EXPERIMENTAL

1,3,5-trifluoronitrobenzene was prepared by the method of Finger and Kruse,[6] and the azeotropic mixture boiling at 70–85°/20 mm. was used in preparation of trifluorodinitrobenzene.[7]

1,3,5-Trifluoro-2,4-dinitrobenzene. To a nitrating mixture of 25 ml. of white fuming (90%) nitric acid and 14 ml. of 30% fuming sulfuric acid was added 14 ml. of 1,3,5-trifluoro-2-nitrobenzene, followed by 10 ml. more of 30% fuming sulfuric acid. The mixture was heated carefully[8] to 75°; then slowly to 100° and held there for 2 hr. The nitration mixture was poured into ice and water, filtered, and washed. The 1,3,5-trifluoro-2,4-dinitrobenzene was separated from the impurities by washing with 150–200 ml. of 75% acetic acid. The acetic acid solution with the dissolved trifluorodinitrobenzene was diluted with approximately 1 l. of ice water, allowed to stand at 0° for about 0.5 hr., and filtered. Repeated recrystallizations from a cyclohexane–petroleum ether (b.p. 30–60°) mixture at 0° gave long white needles of 1,3,5-trifluoro-2,4-dinitrobenzene which melted at 57–58° (lit., m.p. 52–53°).

Anal. Calcd.: C, 32.45; N, 12.62; H, 0.45. Found: C, 33.27; N, 12.65; H, 0.55.

The predominant impurity, 1,3,5-trichloro-2-fluoro-4,6-dinitrobenzene, may be recrystallized from alcohol, giving platelets, m.p. 146–147°.

Anal. Calcd.: C, 24.72; N, 9.61; Cl, 36.94. Found: C, 25.56; N, 9.78; Cl, 35.10.

1,3,5-Trifluoro-2,4,6-trinitrobenzene. A flask with 9 g. of potassium nitrate was chilled in an ice water bath and 28 ml. of 30% fuming sulfuric acid was added slowly. The cold bath was removed, 5 g. of trifluorodinitrobenzene added, and the mixture then heated to 163° for 21 to 24 hr. The time required for the nitration was determined by sampling and infrared spectra.[9] The nitration mixture was poured slowly over 125 ml. of crushed ice. After thorough mixing, the product was filtered rapidly in a sintered glass crucible and washed with a small amount of cold water. Hydrolysis of trifluorotrinitrobenzene was kept at a minimum if ice was kept in the drowned nitration mixture up to the point of washing, where the last of the ice was melted. The solid was dried rapidly in vacuum, pumping to a pressure of about 1 micron; yield, 2.6 g. (43%).

Recrystallization from dry carbon tetrachloride gave long fine needles, m.p. 87°. X-ray analysis showed the crystal structure to be rhombohedral with $A = 16.8$ Å, $\alpha = 118°$ 18′. Hexagonal indices (triple-cell), $a = 29.14$ Å, and $c = 6.576$ Å. The cell contained 21 formula units, which gave a density of 1.92.

Anal. Calcd: C, 26.80; N, 15.73; F, 21 34. Found: C, 26.67; N, 15.16; F, 19.94.

1-Fluoro-2,4,6-trinitrobenzene. A 125-ml. Erlenmeyer flask, fitted with an 18-in. air condenser, was charged with 21 g. of potassium nitrate, 56 ml. of 30% fuming sulfuric acid, and 10 g. of 1-fluoro-2,4-dinitrobenzene. The reaction mixture was heated, with stirring, at 120° (oil bath temperature) for 30–35 hr., then worked up in the same manner as the trifluoronitrobenzene; crude yield, 8.7 g. (70%). Recrystallization from carbon tetrachloride gave a m.p. of 122–123°.[10]

Anal. Calcd: C, 31.19; H, 0.86; N, 18.19. Found: C, 30.97; H, 0.96; N, 18.40.

