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TECHNICAL REPORT 6614

GAS-LIQUID CHROMATOGRAPHY OF THE ALKYL ALPHA CYANOACRYLATES

Reported by: Duane E. Bartak
R. K. Kulkarni

August 1966

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U.S. ARMY MEDICAL BIOMECHANICAL RESEARCH LABORATORY
WALTER REED ARMY MEDICAL CENTER
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ABSTRACT

The purity of the cyanoacrylate monomers was estimated by gas-chromatographic technique. Some of the impurities, like diglyme, cyanoacetates were identified by noting the retention volumes. A plot of the retention volumes vs. number of carbons in the alkyl part of the cyanoacrylates was found to be linear; however, the use of temperature programming to obviate the broadening of the peaks for compounds having higher retention volumes was not successful, due to the shifting of the base line with increase in temperature.

INTRODUCTION

The n-alkyl cyanoacrylate monomers, known for their applications as adhesives, are being investigated by the Army Medical Biomechanical Research Laboratory with regard to tissue reaction, toxicity, and overall suitability as surgical adjuncts.[1] A procedure was necessary to determine the purity of each of the monomers which were synthesized in our laboratory to be used for further research. Gas-liquid chromatography offered a technique which was both fast and accurate for the determination of purities of the monomers and the identification of the impurities that were present.

EXPERIMENTAL

Apparatus: F & M Model 700 gas chromatograph equipped with an F & M dual hydrogen flame ionization detector was used. The recording device was a Model LS11A Westronics recorder.

Column: Columns were prepared from 1/4-inch o.d. stainless steel tubing in lengths of 6 feet. The inert support was 80/100 mesh chromosorb P containing 10% by weight of Silicone Gum Nutrile (F & M Scientific Company).

Chromatograph Conditions: The column temperature was maintained at 165° C for methyl through butyl homologs and 185° for amyl through nonyl homologs. Injection port temperature was 210° at all times. Helium zero-grade gas supplied by Metheson was used as the carrier gas at 25 p.s.i. and at a flow rate of 30 ml/min at outlet measured with soap bubble apparatus with a setting of 3.0 on the flowmeter on the F & M 700 chromatography.

Detector temperature was 230° C with hydrogen setting of 2.5 on the flowmeter at 30 p.s.i., and compressed air at 2.5 arbitrary units setting on the flowmeter at 12 p.s.i.

ANALYSIS

Samples of the monomers prepared were made up at 3-5% by weight in methylene chloride. Nitromethane was also used; however, it was more hydroscopic and therefore difficult to use in presence of monomers prone to polymerize with water. 1.0 μl to 2.0 μl (sample size) were injected with a 10 μl Hamilton syringe into the column. The impurities were identified by comparing retention times of known compounds under identical conditions to that of the impurity in the sample and also by spiking the sample with the suspected impurity and observing

if the impurity peak was superimposed by the added "suspect" with no shoulders or tailing of the impurity peak.

DISCUSSION

Listed in Table I are the monomers prepared and the purity calculated for each monomer and the impurities identified. The corresponding alcohols were present as an impurity to a greater de degree than any other. The presence of alcohols can be explained by reviewing the cyanoacrylate preparation by the cyanoacetate which is the product of esterification of the corresponding alcohol and cyano-acetic acid.[2] Diglyme (diethyleneglycol dimethyl ether) was another impurity identified whose presence can be explained since it is also a starting material in the synthesis of the alkyl cyanoacrylates. Chromatograms # 1 and # 2 are typical chromatograms of n-heptyl and isobutyl cyanoacrylates.

To help further identification and to check the separation of the cyanoacrylate monomers, a mixture of the n-homologous series of methyl through octyl was prepared and injected. Chromatogram # 3 shows the effective separation of 5% monomer mixture by weight in methylene chloride.

The relative retention volumes for each of the cyanoacrylates are calculated and reported in Table II.[3] N-butyl cyanoacrylate is given the value of 1.00.

Graph I illustrates the linearity when the log of the retention time versus the number of carbon atoms in the homologous series is plotted.

Temperature programming was attempted to speed up the analysis of the monomer mixture; however, due to substrate bleeding at higher column temperatures, there was large baseline drifting. Therefore, quantitative results were found not to be acceptable with the large drift of baseline.

