[Contribution from the Research Department of the Union Carbide Plastics Co.]

A New Synthesis of β-Cyanoesters

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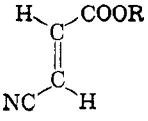
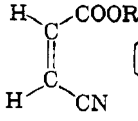
Alkyl and aryl β-cyanoacrylates, ethyl β-cyanopropionate, and ethyl *o*-cyanobenzoate have been prepared by simultaneous dehydration and esterification of the appropriate amic acids with chloroformate esters and triethylamine.

Alkyl β-cyanoacrylates (I and II, R = alkyl) and their derivatives possess a variety of uses which have been disclosed in the patent literature.[1] β-Cyanoesters in general have found use in the synthesis of 2-pyrrolidones, *e.g.* the recent hydrogenation and ring closure of ethyl 3-cyano-2-carboethoxypropionate to 3-carboethoxy pyrrolidone.[2] Wide application of the β-cyanoesters has been hampered by the lack of convenient methods for their preparation. Previous syntheses of these materials have suffered from low yields, expensive starting materials and the hazards attending the use of hydrogen cyanide. Thus, methyl *trans*-β-cyanoacrylate (I, R = CH_3) was prepared from methyl α-chloroacrylate in 31% yield by the concurrent addition of hydrogen cyanide and loss of hydrogen chloride.[3] The product was contaminated with a small amount of the *cis* isomer (II, R = CH_3).[4] A less attractive method for laboratory use involves the addition of gaseous hydrogen cyanide to methyl propiolate.[5] The product was reported to be *trans* and the yield was 25%. Substituted β-cyanoacrylates have been prepared by dehydration of the cyanohydrins formed from acetoacetic esters[6]; this general method has not been applied to the synthesis of the unsubstituted β-cyanoacrylic esters.

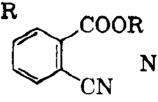
Ethyl *o*-cyanobenzoate (III, R = C_2H_5) has been prepared from ethyl anthranilate by diazotization and treatment with cuprous cyanide.[7] Dimethyl 2,5-dicyanoterephthalate has been obtained from the corresponding dibromo compound by treatment with cuprous cyanide.[8] β-Cyanopropionates



I



II



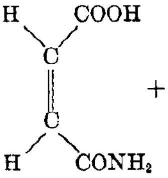
III

$NC(CH_2)_2COOR$

IV

have also been prepared from the appropriate halogen esters.[9]

We have developed a method for the synthesis of the cyanoesters, II, III, and IV in good yields. The starting materials are the corresponding amic acids obtained by the reaction of the appropriate five-membered ring anhydrides with ammonia. Treatment of a solution made from maleamic acid[10] (V) and two equivalents of triethylamine in dichloromethane at 0–5° with two equivalents of ethyl chloroformate resulted in an immediate, mild exothermic reaction. Carbon dioxide was evolved and triethylamine hydrochloride precipitated. A 91% yield of ethyl β-cyanoacrylate which possessed the appropriate infrared spectrum and elemental analysis was obtained (see Equation 1). In a similar



V

$$+ 2ROCOCl + 2N(C_2H_5)_3 \longrightarrow$$

$$II + ROH + 2CO_2 + 2[HN(C_2H_5)_3]^+Cl^- \quad (1)$$

experiment, methyl chloroformate, triethylamine, and maleamic acid at 0–5° gave a 64% yield of a solid, m.p. 30–31°, which had an elemental analysis and infrared spectrum corresponding to methyl β-cyanoacrylate. The synthesis of β-cyanoacrylates from maleamic acid (*cis* unsaturation) at 0–5° suggested that the double bond in the acrylate products possesses the *cis* configuration. The major product obtained by Crawford, McLeish, and Wood[3] from methyl α-chloroacrylate and sodium cyanide was synthesized and was shown to be different from the methyl β-cyanoacrylate prepared above. The assignment of the *trans* configuration by these workers to their major product[4] thus appears to be correct. These assignments have been

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(1) (a) D. T. Mowry, U. S. Patent **2,437,231** (1948) [*Chem. Abstr.*, **42**, 5272 (1948)]; (b) G. F. D'Alelio, U. S. Patents **2,531,408** (1950) [*Chem. Abstr.*, **45**, 1812 (1951)]; **2,850,486** (1958); **2,850,487** (1958).