1,3-Difluoro-2,4,6-trinitrobenzene. A nitration mixture of 9.58 g. of potassium nitrate, 28 ml. of 30% fuming sulfuric acid, and 5 g. of 1,3-difluoro-4,6-dinitrobenzene was placed in an apparatus similar to that used in the fluorodinitrobenzene nitration. After about 35 hr. at 140°, the product was worked up as before; yield, 2.5 g. (41%); recrystallization from dry carbon tetrachloride gave m.p. 147–148°.

Anal. Calcd: C, 28.81; N, 16.80. Found: C, 29.14; N, 16.72.

Trinitrophloroglucinol. Treatment of trifluorotrinitrobenzene with water resulted in the hydrolysis of the fluorine, giving trinitrophloroglucinol, m.p. 166.5–167°. The melting point was not depressed when mixed with an authentic sample, prepared by trinitration of phloroglucinol.

Anal. Calcd: C, 27.60; N, 16.09; H, 1.16. Found: C, 28.05; N, 16.34; H, 1.83.

1-Fluoro-3,5-diethoxy-2,4,6-trinitrobenzene. Trifluorotrinitrobenzene recrystallized from ethanol gave the corresponding fluorodiethoxytrinitrobenzene.

Anal. Calcd: C, 37.63; N, 13.16; H, 3.16; F, 5.95. Found: C, 37.57; N, 13.44; H, 3.32; F, 5.86.

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(7) Use of a fraction with a wider boiling range gave rise to an oil from which it was very difficult to isolate the trifluorodinitrobenzene.

(8) Rapid heating results in uncontrolled boiling of the reaction.

(9) If the dilution of the nitrating mixture was attempted before the nitration is complete, the product was usually a liquid or paste which could not be filtered. Since no other means of rapid separation were available, the product was likely to be lost at this point due to hydrolysis of the fluorines in the trifluorotrinitrobenzene. In order to avoid this problem, approximately 0.02 to 0.1 ml. of the nitration was taken a short time before the estimated time of completion and dropped into a centrifuge cone of crushed ice. The precipitated material was centrifuged out, decanted, and dried in vacuum to approximately 1 micron. (The time of contact of the trifluorotrinitrobenzene with cold water was kept to less than 5 min. during the filtration and centrifugation steps.) The sample was used to determine an infrared spectrum, the disappearance of trifluorodinitrobenzene 8.6- and 9.2-μ bands being taken as the criterion for complete nitration.

(10) Two allotropic forms of fluorotrinitrobenzene exist; m.p. 122–123° and 131–132°. The higher melting form was obtained from the first two preparations, but after repeated recrystallizations it changed to the lower melting form. Upon melting and resolidifying, the lower melting form reverts back to the higher melting allotropic form.

Some Constituents of *Calendula officinalis*

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The composition of the constituents of the medicinal herb, marigold flowers (*Calendula officinalis*), has been the subject of frequent reports. The existence of carotenoid pigments was established by Zechmeister,[1] and the identification of individual components was undertaken by Goodwin.[2] The presence of a bitter principle was reported by Gedeon[3] and has been confirmed by the recent work of Suchý and Herout[4] who propose the name

(1) L. Zechmeister and L. v. Cholnoky, *Z. physiol. Chem.*, **208**, 27 (1932).

(2) T. W. Goodwin, *Biochem. J.*, **58**, 90 (1954).

(3) J. Gedeon, *Pharmazie*, **6**, 547 (1951); **9**, 922 (1954).

(4) M. Suchý and V. Herout, *Collection Czechoslov. Chem. Commun.*, **26**, 890 (1961).

calendin. Considerable discrepancies are apparent in the reports of the occurrence of triterpenoids. Oleanolic acid glycoside was first isolated from this source by Winterstein and Stein[5] and later by Zimmermann,[6] who obtained also the triterpene diols, faradiol (taraxastenediol) and arnidiol (ψ-taraxastenediol) and by Kasprzykówna[7] who further described the isolation of a triterpene monoalcohol, $C_{30}H_{50}O$. The most recent report[3] also indicates the existence of a triterpene diol differing from arnidiol and faradiol.