Due to the fact that standard n-alkyl cyanoacrylate samples were not available, the internal normalization method was employed.[4] Results obtained from this method are independent of sample size within reasonable limits, as the procedure is to sum the areas of all the peaks and divide this value into the area of the individual peak. However, detector response must be approximately the same for all compounds being evaluated to avoid large error in such measurements. Detector

response for the n-alkyl cyanoacrylate and various alcohols and other impurities present in some of the work presently being carried out.

CONCLUSIONS

Gas-liquid chromatograph is a useful tool for the determination of the purities of the alkyl cyanoacrylates. It offers a fast and accurate method for the identification of impurities that may be present.

RECOMMENDATIONS

The investigation of the relative sensitivity of the members of the homologous series of cyanoacrylates, and also the impurities, is necessary for evaluation of the true purities of the samples. This work is already in progress. The gas chromatographic evaluation may be extended to measure the purity of the polymers of cyanoacrylates as well, because they get cracked and depolymerized in the chromatographic columns. More careful work on temperature programming is proposed, using properly equilibrated columns for avoiding the baseline drift commonly experienced, as of now.

Citation of specific commercial equipment, material or trade names in this report does not constitute an official endorsement or approval of the use of such commercial products.

TABLE I

MONOMERS

Cyanoacrylate	Purity	Impurities
Methyl	98.7%	Not identified
Ethyl	99.5%+	None measurable
Propyl	99.5%+	None measurable
Butyl	99.5%+	None measurable
Amyl	99.2%	0.8% Amyl Alcohol
Hexyl	96.8%	1.8% Isomer of Hexyl Cyanoacrylate; 1.4% Hexyl Alcohol
Heptyl	99.1%	0.9% Heptyl Alcohol
Octyl	98.8%	0.3% Octyl Alcohol 0.9% Unidentified
Nonyl	97.9%	2.1% Nonyl Alcohol
Iso-Propyl	99.5%+	None measurable
Iso-Butyl	99.5%+	None measurable
Iso-Amyl	99.5%+	None measurable
Ethyl Hexyl	99.0%	1.0% Ethyl Hexyl Alcohol
Cellosolve	98.0%	2.0% Not Identified

TABLE II

Relative Retention Volumes of N-Alkyl Cyanoacrylates at 170° C

(N-Butyl Cyanoacrylate assigned relative retention volume of 1.00)

	Retention Volume	Relative Retention Volume
Methyl Cyanoacrylate	132 ml	0.48
Ethyl Cyanoacrylate	150 ml	0.56
N-Propyl Cyanoacrylate	199 ml	0.73
N-Butyl Cyanoacrylate	274 ml	1.00
N-Amyl Cyanoacrylate	383 ml	1.40
N-Hexyl Cyanoacrylate	542 ml	1.98
N-Heptyl Cyanoacrylate	765 ml	2.79
N-Octyl Cyanoacrylate	1100 ml	4.01

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1. S. C. Woodward, et al, Annals Surg. 162: 113-122 (1965).

2. USAMBRL Technical Report 6520, Leonard, F., et al, "Synthesis and Degradation of Poly Alkyl Alpha Cyanoacrylates", November 1965.

3. Burchfield, H.P. and Storrs, E.E., Biochemical Applications of Gas Chromatography, N.Y. Academic Press, 1962, pp. 11-14.