(2) W. M. Byrd, Jr., Dissertation Abst., **20**, 517 (1959). See also C. F. Koelsch and C. H. Stratton, *J. Am. Chem. Soc.*, **66**, 1883 (1944).

(3) J. W. Crawford, N. McLeish, and T. K. Wood, U. S. Patent **2,293,967** (1942).

(4) The *cis* and *trans* structural assignments were made on the basis of boiling point comparisons but no rigorous proof of structure was reported.

(5) P. Kurtz, *Ann.*, **572**, 23 (1951).

(6) D. T. Mowry and A. G. Rossow, *J. Am. Chem. Soc.*, **67**, 926 (1945).

(7) M. L. Bender, Y. L. Chow, and F. Chloupek, *J. Am. Chem. Soc.*, **80**, 5381 (1958).

(8) E. A. Lawton and D. D. McRitchie, *J. Org. Chem.*, **24**, 26 (1959).

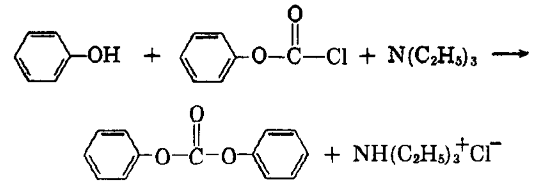
(9) M. Protiva, V. Keřicha, and J. O. Jílek, *Chem. Listy*, **44**, 231 (1950).

(10) R. S. Robinson and E. L. Humburger, U. S. Patent **2,459,964** (1949), Example 1: *Chem. Abstr.*, **43**, 3843 (1949).

confirmed by the NMR spectra of both isomers which have been studied by another group.[11] Both the *cis* and *trans* isomers of methyl β-cyanoacrylate absorb in the 960–970 cm.$^{-1}$ region of their infrared spectra. Absorption in this region can indicate the presence of *trans* unsaturation.[12] However, the intensity of the absorption at 965 cm.$^{-1}$ for the *trans* compound is much greater than that of the *cis* compound. These same observations have been made for the *cis* and *trans* isomers of ethyl β-cyanoacrylate. Therefore, assignment of the structure of the β-cyanoacrylate isomers based on infrared data alone could be misleading.

The use of phosgene and ethanol in the above synthesis in place of ethyl chloroformate gave a fair yield of ethyl *cis*-β-cyanoacrylate although no attempt was made to maximize the yield under these conditions. When the amount of tertiary amine used in this modification of the synthesis was insufficient to neutralize completely the hydrogen chloride produced, chlorinated products were obtained. These products, presumably chloro derivatives of β-cyanopropionates, could be dehydrochlorinated with triethylamine to yield mainly ethyl *trans*-β-cyanoacrylate (I, R = C_2H_5).

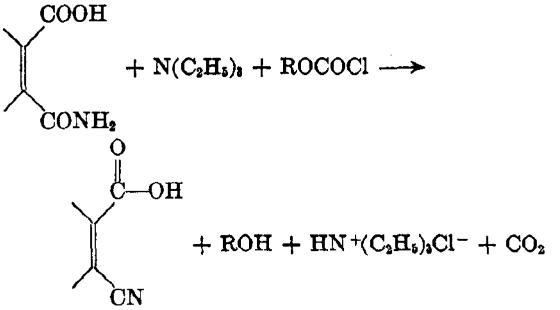
The behavior of the alkyl chloroformates and triethylamine toward maleamic acid was paralleled by phenyl chloroformate; phenyl *cis*-β-cyanoacrylate was prepared in 43% yield. A substantial amount of diphenyl carbonate was also obtained, presumably from the reaction of phenyl chloroformate with the phenol produced in the reaction. (See Equation 2.) The reaction of aryl chloroformate–pyridine complexes with phenol to produce diphenyl carbonate has been previously reported.[13] Other amic acids gave good yields of the corresponding ethyl cyanocarboxylates when subjected to the ethyl chloroformate–triethylamine reagent. Thus, ethyl β-cyanopropionate (IV, R = C_2H_5) and ethyl *o*-cyanobenzoate (III, R = C_2H_5) were synthesized from succinamic acid and phthalamic acid in yields of 69% and 84%, respectively.