The present work, describing the nonsaponifiable constituent fraction from marigold flowers collected in the United States, was undertaken with the primary aim of isolating the alcohol, $C_{30}H_{50}O$, reported by Kasprzykówna.[7] Although the general isolation procedure previously described[7] was employed, there was obtained instead of the previously reported alcohol, an somer which was ident fied as ψ-taraxasterol by characterization as acetate, benzoate, and dihydro derivatives.

The triterpene diol mixture was readily isolated. No attempt was made to effect the difficult separation of arnidiol and faradiol,[8] and their presence was established by (a) catalytic hydrogenation followed by chromic acid oxidation in acetone solution to give dihydrofaradione and (b) chromic acid oxidation in acetone solution followed by acid equilibration to yield faradione. Although the specific rotation value for dihydrofaradione differs considerably from that previously reported,[9] comparison with an authentic sample isolated from the flowers of *Arnica montana* established their identity. The triterpenoid constituents apparently differ considerably with locality of the flower specimens.

The empirical analysis and melting point of the hydrocarbon fraction suggested that it was largely *n*-triacontane, $C_{30}H_{62}$. Vapor phase chromatography has shown, however, that it contains the normal paraffins from C_2H_{54} to $C_{34}H_{70}$.

EXPERIMENTAL[10]

Isolation of neutral extract of calendula flowers. A suspension of powdered flowers (800 g., supplied by S. B. Penick and Co.) in ether (2 l.) was stirred at room temperature for 3 hr., the extract decanted, the process repeated with a further 2 l. of ether, and the combined extract evaporated to yield an orange tar (85.7 g.). This was dissolved in 10% methanolic potassium hydroxide solution, and the solution heated under reflux for 3 hr. The product was isolated by concentration, addition of water, and extraction with ether. Removal of the ether from the washed and dried extract gave an orange-brown gum (37 g.), which on trituration with petroleum ether (b.p. 50–60°) gave a yellow solid (30 g.) which was removed from the petroleum-soluble fraction by filtration.

Examination of petroleum-soluble fraction. The residue obtained by removal of the solvent was crystallized from chloroform-methanol to give a first crop (1.0 g.) of a pale yellow solid (m.p. 61–64°) and a second crop of sticky solid which on crystallization from methanol yielded a white solid (630 mg., m.p. 130–160°).

A solution of the pale yellow solid (550 mg.) was dissolved in light petroleum (b.p. 38–50°) and chromatographed on alumina (Woelm, almost neutral). Elution with the same solvent (60 cc.) gave a white solid (538 mg.) which crystallized from benzene-ethanol as leaflets, m.p. 63.5–65.5°, $[\alpha]_D \pm 0°$.

Anal. Calcd. for $C_{30}H_{62}$: C, 85.22; H, 14.78. Found: C, 85.0; H, 15.0.

A vapor phase chromatographic analysis of this hydrocarbon mixture using an Aerograph A-100-C model and a 5-ft. stainless steel column packed with 20% silicone rubber indicated the composition: hexacosane (2.1%), heptacosane (0.5%), octacosane (16.3%), nonacosane (3.0%), triacontane (33.8%), hentriacontane (3.2%), dotriacontane (29.9%), tritriacontane (3.9%), tetratriacontane (7.3%).

Purification of the second crop, either by crystallization from petroleum ether or by chromatography on alumina [eluted by benzene-methanol (99:1)] gave ψ-taraxasterol as long needles, m.p. 199–205°, $[\alpha]_D$ +49° (*c*, 1.5). This yielded, on acetylation in pyridine solution with acetic anhydride, ψ-taraxasteryl acetate as plates, m.p. 235–237°, $[\alpha]_D$ +59° (*c*, 1.5); reported[11] m.p. 238–240°, $[\alpha]_D$ +56°. Treatment in pyridine solution with benzoyl chloride gave ψ-taraxasteryl benzoate as plates, m.p. 262–270°, vac. m.p. 282–285°, $[\alpha]_D$ +74° (*c*, 2.1); reported[11] m.p. 273–275°, $[\alpha]_D$ +75°.

