TABLE I

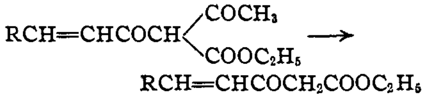
β-SUBSTITUTED ACRYLOYLACETOACETIC ESTERS $R{-}CH{=}CHCO{-}CH\left\langle\begin{matrix}COCH_3\\COOC_2H_5\end{matrix}\right.$

R	Formula	M. p., °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Phenyl[5]	.....	46	75	...	...	..	..
α-Furyl[6]	$C_{13}H_{14}O_5$	48	45	62.40	62.31	5.60	5.50
1-Naphthyl	$C_{19}H_{18}O_4$	80	42	73.55	73.56	5.81	6.26
p-Methoxyphenyl	$C_{16}H_{18}O_5$	65	80	66.20	66.10	6.21	6.14
Cyclohexyl	$C_{15}H_{22}O_4$		45	67.67	67.62	8.27	8.25
3,4-Methylenedioxyphenyl[4]	.....	104	55	...	...	..	..

TABLE II

β-SUBSTITUTED ACRYLOYLACETIC ESTERS, $R{-}CH{=}CHCOCH_2COOC_2H_5$

R	Formula	M. p., °C.	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Phenyl[4]	.....	45–46	82	...	...	..	..
α-Furyl	$C_{11}H_{12}O_4$	60	64	63.46	63.70	5.77	6.05
p-Methoxyphenyl	$C_{14}H_{16}O_4$	44–45	70	67.75	67.55	6.45	6.57
3,4-Methylenedioxyphenyl[4]	$C_{14}H_{14}O_5$	60	64	...	...	..	..



$$RCH{=}CHCOCH\left\langle\begin{matrix}COCH_3\\COOC_2H_5\end{matrix}\right. \longrightarrow RCH{=}CHCOCH_2COOC_2H_5$$

Although reactions of this type have been carried out by Borsche,[4] repetition of this work revealed a need for further study of the process with a view to developing a practical synthesis.

The procedure as finally adopted was as follows. The appropriate substituted acrylic acid was refluxed with 2-3 moles of thionyl chloride and the acid chloride fractionally distilled under reduced pressure, except in the case of the naphthyl derivative, where phosphorus pentachloride in dry benzene was found more advantageous. Yields of from 82–97% of the β-substituted acryloyl chlorides were obtained with melting points or boiling points in good agreement with the values given in the literature.

The conversion of these chlorides to the corresponding acylated acetoacetic esters was accomplished by adding them in dry xylene solution to a freshly prepared suspension of the theoretical quantity of sodium ethylacetoacetate, also in dry xylene. After stirring at room temperature for twenty-four hours, the solution was centrifuged and the xylene removed in vacuum. The phenyl- and naphthylacryloylacetoacetates were thus obtained as dark oils which crystallized on standing and were purified by recrystallization from petroleum ether and alcohol, respectively. In the remaining cases the crude products were converted, by shaking with saturated aqueous copper acetate, into their crystalline copper salts. These in turn were readily converted, by treatment with cold dilute acids, into the pure β-substituted acryloylacetoacetic esters, which could be distilled at low pressures (below 1 mm.) without noticeable decomposition.

β-Substituted acryloylacetic esters were prepared from the above acetoacetic esters by saturating solution of 0.01 mole of the latter in 10 cc. of 1 normal sodium hydroxide with ammonia at 0°. After standing at room temperature for one hour, the solution was filtered and the filtrate acidified with 3 normal sulfuric acid. An oily precipitate resulted which in the case of the phenylacryloyl ester solidified and was recrystallized from petroleum ether. The others were purified by means of their copper salts. This method failed with the naphthyl and cyclohexyl analogs.

Tests for physiological activity were carried out by the pea test[7] method on all the products prepared. All were found to be either inactive or only very slightly active by this assay.[8]

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[4] Borsche, *Ber.*, **66**, 1792 (1933).

[5] Fischer and Kuzel, *ibid.*, **16**, 167 (1883).

[6] Lampe. *Chem. Listy.*, **26**, 454 (1932); *Chem. Abs.*, **27**, 721 (1932).

[7] Thimann and Went, "Phytohormones," The Macmillan Co., New York, N. Y., 1937.

[8] We are indebted to Dr. Paul Burkholder for his helpful cooperation in carrying out the physiological tests.

