in press.
(4) N. Chatterjee and G. N. Barpajari, *J. Indian Chem. Soc.*, **15**, 639 (1938).
(5) "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 446.
(6) I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer, and K. Offermann, *Angew. Chem.*, **77**, 492 (1965).
(7) "Preparative Methods of Polymer Chemistry," 2nd ed, Wiley, New York, N. Y., 1968, p 376.
(8) Reference 5, p 476.
(9) "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 425.
(10) "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1950, p 321.