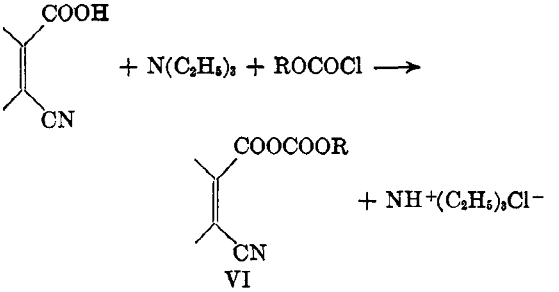
(2)

The ready availability of many five-membered ring anhydrides from Diels-Alder reactions of maleic anhydride provides a variety of starting materials to which the above synthesis of cyanoesters will probably be applicable. Most of the cyanoesters would be difficult to obtain by previous methods.

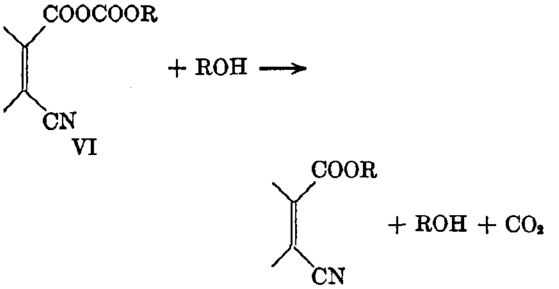
The detailed course of the formation of cyanoesters by the method described above is unknown. One possibility is a stepwise dehydration of the amide group to the nitrile-carboxylic acid (Equation 3) followed by the formation of a mixed carboxylic-carbonic anhydride[14] (Equation 4). Subsequent nucleophilic attack of the alcohol formed in Equation 3 upon this material (VI) would yield the product (Equation 5).



(3)



VI (4)



VI (5)

The dehydration of carboxamides to nitriles with phosgene and pyridine is known.[15] However, the preferred conditions for this reaction are more vigorous than those employed in this cyanoester synthesis. Furthermore, benzamide was only slightly dehydrated to benzonitrile with ethyl chloroformate and triethylamine under conditions which gave a high yield of ethyl *o*-cyanobenzoate from phthalamic acid. The reaction of mixed carbonic-carboxylic anhydrides with alcohols to give esters has been studied by Tarbell and Price.[14a] Again the conditions were more vigorous than those

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[11] We are indebted to Professor E. J. Corey for informing us of these conclusions and for permission to mention them here in advance of their publication.

[12] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York (1954), p. 31.

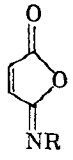
[13] German Patent 116,386 (1900); *cf. Friedlander*, 6, 1160.

[14] (a) D. S. Tarbell and J. A. Price, *J. Org. Chem.*, **22**, 245 (1957); (b) D. S. Tarbell and N. A. Leister, *J. Org. Chem.*, **23**, 1149 (1958).

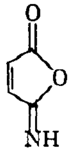
[15] P. M. Brown, D. B. Spiers, and M. Whalley, *J. Chem. Soc.*, 2882 (1957).

employed in this cyanoester synthesis. When the mixed anhydride from benzoic acid and ethyl chloroformate was prepared in the presence of ethanol and the undistilled product compared with the mixed anhydride prepared without ethanol, no differences were noted. When the sample prepared in the presence of ethanol was distilled under reduced pressure, nothing distilled at 1 mm. until the pot temperature reached 140°. At that temperature the pressure increased to 4 mm., a vigorous bubbling started, and some material which may have contained ethyl benzoate was carried over. This material resulted from the pyrolytic decomposition of the mixed anhydride.[16] These results appear to rule out the mechanism shown in Equations 3-5 for this synthesis.

