The Reaction of Tropylmalononitrile and Ethyl Tropylcyanoacetate with Acyl Chloride[1]

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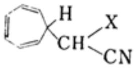
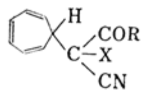
The acylation of tropylmalononitrile (I) or ethyl tropylcyanoacetate (II) would be expected to give a compound of type (A), which, under basic conditions, might be hydrolyzed to a tropyl derivative different from the starting material, might form a heptafulvene by the elimination of hydrogen cyanide, or might give a styrene-type compound through rearrangement.[2] However, the treatment of I or II with acyl chloride in a basic medium led to an unexpected result, which will be described in this paper.



I : X=CN
II : X=$COOC_2H_5$

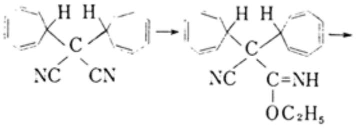


(A)

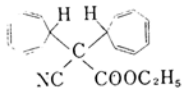
X=CN or $COOC_2H_5$
R=C_6H_5 or CH_3

The reaction of equimolar proportions of benzoyl chloride and I in a pyridine solution afforded compound (III), $C_{17}H_{14}N_2$, and benzoylcyanoacetamide. The former compound was also obtained when I was treated with acetyl chloride in pyridine. The ultraviolet spectrum of III showed a maximum at 255 mμ (log ε = 3.81) due to the tropyl group;[3] the infrared spectrum had a band at 2260 cm^{-1} (CN group). III may, therefore, be supposed to be ditropylmalononitrile. This was comfirmed by a mixed melting point determination with an authentic sample.[4] In the above reaction, and in several of those following, the products were isolated by chromatography on aluminum oxide,[5] which led to the partial conversion of compound (III) into ditropylcyanoacetamide (IV), which was identical with the compounds obtained by reaction of tropylcyanoacetamide with tropylium ions.

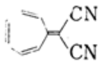
The sodio compound of I, in ethanol, also reacted with acetyl or benzoyl chloride to afford III in a fairly good yield, along with ethyl ditropylcyanoacetate[4] (V). The reaction of I with acyl chlorides in ethanol, in the presence of two molar equivalents of sodium ethoxide, gave compound (VI) $C_{19}H_{20}ON_2$ and 8, 8-dicyanoheptafulvene[4] (VII), besides compounds III, IV and V; the yields are given in Table I. The infrared spectrum of VI showed bands at 2240 (CN), 3345 (NH) and 1658 cm^{-1} (C=N). The mild treatment of VI with acid gave V. Furthermore, VI could be obtained from the reaction of III with sodium ethoxide. From these facts, VI is concluded to be ethyl ditropylcyanoacetimidate.



III VI



V



VII

It is assumed that 8,8-dicyanoheptafulvene (VII) originates not from the intermediate (A), but from dehydrogenation of I, because the preferential elimination of hydrogen cyanide from A should give 8-cyano-8-acylheptafulvene. Indeed, it was found that the treatment of I with one molar equivalent of sodium ethoxide afforded tropylcyanoacetamide, together with a trace of VII, which is probably formed by the dehydrogenation of I with air.

The reaction of ethyl tropylcyanoacetate (II) with benzoyl or acetyl chloride in pyridine afforded ethyl ditropylcyanoacetate (V). The acylation of a sodio compound of II, in ethanol, also afforded V in the yield shown in Table II.

The formation of the ditropyl compounds (III, V, etc.) in the acylation reaction of I or

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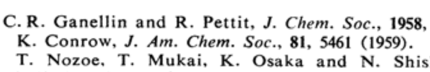
[1] Presented at the 15th Annual Meeting of the Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, October, 1963.

[2] The following reactions would be expected:



Cf. C. R. Ganellin and R. Pettit, *J. Chem. Soc.*, **1958**, 576.

[3] K. Conrow, *J. Am. Chem. Soc.*, **81**, 5461 (1959).