4. Dal Nogare, S. and Juvet, R.S., Jr., Gas-Liquid Chromatography, N.Y. Interscience Publishers, 1965, pp. 256-257.

GRAPH I

24 May 66 DEBRAK 1 Cal

METHYL [illegible] OCTYL CYANOACRYLATE

SILICONE GUM NITRILE

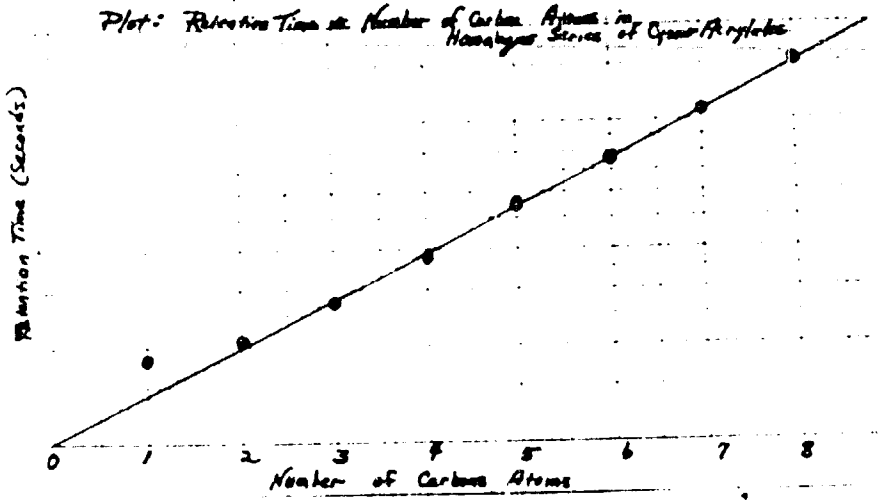
	21	25	24
	30	25	25
	24	12	30
	220	170	235
	—	—	—
	—	—	

10 5 1 in/min

Methylene Chloride Solvent

24 May 66 DEBRAK

Plot: Retention Time vs. Number of Carbon Atoms in Homologous Series of Cyanoacrylates



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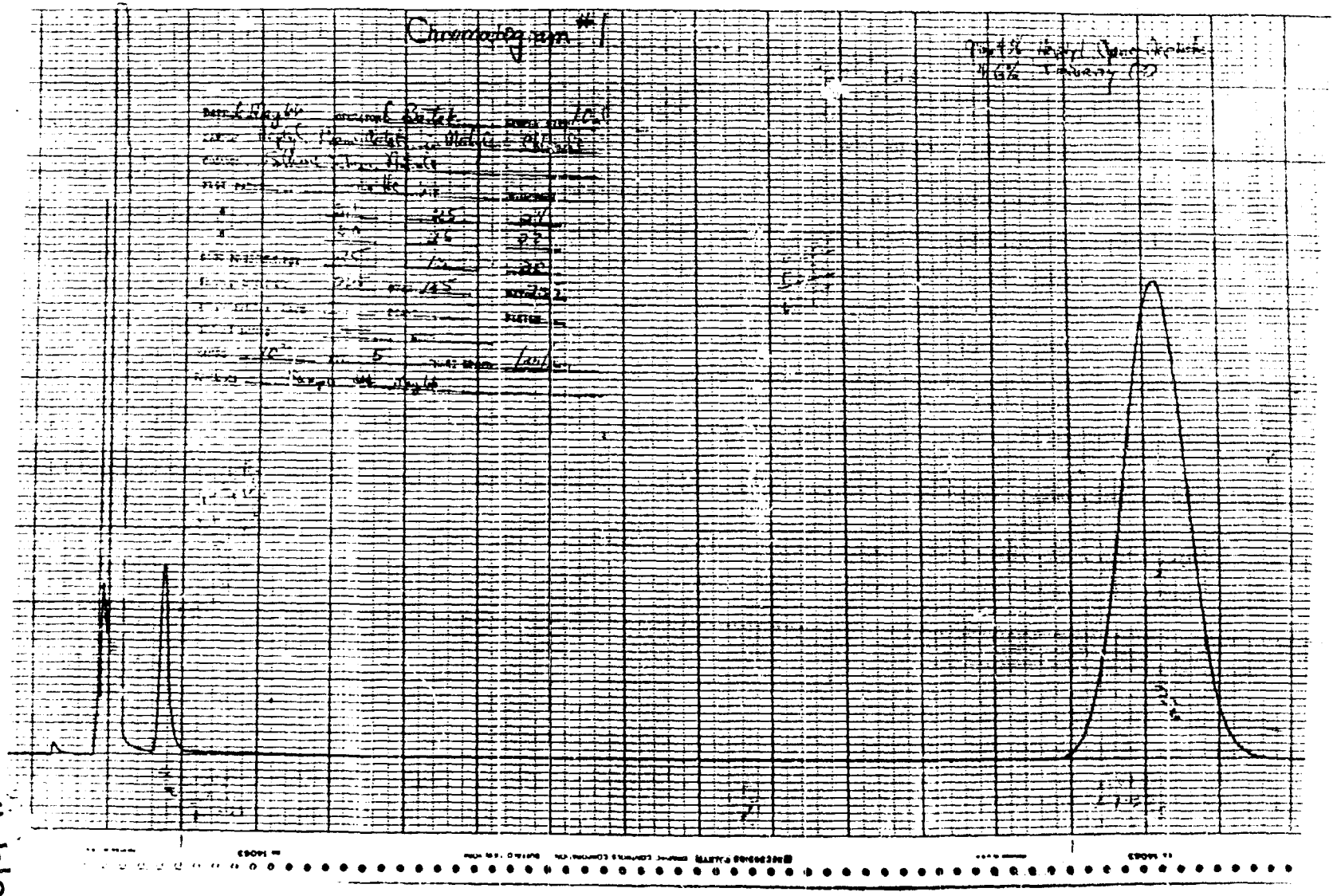