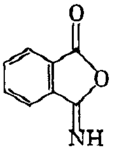
The necessary proximity of the acid and amide group for good reactivity in this synthesis is emphasized by the failure of terephthalamic acid to give ethyl *p*-cyanobenzoate. This experiment indicates that interaction[17] of the reacting groups is probably a requirement for facile reaction. Furthermore, the related synthesis of *N*-substituted isomaleimides (VII) from *N*-substituted maleamic acids suggests that the isoimides VIII, IX, and X may be intermediates in these reactions.[18] In the synthesis of ethyl *cis*-β-cyanoacrylate, formation of isomaleimide (VIII) would require one mole each of triethylamine and ethyl chloroformate and would yield one mole of ethanol. Addition of this ethanol to the carbonyl group of isomaleimide would yield a species (XI) that could lose a proton in either of two ways by attack of the second mole of triethylamine. The ions (XIIa, XIIb) could both undergo ring-opening as indicated, to yield *O*-anions which could react with the second mole of ethyl chloroformate. The intermediates formed in this step should be capable of facile decomposition through the indicated *quasi*-six membered ring transition states[19] (XIIIa, XIIIb) to yield the observed products. A choice between these two possible mechanistic routes cannot be made on the basis of the available evidence.



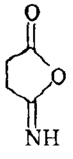
VII



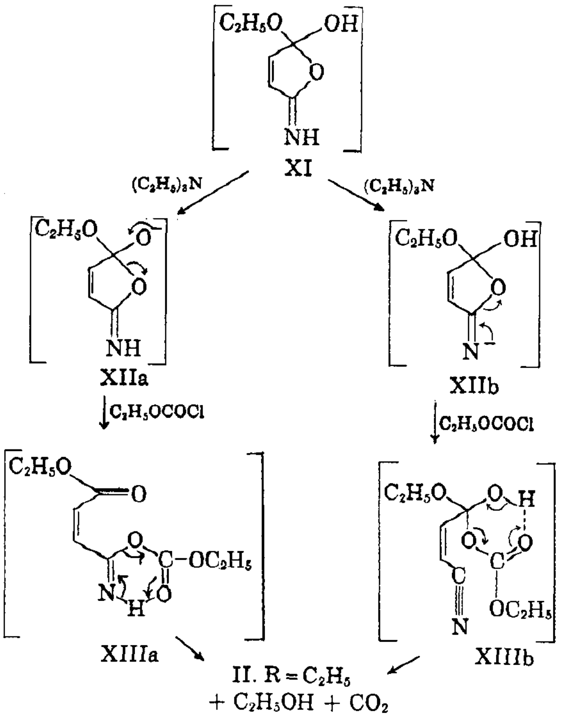
VIII



IX



X



EXPERIMENTAL[20]

Starting materials. Maleamic acid was prepared by the method of Robinson and Humburger.[10] It was not necessary to bubble ammonia into the solution of maleic anhydride. Instead, ammonia was run in over the surface of the solution at 60-75° and was absorbed until the theoretical quantity had been added. The yields obtained were in the range of 90-97% of white crystals, m.p. 165-168°, (lit.[10] m.p. 166°).

