NASA TM-77886

NASA-TM-77886 19850021698

NASA TECHNICAL MEMORANDUM NASA TM-77886

CONDENSATION OF ANHYDRIDES OF DICARBOXYLIC ACIDS WITH COMPOUNDS CONTAINING ACTIVE METHYLENE GROUPS.
I. CONDENSATION OF PHTHALIC ANHYDRIDE WITH ACETOACETIC AND MALONIC ESTERS

V. P. Oshkaya and G. Ya. Vanag

Translation of "Kondensatsiya angidridov dikarbonovykh kislot s soyedineniyami, soderzhashchimi aktivnyye metilenovyye gruppy. I. Kondensatsiya ftalevogo angidrida s atsetouksusnym i malonovym efirami," Izvestiya Akademii nauk Latviyskoy SSR, Seriya khimicheskaya, No. 3, 1964, pp. 271-276.

(Latvijas PSR Zinatnu Akademijas Vestis, Kimijas Serija)

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D.C. 20546 JUNE 1985

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         INVALID COMMAND
  3      2      2 UTP/CONDENSATION *+2 ANHYDRIDES *+2 DICARBOXY
           DISPLAY 03/2/1
       85N30010*#   ISSUE 19   PAGE 3227   CATEGORY 23   RPT#: NASA-TM-77886 NAS
       1.15:77886   CNT#: NASW-4005   85/06/00  12 PAGES   UNCLASSIFIED DOCUMENT
UTTL: Condensation of anhydrides or dicarboxylic acids with compounds containing
      active methylene groups.  Part 1:  Condensation of phthalic anhydride with
      acetoacetic and malonic ester
AUTH: A/OSHKAYA, V. P.;  B/VANAG, G. Y.
CORP: National Aeronautics and Space Administration, Washington, D.C.
      AVAIL.NTIS
SAP:  HC A02/MF A01
CIO:  LATVIA Transl. by Kanner (Leo) Associates, Redwood City, Calif.  Original
      doc. prep. by Latvian State Univ.   Transl. into ENGLISH from Izv. Akad.
      Nauk Latv. SSR, Ser. Khim. (Latvia), no. 6, 1964  p 271-276
MAJS: /*ANHYDRIDES/*CONDENSING/*DICARBOXYLIC ACIDS/*ESTERS/*MALEATES/*METHYLENE
      /*PHTHALATES
MINS: / ACETIC ACID/ ALIPHATIC COMPOUNDS/ CHEMICAL REACTIONS/ FATTY ACIDS/
      HYDROCARBONS
ABA:  E.A.K.
ABS:  Phthalic anhydride was condensed with acetoacetic ester in acetic
      anhydride and triethylamine solution, and when phthalyl chloride was
      reacted with sodium acetoacetic ester compounds were formed of the
      phthalide and indandione series: phthalylacetoacetic ester and a
      derivative of indan-1,3-dione which after boiling with hydrochloric acid
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NASA-TM-77886 1985

CONDENSATION OF ANHYDRIDES OF DICARBOXYLIC ACID WITH COMPOUNDS CONTAINING ACTIVE METHYLENE GROUPS. Part I: CONDENSATION OF PHTHALIC ANHYDRIDE WITH ACETOACETIC AND MALONIC ESTERS. (Kondensatisiya angidridov dikarbonovykh kislt s soyedineniyami, soderzhaschimi aktivnyye metilenovyye gruppy. I. Kondensatsiya ftalevogo angidrida s aesetouksusnym i malonovym efirami). V.P. Oshkaya and G.Ya. Vanag. June 1985. 10p. (Eng. trans.).

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Latvijas PSR Zinatnu Akademijas 1964
Vestis, Kimijas Serija, no.6, N85-30010#
p.271-276 (USSR) N-155,444

STANDARD TITLE PAGE

1. Report No. NASA TM-77886
2. Government Accession No.
3. Recipient's Catalog No.
4. Title and Subtitle CONDENSATION OF ANHYDRIDES OF DICARBOXYLIC ACIDS WITH COMPOUNDS CONTAINING ACTIVE METHYLENE GROUPS. I. CONDENSATION OF PHTHALIC ANHYDRIDE WITH*
5. Report Date June 1985
6. Performing Organization Code
7. Author(s) V. P. Oshkaya and G. Ya. Vanag
8. Performing Organization Report No.
9. Performing Organization Name and Address