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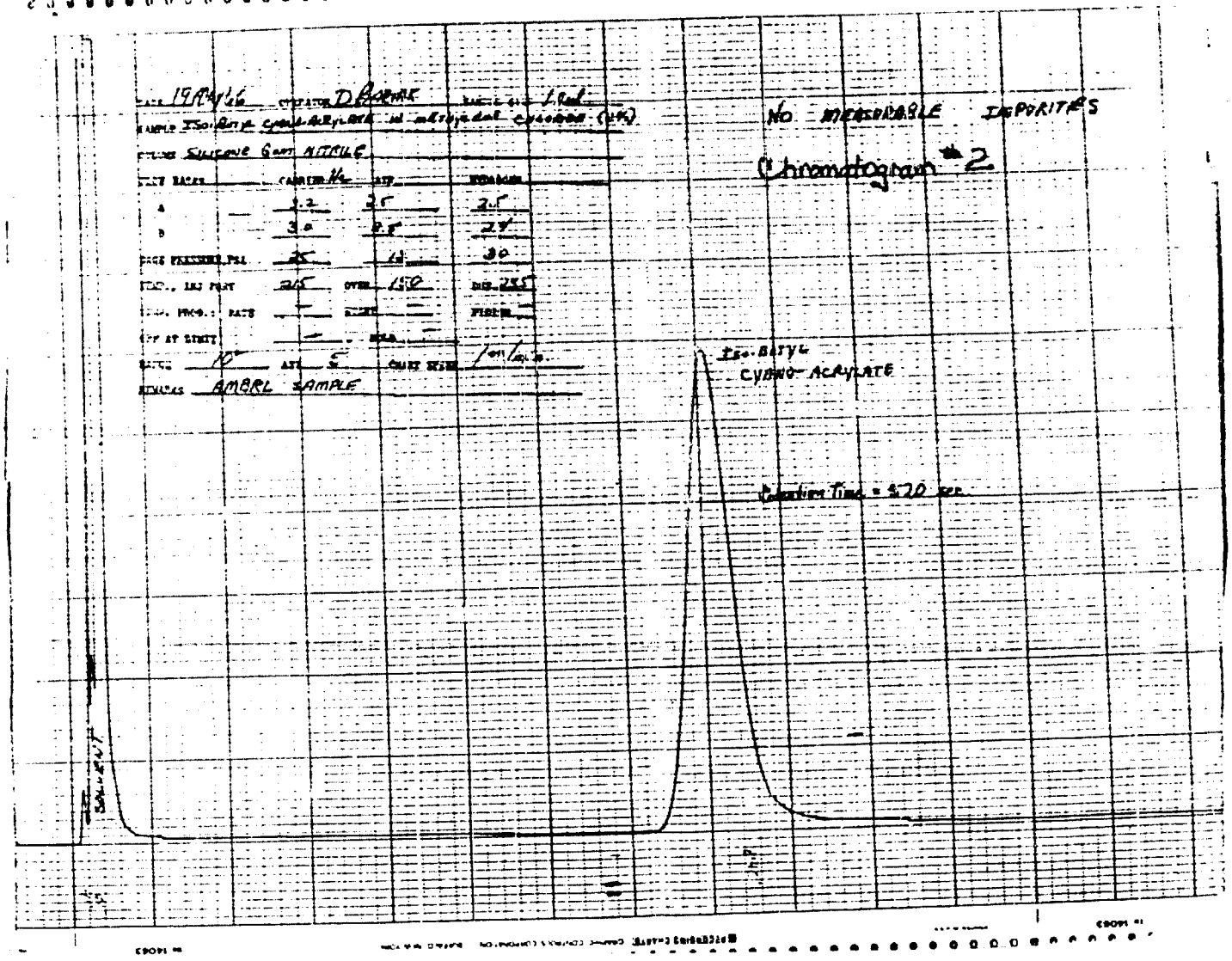