Phthalamic acid and succinamic acids were obtained by reaction of the appropriate anhydrides with concd. aqueous ammonia followed by acidification.[21]

Terephthalamic acid was prepared by the method of Kattwinkel and Wolffenstein.[22]

Methyl cis-β-cyanoacrylate. To 95 g. (0.83 mole) of maleamic acid in 1 l. of dichloromethane at 0-5°, 170 g. (1.7 mole) of triethylamine was added with stirring. The mixture was cooled to 0-5° and 170 g. (1.8 moles) of methyl chloroformate was added dropwise with stirring while the temperature was maintained below 5°. Carbon dioxide was evolved during the addition and for a short time after it was completed. The mixture was allowed to remain for 16 hr. at room temperature. Triethylamine hydrochloride was removed by filtration and the solvent was removed by distillation under reduced pressure. The residue was taken up in ether and filtered to remove the remainder of the amine salt. The ether was removed under reduced pressure and the residue was added to water and allowed to crystallize at 5°. The crystals were collected and dried under vacuum; 59 g. (64%), m.p. 30-31°, was obtained. The infrared spectrum

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[16] T. B. Windholz, *J. Org. Chem.*, **23**, 2044 (1958); A. Einhorn, *Ber.*, **42**, 2772 (1909); T. Wieland and H. Bernhard, *Ann.*, **572**, 190 (1951).

[17] M. L. Bender, F. Chloupek, and M. C. Neveu, *J. Am. Chem. Soc.*, **80**, 5380, 5384 (1958).

[18] Robert J. Cotter, Carol K. Sauers, and John M. Whelan, *J. Org. Chem.*, **26**, 10 (1961).

[19] E. S. Gould, *Mechanism and Structure in Organic Chemistry*, Henry Holt Co., New York, 1959, p. 500-504.

[20] Melting points are corrected and boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Infracord Spectrophotometer, model 137. Vapor phase chromatographic analyses were obtained on a Perkin-Elmer Vapor Fractometer, model 154-C. Microanalyses were performed by Drs. G. Weiler and F. Strauss, Oxford, England, and by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

[21] E. Chapman and H. Stephen, *J. Chem. Soc.*, **127**, 1793 (1925).

[22] P. Kattwinkel and R. Wolffenstein, *Ber.*, **37**, 3221 (1904).

of a liquid film of this product possessed absorption at 2220 cm.$^{-1}$ (w), 1730 cm.$^{-1}$ (s) and 1630 cm.$^{-1}$ (m) indicating the presence of the nitrile, ester, and double bond groups, but no strong absorption near 970 cm.$^{-1}$ Vapor phase chromatography showed no contamination with the methyl *trans-β*-cyanoacrylate prepared below. Upon admixture of this product with the *trans* isomer the melting point was depressed below 25°.

Anal. Calcd. for $C_5H_5O_2N$: C, 54.05; H, 4.54; N, 12.61. Found: C, 53.94; H, 4.43; N, 12.65.

Methyl trans-β-cyanoacrylate. The method of Crawford, McLeish, and Wood[8] (Example I) was followed with the following modifications. After the addition of the sodium cyanide solution the reaction mixture was allowed to stir for *ca.* 16 hr. at room temperature. At the end of this time the organic layer was separated from the aqueous layer and the aqueous layer extracted with several portions of dichloromethane. When the aqueous layer was not extracted completely, the yield of the product was very low. The dichloromethane extracts and the organic layer from the reaction mixture were combined and the solvents removed by distillation at atmospheric pressure. The residue was distilled through a short Vigreux column, yielding 32% b.p. 85–88° (35 mm.) of a clear liquid which solidified on cooling. Recrystallization from 1:1 1-propanol-water afforded white crystals, m.p. 32–34° (lit.[8] m.p. 34°). The retention time of this material on a Carbowax column at 140° and 25 p.s.i. was 2.9 min. The retention time of methyl *cis-β*-cyanoacrylate prepared above was 9.3 min. under the same conditions. The infrared spectrum of the *trans* isomer was similar to that of the *cis* isomer with the addition of a strong absorption band at 965 cm.$^{-1}$

Ethyl cis-β-cyanoacrylate. This compound was prepared by essentially the same procedure as the one used for methyl *cis-β*-cyanoacrylate except that ethyl chloroformate was used in place of methyl chloroformate. The product was obtained in 100% yield by distillation of the residue obtained from the ether solution through a Vigreux column. It distilled at 50–54° (0.2 mm.) n_D^{25} 1.4491 and was shown to be 91.4% pure by vapor phase chromatography on a silicone column (Perkin-Elmer column "C") at 190° and 25 p.s.i. The retention time was 2.65 min. The infrared spectrum of a liquid film showed bands at 2220 cm.$^{-1}$ (w), 1730 cm.$^{-1}$ (s), 1630 cm.$^{-1}$ (w), 980 cm.$^{-1}$ (very weak) indicative of the ethyl *cis-β*-cyanoacrylate structure.