Leo Kanner Associates
Redwood City, California 94063

10. Work Unit No.
11. Contract or Grant No. NASW-4005
13. Type of Report and Period Covered Translation
12. Sponsoring Agency Name and Address National Aeronautics and Space Administration, Washington, D.C. 20546
14. Sponsoring Agency Code
15. Supplementary Notes

Translation of "Kondensatsiya angidridov dikarbononvykh kislot s soyedineniyami, soderzhashchimi aktivnyye metilenovyye gruppy. I. Kondensatsiya ftalevogo angidrida s atsetouksusnym i malonovym efirami," Izvestiya Akademii nauk Latviyskoy SSR, Seriya khimicheskaya, No. 6, 1964, pp. 271-276.

16. Abstract

When phthalic anhydride was condensed with acetoacetic ester in acetic anhydride and triethylamine solution, as well as when phthalyl chloride was reacted with sodium acetoacetic ester, compounds of the phthalide and indandione series were formed: phthalylacetoacetic ester and a derivative of indan-1,3-dione which after boiling with hydrochloric acid yielded indan-1,3-dione.

Phthalylmalonic ester was obtained from phthalic anhydride and malonic ester in the presence of triethylamine.

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*ACETOACETIC AND MALONIC ESTER

17. Key Words (Selected by Author(s))
18. Distribution Statement Unclassified-Unlimited
19. Security Classif. (of this report) Unclassified
20. Security Classif. (of this page) Unclassified
21. No. of Pages 10
22.

N-85-30010#
N-155,444

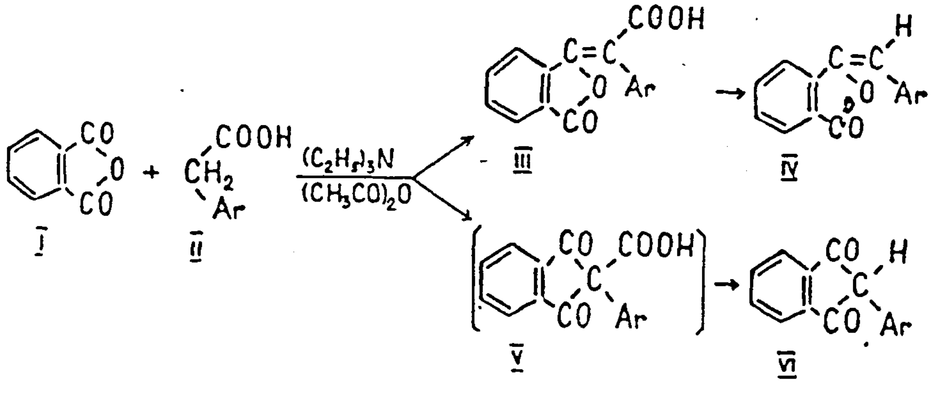
CONDENSATION OF ANHYDRIDES OF DICARBOXYLIC ACIDS WITH COMPOUNDS CONTAINING ACTIVE METHYLENE GROUPS.

I. CONDENSATION OF PHTHALIC ANHYDRIDE WITH ACETOACETIC AND MALONIC ESTER

V. P. Oshkaya and G. Ya. Vanag

Latvian State University,
Latvian SSR Academy of Sciences Institute of Organic Chemistry

In some of our works [1-3] we have already attempted to prove that /271* phthalic anhydride and its homologs, in a solution of acetic anhydride in the presence of triethylamine, react with aryl acetic acids according to two reaction outlines. Depending on the amount of triethylamine and the temperature conditions, either a Perkin reaction occurs and derivatives of 3-methylenephthalide (III; IV) are produced, or there is direct formation of derivatives of indan-1,3-dione (V; VI). In aryl acetic acids the active methylene group is located between a carboxyl group and an aryl radical, so when the condensation reaction proceeded according to the latter outline, the corresponding 2-aryl indan-1,3-diones were isolated (VI).