[4] T. Nozoe, T. Mukai, K. Osaka and N. Shishido, This Bulletin, **34**, 2385 (1961).

[5] This transformation did not occur when a neutralized aluminum oxide was used.

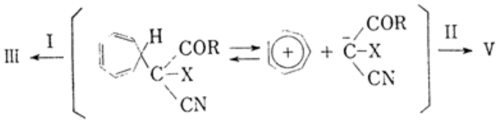
TABLE I. THE RESULTS OF THE ACYLATION OF I

Medium	Reagent	Yield of products, % III	IV	V	VI	VII
In pyridine	C_6H_5COCl	82	14			
	CH_3COCl	58	6.3			
In ethanol 1 mol. equiv. of $NaOC_2H_5$	C_6H_5COCl	89	7	4		
	CH_3COCl	67	5.4			
In ethanol 2 mol. equiv. of $NaOC_2H_5$	C_6H_5COCl	35		5.5	2.6	1.5
	CH_3COCl		21	1.4	20	0.5

TABLE II. THE YIELDS (%) OF V IN ACYLATION OF II

Reagent	In pyridine	In ethanol 1 mol. equiv. of $NaOC_2H_5$	In ethanol 2 mol. equiv. of $NaOC_2H_5$
C_6H_5COCl	45	64	21
CH_3COCl	3.6	50	30

II can be explained as is shown in the following scheme, the first step of which is assumed to be the formation of compound A. The presence of three electron-with drawing groups in A, and the stabilization of the resulting tropylium ions, constitute a strong driving force for the cleavage of A to tropylium ions. The products III or V can result from the reaction of the tropylium ions with I or II.[4)] As another pathway to III or V, a nucleophilic attack of I or II on A before its cleavage is also possible.



(A)

It has been pointed out previously that, in general, the fragmentation of tropyl derivatives is brought about by attack Lewis acids[3)] or electrophilic reagents.[6)] However, it should be emphasized that, in this case, the formation of tropylium ions (or their precursors) occurs readily, even in a basic medium, during the reaction of I or II with acyl chloride.

Attempted acylation of other tropyl compounds containing active methylenes, such as diethyl tropylmalonate, tropylacetylacetone and tropyldibenzoylmethane, did not afford any ditropyl compound, but it did result in the recovery of the starting materials. This is of interest when compared with the fact that diethyl tropylmalonate did not react with tropylium ions.[4)]

Experimental[7,8)]

The Reaction of Tropylmalononitrile (I) with Acyl Chloride in Pyridine.—*a) With Benzoyl Chloride.*—To a solution of 1 g. (6 mmol.) of I in 3 ml. of pyridine, 0.9 g. (6 mmol.) of benzoyl chloride was added under cooling with ice. After it had been stirred for 20 hr. at room temperature, the reaction mixture was poured into water and extracted with benzene. The benzene-extract was then washed with 2 N hydrochloric acid and 2 N sodium hydroxide successively, dried over sodium sulfate, and evaporated to give 1.92 g. of a brown oil. This oil was dissolved in benzene and chromatographed, using 60 g. of aluminum oxide (Grade I). The evaporation of the benzene-elute gave 650 mg. of colorless crystals (m.p. 103—105°C), which, on recrystallization from ethanol, afforded ditropylmalononitrile (III)[3)] as colorless crystals (m.p. 106—108°C). The evaporation of the elute with benzene-methanol (5:1) gave 115 mg. of colorless crystals (m.p. 155—162°C), which, on recrystallization from petroleum ether-benzene, gave colorless crystals (m.p. 167°C). They were found to be identical with ditropylcyanoacetamide (IV), which was synthesized as will be described later. The alkaline washings were acidified with 6 N hydrochloric acid and extracted with ether. The ether-extract was dried over sodium sulfate and evaporated to give colorless crystals (m.p. 98—105°C), which, on recrystallization from benzene, gave 30 mg. of colorless crystals (m.p. 134—135°C), assumed to be benzoylcyanoacetamide.