An analytical sample redistilled through a semimicro column boiled at 53–54° (0.15 mm.), n_D^{25} 1.4510.

Anal. Calcd. for $C_6H_7O_2N$: C, 57.60; H, 5.64; N, 11.20. Found: C, 57.74; H, 5.62; N, 11.20.

When only 1 mole each of ethyl chloroformate and triethylamine per mole of maleamic acid was used, the yield of ethyl *cis-β*-cyanoacrylate was 33% based on maleamic acid and no other product was isolated.

Preparation of ethyl cis-β-cyanoacrylate with ethyl chloroformate prepared in situ. Phosgene, 114 g. (1.15 moles), was dissolved in 600 ml. of dichloromethane at 0° and 54 g. (1.17 moles) of ethanol was added with gentle stirring. Then 57 g. (0.5 mole) of maleamic acid in a solution of 116 g. (1.15 mole) of triethylamine and 140 ml. dichloromethane was added dropwise with stirring while the reaction was cooled with an ice salt bath. Another 116 g. of triethylamine was added dropwise with stirring and the reaction was stirred overnight during which time it came to room temperature. One liter of cold 10% sodium hydroxide solution was added and the aqueous layer was saturated with sodium chloride. The organic layer was separated and the dichloromethane and triethylamine were recovered by distillation. The residue was distilled through a short Vigreux column and the main fraction, b.p. 59–62° (0.4 mm.), was collected, 35.2 g. (56%). The infrared spectrum indicated that ethyl *cis-β*-cyanoacrylate prepared in this manner was contaminated by a small amount of the *trans* isomer.

In another experiment an excess of phosgene was bubbled into a solution of 57 g. (0.5 mole) of maleamic acid, 46 g. (1.0 mole) of ethanol and 101 g. (1.0 mole) of triethylamine in 1 l. of dichloromethane. The solution was allowed to remain for *ca.* 48 hr. at room temperature and the triethylamine hydrochloride was removed by filtration and by washing the filtrate with water. After the solvent was removed the residue was distilled, 40 g., b.p. 40–70° (0.4 mm.). This material contained several halogen-containing compounds as was shown by positive Beilstein tests on several fractions obtained by vapor phase chromatography. The material not used in the analyses was dehydrohalogenated with a mixture of 20 ml. of triethylamine and 80 ml. of ether. After removal of the amine salt and the solvent, the product was distilled under reduced pressure (0.4–0.5 mm.). Three fractions were collected: 10.1 g., b.p. 42–43°; 5 g., b.p. 43–49°; 5 g., b.p. 49–53°. The infrared spectra of these fractions exhibited strong absorption at 975 cm.$^{-1}$ The first fraction was redistilled for analysis, b.p. 37–38° (0.23 mm.), n_D^{25} 1.4480.

Anal. Calcd. for $C_6H_7O_2N$: C, 57.60; H, 5.64; N, 11.20. Found: C, 57.57; H, 5.76; N, 11.23.

Phenyl cis-β-cyanoacrylate. This compound was prepared by essentially the same procedure as the one used for methyl *cis-β*-cyanoacrylate except that phenyl chloroformate was used in place of methyl chloroformate. The crude residue obtained after distilling the methylene chloride [26 g., (75%), m.p. 39–50°] was passed through a column of Florisil in benzene. The benzene eluates were evaporated and the residue recrystallized from 1:1 pentane-ether. Eight grams (23%) of phenyl *cis-β*-cyanoacrylate was obtained, m.p. 54–56°.