With further development of this method of synthesis, it seemed of interest to study the interaction of phthalic anhydride with compounds containing an active methylene group of another type than in aryl acetic acids, and thereby directly produce other groups of indandione compounds. Selected for experiments were the ethyl ester of acetoacetic acid and the diethyl ester of malonic acid, in which

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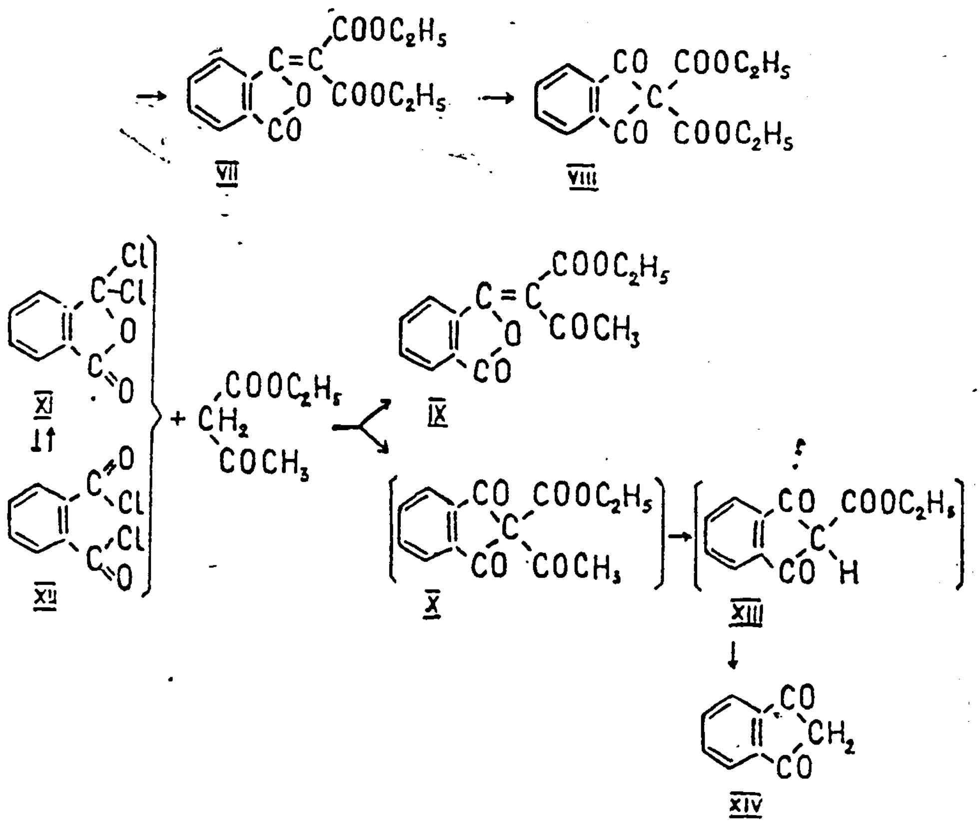
*Numbers in the margin indicate pagination in the foreign text.

the active methylene group is adjacent to the carbethoxyl group.

The use of substituted acetic acids in the form of their esters in Perkin's reactions is quite atypical and relatively rarely described [4]. True, as early as 1881 Gabriel reported attempts to condense phthalic anhydride with malonic and acetoacetic esters in the presence of sodium/272 acetate [5]. The reaction was conducted at a temperature of 130-150°, and the expected phthalylmalonic (VII) and phthalylacetoacetic (IX) esters were not isolated. Obtained in low yields were the products of further transformation of the supposed primary reaction products -- phthalylmalonic and phthalylacetoacetic esters -- specifically, tri-*o*-benzoylene benzene, 3-methylene phthalide, and some other products of unestablished structure.



The production of phthalylmalonic and phthalylacetoacetic esters later was mentioned many times; condensation of phthalyl chloride with sodium malonic and sodium acetoacetic esters was used for the synthesis [6-12]. On the question of the structure of the reaction products -- whether they are derivatives of the phthalide (VII and IX) or of indan-1,3-dione (VIII and X) -- the authors disagree [6-12]. These questions were especially carefully investigated by Ruggli and Zickendraht [12], using phthalylacetoacetic ester as an example.

With disodium acetoacetic ester, phthalylchloride reacts mostly in its asymmetric form (XI), yielding about 60% phthalide derivative -- phthalylacetoacetic ester (IX). Also isolated from the reaction mixture, however, are small amounts of the ethyl ester of indan-1,3-dione-2-carboxylic acid (XIII) and indan-1,3-dione (XIV), which is evidence that phthalylchloride in this condensation yields derivatives also responding to its symmetric form (XII). In our experiments on condensation of phthalic anhydride with acetoacetic ester in a solution of acetic anhydride and triethylamine at room temperature, phthalylacetoacetic ester is produced with a small yield, even at 1:4:4:48 /273 molar ratios of triethylamine, phthalic anhydride, acetoacetic ester, and acetic anhydride. The reaction product from the unreacted phthalic anhydride is purified by recrystallization from ethyl alcohol; phthalic anhydride esterifies and remains in solution, while phthalylacetoacetic ester is crystallized out with very minor losses.