Found: C, 64.03; H, 4.12; N, 14.51. Calcd. for $C_{10}H_8O_2N_2$: C, 63.82; H, 4.29; N, 14.89%.

b) With Acetyl Chloride.—The reaction of 2.0 g. (13 mmol.) of I and 1.02 g. (13 mmol.) of acetyl chloride was carried out in a pyridine solution as has been described in a). The evaporation of the benzene extract gave 1.1 g. of a neutral oil, which crystallized when allowed to stand. The recrystallization of crystals from ethanol gave 572 mg. of ditropylmalononitril (m.p. 105—107°C). The mother liquor was then evaporated, and the residue was dissolved in benzene and chromatographed by passing it through a column containing 15 g. of aluminum oxide (Grade I). A further 350 mg. of III (m.p. 105—107°C) were obtained from the benzene elute, and 107 mg. IV (m.p. 165—167°C),

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6) T. Mukai and H. Tsuruta, This Bulletin, 37, 1018 (1964).

7) All melting points are uncorrected.

8) The microanalyses were carried out by Miss A. Iwanaga and Miss M. Suzuki, to whom the authors wish to express their gratitude.

from the elute with ether-methanol (5 : 1). The alkaline washings were acidified and extracted with ether. The evaporation of the ether-extract gave 320 mg. of an acidic, viscous oil.

The Synthesis of Tropylcyanoacetamide and Ditropylcyanoacetamide (IV).—a) To a solution of 6.5 g. (30 mmol.) of tropyl bromide dissolved in 15 ml. of water, 2.5 g. (30 mmol.) of cyanoacetamide was added. The reaction mixture was neutralized to pH 6 by the addition of a 6 N sodium hydroxide solution and stirred at room temperature for 2 hr., during which time colorless crystals separated out. Filtration, followed by recrystallization from benzene, afforded 4.8 g. of tropylcyanoacetamide as colorless needles (m. p. 144—145°C).

Found: C, 69.21; H, 5.44; N, 15.74. Calcd. for $C_{10}H_{10}ON_2$: C, 68.95; H, 5.79; N, 16.08%.

b) To a solution of 77 mg. (0.45 mmol.) of tropyl bromide in 3 ml. of pyridine, 50 mg, (0.3 mmol.) of tropylcyanoacetamide was added, and the reaction mixture was allowed to stand for 12 hr. at room temperature. After the pyridine had been evaporated under reduced pressure, the residue was poured into water and extracted with benzene. The benzene-extract was washed with dilute hydrochloric acid and then with water and dried over sodium sulfate. The evaporation of benzene gave crystals, which, on recrystallization from ethanol, gave 76 mg. of ditropylcyanoacetamide (IV) as colorless crystals (m. p. 167°C).

Found: C, 76.83; H, 5.90; N, 9.99. Calcd. for $C_{17}H_{16}ON_2$: C, 77.25; H, 6.10; N, 10.60%.

Ditropylcyanoacetamide (IV) was also obtained in the chromatography of III using aluminum oxide. A benzene solution of 200 mg. of III was passed through a column containing 6 g. of alumina (Grade 1). From the benzene elute, 170 mg. of III was recovered, while 25 mg. of IV (m. p. 165—167°C) was obtained from the elute with ether-methanol (1 : 1).