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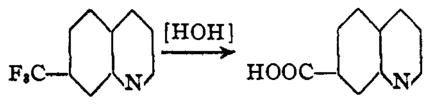
5- and 7-Trifluoromethylquinolines

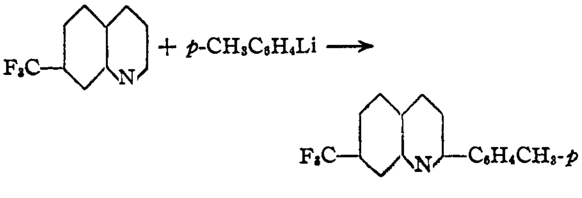
BY HENRY GILMAN AND DENNIS BLUME

In connection with a study of fluorine derivatives of polynuclear heterocycles, 5- and 7-trifluoromethylquinolines have been prepared. The Skraup synthesis was used, starting with *m*-trifluoromethylaniline, and the 7-isomer was formed predominantly.

The structures of the two compounds were established by acid hydrolysis to the known quinolinecarboxylic acids



Addition of organolithium compounds occurs normally. For example, *p*-tolyllithium gives a dihydro derivative which on oxidation by nitrobenzene yields 2-*p*-tolyl-7-trifluoromethylquinoline.



Experimental

Skraup Reaction with *m*-Trifluoromethylaniline.—To a mixture of 64.4 g. (0.40 mole) of *m*-trifluoromethylaniline[1] and 120 g. (1.3 moles) of glycerol was added 56.5 g. (0.40 mole) of arsenic acid and 110 g. (1.1 moles) of concentrated sulfuric acid. The reaction mass was shaken well before being placed under a reflux condenser. The mixture was heated cautiously until the reaction started, and then the burner was removed. When the initial reaction had subsided, the mixture was refluxed for four hours by heating on a sand-bath. After cooling, the contents were poured into one liter of cold water and allowed to stand overnight. The solution was partially neutralized with 65 g. of solid sodium hydroxide, filtered, and after complete neutralization extracted three times with ether. The total volume of the ether extracts was 800 cc. After drying the ether solution over calcium chloride, and removing the ether by distillation, the quinoline compounds distilled over the range 80–100° (3 mm.), and the yield was 44.5 g. (56.5%).

7-Trifluoromethylquinoline.—Upon redistillation at atmospheric pressure, the fraction (10 g., 12.7%) distilling between 205–218° consisted chiefly of 5-trifluoromethylquinoline; and the fraction (34 g., 43%) distilling over at 218–225° was largely 7-trifluoromethylquinoline. When the latter, higher-boiling fraction was cooled, crystallization set in. Recrystallization from 60% ethanol gave a product melting at 66–68°. Redistillation of these crystals gave 7-trifluoromethylquinoline which boiled at 219–221° (731 mm.). The yield of pure compound was 25 g. or 31.8%.

Anal. Calcd. for $C_{10}H_6NF_3$: N, 7.11. Found: N, 6.91 and 7.01.

The compound was hydrolyzed by refluxing 0.5 g. in 10 cc. of 80% sulfuric acid for three hours on a sand-bath.[2] After neutralization with sodium hydroxide and recrystallization from water the 7-quinolinecarboxylic acid melted at 246–247° (cor.). The melting point reported by Skraup and Brunner[3] is 247°.

5-Trifluoromethylquinoline.—The fraction distilling between 205–218° was first partially purified by forming the oxalic acid salt in ethanol. To the salt (which melted between 120–126°) was added water and ether, and then 20% potassium hydroxide. The ether layer was separated, dried over calcium chloride, and the ether removed by distillation. The 5-trifluoromethylquinoline distilled at 214–215° (732 mm.); d^{32}_4 1.272; n^{32}_D 1.528. The yield of pure product was 4.5 g. or 5.7%.

Anal. Calcd. for $C_{10}H_6NF_3$: N, 7.11. Found: N, 7.07.

Hydrolysis, by the procedure used with the 7-isomer, gave 5-quinolinecarboxylic acid which melted at 341–343°. The melting point reported by V. Jakubowski[4] is 338–340°.