When the amount of employed triethylamine is increased, the yield of phthalylacetoacetic ester also increases, and at component molar ratios of 1:1:1:4 it reaches about 45% of theoretical. No further increase in yield is observed when more triethylamine is employed. At molar ratios of triethylamine, phthalic anhydride, and acetoacetic ester of 1:1:1 the forming phthalylacetoacetic ester crystallizes out of the reaction mixture in relatively pure form, but although phthalylacetoacetic ester is formed with increased quantities of triethylamine, it remains in solution together with the other reaction products. The number of these side reactions continues to increase with further increases of the triethylamine concentration. Under these conditions an oily precipitate is yielded when the reaction mixture is decomposed with ice and hydrochloric acid. Since phthalylacetoacetic ester remains virtually unchanged when boiled with a dilute hydrochloric acid solution, this can be used to separate the reaction products; after brief heating of the mixture of products diluted with hydrochloric acid, the solution is filtered and the indan-1,3-dione (XIV) is crystallized out of the filtrate, reaching a yield of 23% of theoretical. In this case, too, the same intermediate products (X; XIII) apparently form upon condensation as with the condensation of phthalylchloride with sodium acetoacetic ester.

Observed in the IR absorption spectra of phthalylacetoacetic ester, taken in the carbonyl-group absorption region, a number of extremely strong maxima are observed (at 1797 cm^{-1} [78%], 1739 cm^{-1} [77%], 1658 cm^{-1} [59%], and 1628 cm^{-1} [74%]), of which the maximum at 1797 cm^{-1} can be referred with confidence to the lactone ring of the phthalide [13, 14][1]. Thus the spectroscopic data we obtained agree fully with the conclusions of Ruggli and Zikendraht [12], made on the basis of chemical studies; phthalylacetoacetic ester has a phthalide (IX) structure, not that of indan-1,3-dione (X).

In a solution of triethylamine and acetic anhydride, phthalic anhydride with the diethyl ester of malonic acid yields phthalylmalonic ester (VII). The yield of the latter at room temperature and equimolar ratios of the reacting components reaches 60.3%, i.e., more than the yield of phthalylacetoacetic ester under the same conditions. As is observed in the synthesis of phthalylacetoacetic ester, further increase in the quantity of triethylamine reduces the yield of phthalylmalonic ester. At the temperature of a water bath and with 1:1 molar ratios of triethylamine and malonic acid, a mixture of oily products is obtained, the further treatment of which did not lead to isolation of indan-1,3-dione, as occurred with the condensation of phthalic anhydride with acetoacetic acid.

These data, like those we obtained before [1-3], indicate that the usual Perkin reaction proceeds in a solution of acetic anhydride and triethylamine, at room temperature and with small amounts of

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[1] The following maxima were observed in the IR spectra of the phthalylmalonic ester later obtained: at 1791 cm^{-1} (79%), 1728 cm^{-1} (85%), and 1648 cm^{-1} (76%), of which the first belongs also to the carbonyl group of the phthalide ring.

triethylamine: the carbonyl group oxygen of phthalic anhydride condenses. At higher temperature and with greater quantities of triethylamine, /274 condensation with the active methylene group proceeds so that, instead of the anhydride oxygen of phthalic anhydride, the carbon of an active methylene group stands between the two carbonyl groups in the final product. In the literature it is rarely mentioned that, together with a phthalide derivative, derivatives of indan-1,3-dione are isolated as side products during the Perkin condensation of phthalic anhydride [15]. The mechanism of this last reaction, which competes with Perkin's reaction, should be explained in the future, with more detailed study of the condensation reaction occurring in a solution of acetic anhydride and triethylamine between phthalic anhydride and compounds containing active methylene groups.