Anal. Calcd. for $C_{10}H_7O_2N$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.40; H, 4.21; N, 8.28.

The mother liquor from the recrystallization was evaporated and a sample of the residue (17 g.) subjected to vapor phase chromatography. This crude material contained 56% diphenyl carbonate, 2.3% phenol, 40% phenyl *cis-β*-cyanoacrylate and 1.6% of an unknown component. Thus, the total yield of phenyl *cis-β*-cyanoacrylate was 14.8 g. or 43%.

The infrared spectrum of the phenyl *cis-β*-cyanoacrylate showed absorption at 2200 cm.$^{-1}$ (w), 1730 cm.$^{-1}$ (s), 1600 cm.$^{-1}$ (m), 1620 cm.$^{-1}$ (s), 955 cm.$^{-1}$ (w) and 685 cm.$^{-1}$ (s).

Ethyl β-cyanopropionate. This compound was prepared by essentially the same procedure as the one used for methyl *cis-β*-cyanoacrylate. The starting materials were succinamic acid (m.p. 153–157°) and ethyl chloroformate. After removing the methylene chloride from the product, the residue was distilled through a semimicro column; 69% of a clear liquid was obtained, b.p. 54.3–55.5° (0.35 mm.), n_D^{25} 1.4228 (lit.[23] for ethyl β-cyanopropionate, b.p. 221°). The infrared spectrum of a liquid film possessed absorption at 2260 cm.$^{-1}$ (w), 1740 cm.$^{-1}$ (s), and no absorption from 1600–1700 cm.$^{-1}$ A weak broad band had appeared at 960 cm.$^{-1}$

Anal. Calcd. for $C_6H_9O_2N$: C, 56.68; H, 7.14. Found: C, 56.63; H, 7.03.

Ethyl o-cyanobenzoate. This compound was prepared by essentially the same procedure as the one used for methyl *cis-β*-cyanoacrylate. The starting materials were phthalamic acid and ethyl chloroformate. After removal of the methylene chloride, the residue was taken up in ether and filtered to remove the remainder of the amine salt. After removal of the ether under reduced pressure, the crude product remained. Recrystallization from benzene-pentane yielded 84% of white crystals, m.p. 62–65°. Ethyl *o*-cyanobenzoate has a reported m.p. 66.5–67°,[9] 70°.[24] The infrared spectrum of a melted film possessed absorption at 1725 cm.$^{-1}$ (s) and 2220 cm.$^{-1}$ (w).

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(23) O. Dalmer, C. Diehl, E. Feske, and H. Pieper, German Patent 597,305 (1934); *Chem. Abstr.*, **28**, 5078 (1934).

(24) G. Muller, *Ber.*, 19, 1491 (1886).

Anal. Calcd. for $C_{10}H_9O_2N$: C, 68.56; H, 5.18; N, 8.02. Found: C, 68.72; H, 5.43; N, 7.92.

Reaction of terephthalamic acid with ethyl chloroformate and triethylamine. A solution of terephthalamic acid (1.4 g., 0.0085 mole) and triethylamine (1.72 g., 0.017 mole) in 20 ml. of dichloromethane was cooled to 0–5° and 1.9 g. (0.018 mole) of ethyl chloroformate was added. Stirring was continued for 3.5 hr. at room temperature after the addition. The mixture was filtered to remove triethylamine hydrochloride and the solvent was removed under reduced pressure. The residue was washed several times with ether. The ether-insoluble material (1.4 g.) melted at 140–155°. The ether-soluble material (0.2 g.) melted with decomposition at 90–95°. The infrared spectra and melting points of these products preclude the presence of more than a trace of ethyl *p*-cyanobenzoate which has a reported melting point of 50°.[25]