The Reaction of a Sodio Compound of Tropylmalononitrile (I) with Acyl Chloride in Ethanol. —*a) With Benzoyl Chloride.*—To a solution of sodium ethoxide prepared from 450 mg. (19 mmol.) of sodium and 20 ml. of absolute ethanol, 3 g. (19 mmol.) of I was added; the mixture was then stirred for 1 hr. at room temperature. Under cooling with ice, 2.7 g. (19 mmol.) of benzoyl chloride was added, drop by drop, to the solution. After it had been stirred for 24 hr. at room temperature, the reaction mixture was poured into water and extracted with benzene. The benzene extract afforded 3.51 g. of a neutral oil by the usual treatment. The oil crystallized on standing; these crystals, on recrystallization from ethanol, afforded 705 mg. of III (m. p. 104—105°C). The filtrate was evaporated, and the residue was dissolved in benzene and chromatographed using 60 g. of aluminum oxide (Grade I). The evaporation of the benzene elute gave 1.50 g. of III as colorless prisms (m. p. 105—106°C). The ether elute gave 125 mg. of V as colorless needles (m. p. 125—126°C). From the elute with ether-methanol (5 : 1), 197 mg. of IV (m. p. 167—169°C) was obtained. The alkaline solution, after the extraction with benzene, was acidified with 6 N hydrochloric acid and extracted with ether. From the ether-extract, 770 mg. of an acidic oil was obtained in the usual way; this crystallized on standing. Filtration, followed by recrystallization from benzene, gave 705 mg. of benzoylcyanoacetamide (m. p. 134—135°C).

b) With Acetyl Chloride.—In the same way as in a), 2.3 g. of neutral oil and 100 mg. of an acidic oil were obtained from the reaction of 2 g. (13 mmol.) of I, 300 mg. (13 mmol.) of sodium in ethanol and 1.02 g. (13 mmol.) of acetyl chloride. On being allowed to stand, the neutral oil gave crystals, which, on recrystallization from ethanol, gave 630 mg. of III (m. p. 105°C). The filtrate was evaporated, dissolved in benzene, and chromatographed by passing it through a column containing 23 g. of aluminum oxide (Grade I). The benzene elute gave 480 mg. of III (m. p. 105—106°C). Elution with ether-methanol (10 : 1) afforded 90 mg. of IV (m. p. 166°C).

The Reaction of Tropylmalononitrile (I) with Acyl Chloride in the Presence of 2 Molar Equivalents of Sodium Ethoxide. — *a) With Benzoyl Chloride.*—To a solution of sodium ethoxide prepared from 584 mg. (26 mmol.) of sodium and 20 ml. of absolute ethanol, 1.95 g. (13 mmol.) of I and then 1.5 ml. (13 mmol.) of benzoyl chloride were added drop by drop under cooling with ice. After it had been stirred for 21 hr. at room temperature, the reaction mixture was treated in the usual way to give 2.46 g. of a neutral oil containing crystals. The addition of a small amount of ethanol, followed by filtration, afforded 496 mg. of colorless crystals, (m. p. 101—107°C), which, on recrystallization from ethanol, yielded 385 mg. of VI as colorless prisms (m. p. 114—115°C).

Found: C, 77.99; H, 6.33; N, 9.31. Calcd. for $C_{19}H_{20}ON_2$: C, 78.05; H, 6.90; N, 9.58%.

The combined filtrate was evaporated, dissolved in benzene, and chromatographed using 70 g. of aluminum oxide (Grade I). The evaporation of the benzene elute gave 530 mg. of colorless crystals, (m. p. 95—102°C), which, on recrystallization from ethanol, gave 140 mg. of III (m. p. 106—107°C). Elution with benzene-ether (5 : 1) gave 150 mg. of crystals with an oil, which, on recrystallization from ethanol, gave 30 mg. of red crystals (m. p. 140—170°C) from the scarcely soluble portion and 103 mg. of colorless crystals (m. p. 121—124°C) from the easily soluble portion. The recrystallization of the former from ethanol gave 8, 8-dicyanoheptafulvene (VII) (m. p. 199°C), while the latter gave V (m. p. 125°C). Elution with ether-methanol (10 : 1) afforded 300 mg. of crystals (m. p. 130—140°C), which, on recrystallization from ethanol, gave tropylcyanoacetamide (m. p. 140—142°C).