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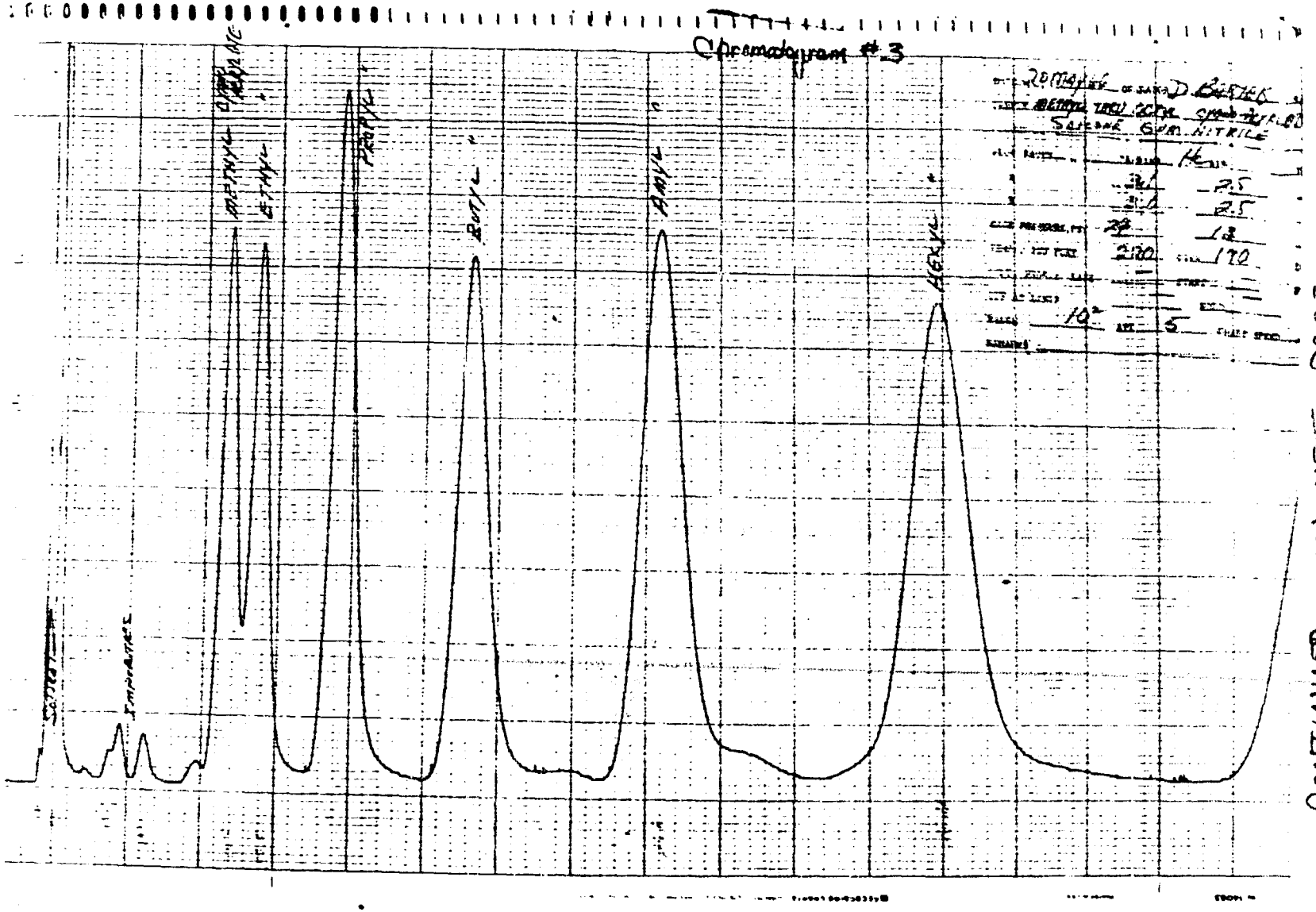