Mixed anhydride of benzoic and ethylcarbonic acids prepared in presence of ethanol. A stirred solution of 12.2 g. (0.1 mole) of benzoic acid, 4.6 g. (0.1 mole) of ethanol and 10.1 g. (0.1 mole) of triethylamine in 100 ml. of dichloromethane was stirred at 0° while ethyl chloroformate (10.8 g., 0.1 mole) was added dropwise over 30 min. The temperature was kept below 0° during the addition. After the addition the external cooling bath was removed and the reaction mixture was stirred for 3 hr. The mixture was filtered and the filtrate washed with water, 5% sodium carbonate solution, water and dried over magnesium sulfate. The drying agent was removed by filtration and the solvent removed under reduced pressure. The clear, colorless liquid which remained, n_{D}^{25} 1.4930, showed absorption in the carbonyl region of its infrared spectrum (liquid film) at 1775 cm.$^{-1}$ (s) and 1715 cm.$^{-1}$ (w). The spectrum was identical with that for the mixed anhydride of benzoic and ethyl carbonic acids (n_{D}^{25} 1.4941) obtained by the procedure described above[14] except that no ethanol was added and the reaction time was 1 hr. An attempt was made to distill the crude product in a semimicro distilling apparatus. A vacuum of 1 mm. was applied and the distillation pot heated slowly. Nothing distilled until the temperature of the pot reached 140°; then the pressure rose to 4 mm. and vigorous decomposition of the product began.

Dehydration of benzamide with ethyl chloroformate and triethylamine. A solution of 2.8 g. (0.023 mole) of benzamide in 25 ml. of acetone and 2.3 g. (0.023 mole) of triethylamine was cooled to 0–5°. Ethyl chloroformate (2.5 g., 0.023 mole) was added dropwise with stirring. After the addition, the cooling bath was removed and the reaction was stirred at room temperature for 3 hr. The reaction mixture was diluted with water and extracted three times with dichloromethane. The dichloromethane extracts were dried over magnesium sulfate and solvent was removed under vacuum. An infrared spectra of the solid residue (2.4 g.) indicated traces of benzonitrile. The residue was washed with ether which left a white solid (2.0 g.), m.p. 119–121.5°. Recrystallization from aqueous ethanol raised the melting point to 123–125°. A mixture melting point with the starting benzamide (m.p. 125–127.8°) was 124–127°.

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[CONTRIBUTION FROM THE RESEARCH DEPARTMENT OF THE UNION CARBIDE PLASTICS CO.]

The Synthesis of *N*-Substituted Isomaleimides

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N-Alkyl and *N*-aryl substituted isomaleimides and bisisomaleimides have been prepared by dehydration of the corresponding *N*-substituted maleamic acids with *N,N'*-dicyclohexylcarbodiimide, ethyl chloroformate-triethylamine, and trifluoroacetic anhydride–triethylamine. *N*-Substituted isomaleimides were isomerized to the symmetrical *N*-substituted maleimides in the presence of sodium acetate or triethylammonium acetate. An improvement in the synthesis of *N*-alkyl maleimides is also reported.

The synthesis of three isomaleimides has been previously recorded in the literature. Piutti[1] has claimed the preparation of *N*-(*p*-methoxyphenyl)isomaleimide (I, R = *p*-$CH_3OC_6H_5$—) and *N*-(*p*-ethoxyphenyl)isomaleimide (I, R = *p*-C_2H_5-OC_6H_5—) by acetyl chloride dehydration of the corresponding maleamic acids (II). Roderick[2] has recently shown that the compounds obtained by Piutti do not possess the isomaleimide structure but instead are the α-chloro-*N*-(*p*-alkoxyphenyl)-succinimides. Tsou, Barnett, and Seligman[3] have dehydrated *N*-(4-hydroxy-1-naphthyl)maleamic acid with trifluoroacetic anhydride and obtained *N*-(4-hydroxy-1-naphthyl)isomaleimide. This is the only substantiated example of an isomaleimide in the literature. Attempts[3] to prepare other isomaleimides using the trifluoroacetic anhydride reagent were unsuccessful. Mild dehydration of phthalanilic acid with acetyl chloride was shown to give the hydrochloride of *N*-phenylisophthalimide which on careful treatment with potassium hydroxide solution allowed the isolation of *N*-

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