b) With Acetyl Chloride.—As has been described in a), 1.75 g. of a neutral oil was obtained from the reaction of 1.95 g. (13 mmol.) of I with 1.02 g. (13 mmol.) of acetyl chloride in the presence of 2 mol. equivalents of sodium ethoxide in an ethanolic solution. The oil crystallized partly when allowed to stand. Filtration, followed by recrystallization from ethanol, afforded 360 mg. of VI as colorless needles (m. p. 114—115°C). The filtrate was then evaporated, dissolved in benzene and chromatographed by passing it through a column containing 50 g. of aluminum oxide (Grade I). The evaporation of the elute with benzene-ether (5 : 1) yielded 450 mg. of an oil, which crystallized on standing. The recrystallization of the crystals from ethanol gave 250 mg. of the starting material (I) (m. p. 60—62°C) as colorless prisms. Elution with ether gave 70 mg. of orange crystals, which, on recrystallization from benzene, afforded 10 mg. of red needles (m. p. 140—170°C), mainly composed of 8, 8-dicyanoheptafulvene (identified by its infrared spectrum). The benzene filtrate was evaporated to give crystals which, on recrystallization from ethanol, afforded 25 mg. of V (m. p. 120—123°C). The evaporation of the elute with ether-methanol (1 : 1) afforded 350 mg. of crystals (m. p. 140—142°C), which, on recrystallization from ethanol, gave IV (m. p. 168—169°C).

The Hydrolysis and Synthesis of Ethyl Ditropylcyanoacetimidate (VI).—*a) The Hydrolysis of VI.*—A solution of 100 mg. of VI dissolved in a mixture of 1 ml. each of 2 N hydrochloric acid and ethanol was refluxed for 30 min. After neutralization with 2 N sodium hydroxide, the reaction mixture was extracted with benzene. The benzene extract was then washed with water, dried over sodium sulfate, and evaporated to give 60 mg. of an yellow oil, which crystallized on cooling. Recrystallization from ethanol gave V as pale yellow needles (m. p. 126—127°C).

b) The Synthesis of VI.—To a solution of sodium ethoxide prepared from 600 mg. (24 mmol.) of sodium and 20 ml. of absolute ethanol, 500 mg. (2 mmol.) of III was added; the reaction mixture was stirred at room temperature for 20 hr., during which time colorless crystals separated out. After the evaporation of the ethanol, the reaction mixture was poured into water and extracted with benzene. The extract was washed with water, dried over sodium sulfate, and evaporated to give colorless needles, which, on recrystallization from ethanol, afforded 150 mg. of VI as colorless needles (m. p. 110—111°C). The residue from the mother liquor was recrystallized from ethanol to give 153 mg. of IV (m. p. 167°C).

The Reaction of Tropylmalononitrile (I) with Sodium Ethoxide in Ethanol.—To a solution of sodium ethoxide prepared from 46 mg. (2 mmol.) of sodium and 4 ml. of absolute ethanol, 312 mg. (2 mmol.) of I was added under cooling with ice. After it had been stirred for 24 hr. at room temperature, the solution was poured into water and extracted with ether; the usual treatment of the ether-extract then gave 300 mg. of an oil. The oil was dissolved in benzene and chromatographed by passing it through a column containing 9 g. of aluminum oxide (Grade I). The evaporation of the benzene elute gave 73 mg. of the starting material (I) (m. p. 62°C). Elution with benzene-ether gave 20 mg. of 8, 8-dicyanoheptafulvene (VII) (m. p. 199°C), while elution with ether-methanol gave 120 mg. of tropylcyanoacetamide (m. p. 145°C).

The Reaction of Ethyl Tropylcyanoacetate (II) with Acyl Chloride in Pyridine.—*a) With Benzoyl Chloride.*—To a solution of 2 g. (11 mmol.) of II dissolved in 4 ml. of pyridine, 1.55 g. (11 mmol.) of benzoyl chloride was added drop by drop under cooling with ice. The mixture was stirred under cooling for 1 hr. and at room temperature for 20 hr. The solution was then poured into water and extracted with benzene. The benzene-extract was successively washed with 2 N hydrochloric acid, 2 N sodium hydroxide and water, dried over sodium sulfate, and evaporated to give 2 g. of a brown oil, which crystallized on standing. Filtration, followed by recrystallization from ethanol, gave 485 mg. of ethyl ditropylcyanoacetate (V) (m. p. 125—127°C).[8] The ethanolic filtrate was evaporated, dissolved in benzene, and chromatographed using aluminum oxide. The evaporation of the benzene elute gave 143 mg. of V (m. p. 124—126°C), and the following benzene elute gave 95 mg. of a brown oil, which was identified with the starting material (II) by a comparison of their infrared spectra.