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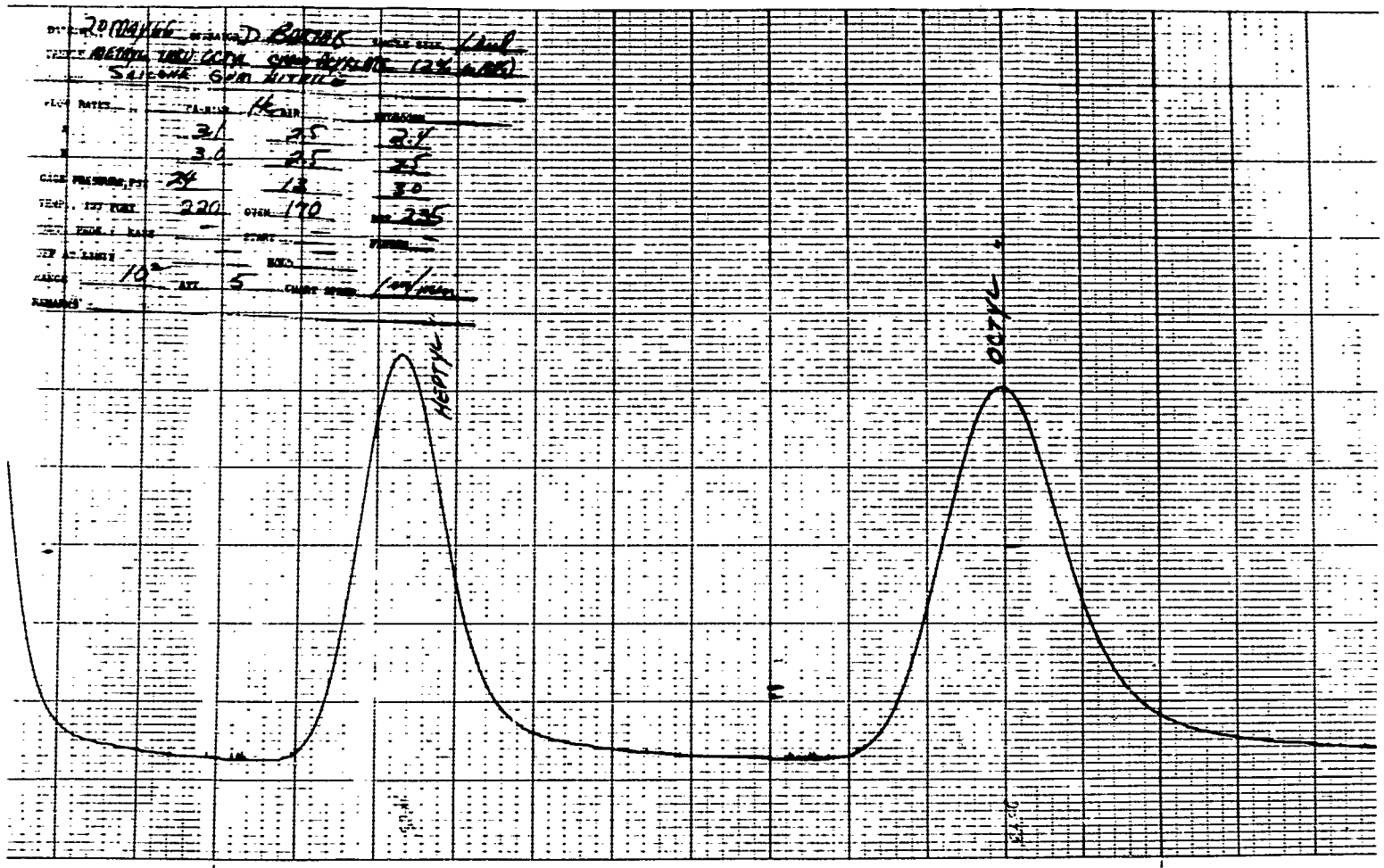
20 MAY 66
D. BARNES
METHYL TRICOSYL CYCLOHEXANE (2% w/w)
SILICONE GUM RUBBER
FLOW RATES
He
3.1
2.5
2.4
3.0
2.5
2.5
24
13
30
220
OVEN 170
225
10
ATT 5
1 cm/min
HEPTYL
OCTYL

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KEY WORDS
Gas Chromatography of Cyanoacrylates
Purity of Cyanoacrylates by Gas Chromatography
GLC
Determination of Cyanoacrylates by GLC

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