2-*p*-Tolyl-7-trifluoromethylquinoline.—To 16.8 g. (0.085 mole) of 7-trifluoromethylquinoline dissolved in 50 cc. of dry ether was added, over a two-hour period with stirring, 64 cc. of an ether solution containing 0.093 mole of *p*-tolyllithium.[5] The mixture was refluxed gently for three hours, and then cooled and poured into 35 g. of ice-water. The ether layer was separated, the water layer was extracted three times with ether, and to the 350 cc. of ether solution was added 10 cc. (0.098 mole) of nitrobenzene. This ether solution was added dropwise to a Claisen flask heated by a boiling water-bath. After the ether was removed, reduced pressure was applied and the nitrobenzene and any initial quinoline compound was separated by distillation. The fraction distilling between 188–195° (6 mm.) was collected (20.2 g. or 83% yield of crude material). Recrystallization from 350 cc. of 95% ethanol gave 15.1 g. or a 61% yield of compound melting at 131–133°.

Anal. Calcd. for $C_{17}H_{12}NF_3$: N, 4.88. Found: N, 4.74.

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[1] The *m*-trifluoromethylaniline was prepared by a modification of the method outlined by Swarts, *Bull. acad. roy. Belg.*, [3] **35**, 390 (1898).

[2] This was done in accordance with general directions of Simons and Ramler, This Journal, **65**, 389 (1943).

[3] Skraup and Brunner, *Monatsh.*, **7**, 519 (1886).

[4] V. Jakubowski, *Ber.*, **43**, 3027 (1910). Our melting point determination, carried out in a sealed tube, was probably accurate to ±3°.

[5] Gilman, Zoellner and Selby, This Journal, **54**, 1957 (1932).

Sulfonation of Some Naphthalene Derivatives in the Presence of Boron Trifluoride[1]

By G. F. Hennion and Claude J. Schmidle

The pronounced catalytic effect of boron trifluoride in the sulfonation of several aromatic compounds was reported some time ago.[2] Since boron trifluoride is one of the strongest acceptor reagents known, it was deemed important to determine whether this new method might result in unusual orientations of the $-SO_3H$ group in typical aromatic donor compounds. Both of the naphthylamines and β-naphthol were selected for this purpose to establish the orientation effects of the groups $-NH_2:BF_3$ and $-OH:BF_3$.

We wish to report now that the sole function of boron trifluoride in these cases appears to be that of a strong dehydrating catalyst since the ordinary sulfonic acid derivatives were formed. Thus while no unusual directing influence was observed, improved yields of clean products were obtained quickly at somewhat lower temperatures than ordinarily used.

Experimental

Sulfonation of α-Naphthylamine.—Thirty-six grams of the amine was sifted into 144 g. of concentrated sulfuric acid in a three-necked flask equipped with a mechanical stirrer, thermometer and inlet tube. Boron trifluoride (26 g.) was admitted at 75–80°, the absorption requiring about one hour. The product was diluted with 300 cc. of cold water. The crystalline deposit left only 5 g. of unreacted amine when extracted with 2 *N* sodium hydroxide, indicating about 86% sulfonation. The product was essentially naphthionic acid as shown by comparison with an authentic sample.[3]

A control experiment, performed in exactly the same manner but without boron trifluoride, showed 60% sulfonation.

Sulfonation of β-Naphthylamine.—Forty-eight grams of the amine sulfate was treated with 134 g. of concentrated sulfuric acid and allowed to absorb 85 g. of boron trifluoride at 50–55° during thirty minutes. After another thirty minutes, sulfonation was 95% complete. The crude dry sodium salts were fractionated by extraction with boiling alcohol. The insoluble portion (48%) was identified as the 8-sulfonic acid.[4] The alcohol soluble material proved to be the 5-sulfonic acid (52%). The benzyl-iso-thiouronium salts melted at 102–103° and 172–174°, respectively.

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[1] Paper XXIX on organic reactions with boron trifluoride; previous paper, *ibid.*, **65**, 1603 (1943).

[2] Thomas, Anzilotti and Hennion, *Ind. Eng. Chem.*, **32**, 408 (1940).

[3] The benzyl-iso-thiouronium derivative melted at 103–104° and the mixed m. p. with a sample made from authentic naphthionic acid was 102–104°. Since these compounds were not analyzed, it should be noted that Chambers and Watt, *J. Org. Chem.*, **6**, 376 (1941), report 195° for the melting point.

[4] Green and Vakil, *J. Chem. Soc.*, **113**, 35 (1918).