b) With Acetyl Chloride.—The reaction of 2 g. (11 mmol.) of II and 0.865 g. (11 mmol.) of acetyl chloride was carried out as in a). Only 52 mg. of V was obtained as colorless crystals (m. p. 127—128°C). The acidification of the alkaline washings, followed by extraction with ether and the usual treatment of the ether-extract, gave 1.12 g. of an acidic oil which contained the starting material (II) (identified from the infrared spectrum).

The Reaction of a Sodio Compound of Ethyl Tropylcyanoacetate (II) with Acyl Chloride in Ethanol.—*a) With Benzoyl Chloride.*—A sodio compound of II was obtained from 253 mg. (11 mmol.) of sodium and 2 g. (11 mmol.) of II in 10 ml. of absolute ethanol. To this solution, 1.55 g. (11 mmol.) of benzoyl chloride was added under cooling with ice. After it had been stirred for 20 hr. at room temperature, the mixture was poured into water and extracted with benzene. The benzene extract was washed with water, dried over sodium sulfate, and evaporated to give 2.1 g. of an oil, which crystallized on cooling. Filtration, followed by recrystallization from ethanol, gave 510 mg. of V as colorless crystals (m. p. 124—125°C). The ethanolic filtrate was evaporated, and the residue was dissolved in benzene and chromatographed using 40 g. of aluminum oxide (Grade I). The evaporation of the benzene elute gave 380 mg. of V (m. p. 124—125°C). After the mother liquor from the benzene extract had been acidified and extracted with ether, the ether-extract was dried over sodium sulfate and evaporated to give 587 mg. of an acidic oil containing crystals of ethyl benzoylcyanoacetate (m. p. 39.5—40.0°C)[9]

b) With Acetyl Chloride.—When the reaction of 2 g. (11 mmol.) of II with 0.864 g. (11 mmol.) of acetyl chloride was carried out in the same way as in a), and 1.4 g. of a neutral oil was obtained; this crystallized partly. Filtration, followed by recrystallization from ethanol, afforded 605 mg. of V (m. p. 126—127°C). The filtrate was evaporated, dissolved in benzene, and chromatographed using aluminum oxide (Grade I) to give 106 mg. of V and 150 mg. of II.

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[9] M. Haller, *Bull. soc. chim. France* [2], **45**, 271 (1886).

The Reaction of Ethyl Tropylcyanoacetate (II) and Acyl Chloride in Ethanol in the Presence of 2 Molar Equivalents of Sodium Ethoxide.—*a) With Benzoyl Chloride.*—To a solution of 506 mg. (22 mmol.) of sodium dissolved in 15 ml. of absolute ethanol, 2 g. (11 mmol.) of II was added, and then 1.55 g. (11 mmol.) of benzoyl chloride was added under cooling with ice. The usual treatment of the reaction mixture afforded 1.40 g. of a neutral oil, which crystallized partly, and 1.26 g. of an acidic oil. The former was filtered and recrystallized from ethanol to give 298 mg. of V as colorless needles (m. p. 124—125°C).

b) With Acetyl Chloride.—As has been described in a), 2 g. (11 mmol.) of II was acetylated with 0.864 g. (11 mmol.) of acetyl chloride in the presence of 2 molar equivalents of sodium ethoxide. From the reaction mixture, 760 mg. of a neutral oil, which crystallized partly, and 690 mg. of an acidic oil were obtained. When the crystals obtained from the neutral oil by chromatography were recrystallized from ethanol, 415 mg. of V (m. p. 126—127°C) were obtained.

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