Experimental Part

Condensation of Phthalic Anhydride with Diethylmalonic Ester

Production of Phthalylmalonic Ester (VII)

29.6 g (0.2 mole) of phthalic anhydride and 32.0 g (0.2 mole) of the diethyl ester of malonic acid are dissolved by heating in 80.0 g (0.08 mole) of acetic anhydride, cooled to room temperature, and 20.2 g (0.2 mole) of triethylamine is added. The solution gradually takes on a dark color. The flask is covered with a calcium chloride tube and left at room temperature for two days, after which its contents are poured out into 300 g of ice and 100 ml of concentrated hydrochloric acid. A light-yellow oily substance is yielded which rapidly crystallizes. It is filtered, rinsed with water, and dried. The weight is 46.7 g (80.5%) and the melting point 67-69°. After crystallization from 70 ml of ethyl alcohol, 35.0 g (60.3%) of diethyl ester of phthalylmalonic acid is obtained, with a melting point of 74-75° (according to the literature [8], the melting point is 74-75°).

Found %: C 62.23, H 4.89. $C_{15}H_{14}O_6$ (VII). Calculated %: C 62.06, H 4.86.

Condensation of Phthalic Anhydride with Acetoacetic Ester

Production of the Ethyl Ester of Phthalylacetoacetic Acid (IX)

15.0 g (0.1 mole) of phthalic anhydride and 13.0 g (0.1 mole) of acetoacetic ester are dissolved, with slight heating, in 50 g (0.5 mole) of acetic anhydride and 10.1 g (0.1 mole) of triethylamine is added. The solution takes on a dark color and is highly heated. It is left at room temperature in a flask covered with a calcium chloride tube. Two days later the crystallized precipitate is filtered out and rinsed with acetic acid, then ether. After drying, the white crystals weigh 11.25 g (43.3%) and melt at 124-125°. After recrystallization from 350 ml of ethyl alcohol the weight is 8.9 g and the melting point 124-125°.

Found %: C 64.42, H 4.60. $C_{14}H_{12}O_5$ (IX). Calculated %: C 64.61, H 4.65.

After filtering out the phthalylacetoacetic ester, the solution is dissociated with ice (100 g) and hydrochloric acid (30 ml). A brown precipitate is isolated, which after drying weighs 2.1 g. A second crystallization yields a small amount of the yellowish phthalylacetoacetic ester.

Stability of the Ethyl Ester of Phthalylacetoacetic Acid in an Acid Medium

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In 100 ml of water, acidified with 5 ml of concentrated hydrochloric acid, 5.0 g of phthalylacetoacetic ester (melting point 124-125°) is heated until the solution boils, boiled for about 3 min, and the colorless solution is filtered to remove the precipitate, which weighs 4.8 g after drying and melts at 122-124°. A small amount of well-formed crystals of phthalylacetoacetic ester, melting point 124-125°, crystallizes in the cooled filtrate.

Production of Indan-1,3-dione (XIV)

The condensation reaction is conducted as described above, using 30 g (0.2 mole) of phthalic anhydride, 26 g (0.2 mole) of acetoacetic ester, 30 g (0.3 mole) of acetic anhydride, and 60.7 g (0.6 mole) of triethylamine. The next day the crystallized phthalylacetoacetic ester (yield 6.3 g [12.1%], melting point 122-124°) is filtered out and the filtrate poured into a mixture of 500 g of ice and 200 ml of concentrated hydrochloric acid. A yellow oil is yielded which thickens and becomes a solid precipitate; this is separated and rinsed with water. The obtained brown, heterogeneous product (weight 27.3 g) is drenched with 400 ml of hot water and 40 ml of concentrated hydrochloric acid, heated to boiling, and filtered, the filtrate cooled with water. Characteristic crystals of indan-1,3-dione are isolated. The weight is 6.8 g (23.3%), the melting point 124-126°. After crystallization from a mixture of benzene and dioxane the melting point is 127-129°. The substance does not produce melting-point depression with known indan-1,3-dione.

Conclusions

Forming with the condensation of phthalic anhydride with acetoacetic ester in a solution of acetic anhydride and triethylamine, as with the interaction of phthalylchloride and sodium acetoacetic ester, simultaneously are compounds of the phthalide and indandione series: phthalylacetoacetic ester and a derivative of indan-1,3-dione, giving indan-1,3-dione upon boiling with hydrochloric acid.

Phthalylmalonic ester is produced from phthalic anhydride and malonic ester in acetic anhydride in the presence of triethylamine.

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