Examination of yellow solid. (a) The yellow solid (3.0 g.) was extracted with petroleum ether (b.p. 40–50°, 350 cc.) in a Soxhlet apparatus. After 3 hr., the yellow extract became cloudy, and a resin (880 mg.) separated on the walls of the flask. After cooling, the clear extract was decanted from the resin and filtered through a column (7 × 1″) of alumina. Elution with petroleum ether (800 cc.) yielded the hydrocarbon mixture (44 mg., m.p. 57–62°), and elution with benzene-methanol (99:1, 350 cc.) gave an orange gum (980 mg.). Two crystallizations from chloroform-methanol and one from petroleum ether gave ψ-taraxasterol, m.p. 193–197°, $[\alpha]_D$ +43°, identified by preparation of the acetate, m.p. 235–238°. An insoluble residue (811 mg.) remained in the extraction thimble.

(b) In another experiment, the orange gum (2.49 g.), isolated as in (a), was acetylated in pyridine (10 cc.) using acetic anhydride (10 cc.) and chromatographed. The only crystalline material (420 mg.) obtained, isolated by elution with petroleum ether–benzene (1:1, 750 cc.), was identified as ψ-taraxasteryl acetate, m.p. 231–234°, $[\alpha]_D$ +55° (*c*, 2.2). On catalytic hydrogenation with platinum oxide in cyclohexane–acetic acid solution, it gave taraxastanyl acetate, m.p. 262–265°, $[\alpha]_D$ +19° (*c*, 1.8); reported[12] m.p. 262–263°, $[\alpha]_D$ +23°.

Hydrolysis of the acetate with lithium aluminum hydride in ether solution gave taraxastanol, m.p. 223–225°, $[\alpha]_D$ +5° (*c*, 1.8); reported[13] m.p. 222–223°, $[\alpha]_D$ +11°.

Identification of arnidiol-faradiol mixture. (a) The petroleum ether-insoluble residue from (a) above was extracted with benzene to give a glass (*ca.* 0.5 g.) which was chromatographed on alumina. The mixed diols (360 mg.) were eluted

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(10) Melting points were determined on a Gallenkamp melting point apparatus. Rotations were measured in chloroform. Merck acid-washed alumina was used for chromatography, except where otherwise stated.

(11) T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 1905 (1954).

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(13) D. W. Haines and F. L. Warren, *J. Chem. Soc.*, 2554 (1949).

with benzene-chloroform (3:1), taken up in acetic acid, and hydrogenated using platinum catalyst to yield the dihydrodiols (m.p. 220–227°, no color with tetranitromethane). A solution of the dihydrodiols (0.85 g.) in acetone (300 cc.) was cooled to 10° and treated with a solution (1 cc.) of chromium trioxide in dilute sulfuric acid (prepared by dissolving 2.672 g. of chromium trioxide in 2.3 cc. of concd. sulfuric acid and making up to 10 cc. with water). After 5 min., the mixture was poured into water (500 cc.), the precipitate collected, dried, and crystallized from methanol to give dihydrofaradione, m.p. 184–187°, $[\alpha]_D$ −18° (*c*, 2.9), undepressed by a specimen, m.p. 187—189°, $[\alpha]_D$ −22°, isolated similarly from arnica flowers; reported[9] for dihydrofaradione (dihydroarnidione), m.p. 183° $[\alpha]_D$ −61°.

(b) The mixed diols (1.0 g.) were oxidized with 1.2 cc. of the standard chromium trioxide agent, the crude water-insoluble precipitate dissolved in a mixture (40 cc.) of ethanol-benzene–sulfuric acid (volume ratio, 10:5:1) and heated under reflux for 4 hr. The product, isolated in the usual way by aqueous dilution and ether extraction, was dissolved in benzene and chromatographed. The fraction eluted by benzene was crystallized once from ether–petroleum ether and once from methanol to give faradione as long laths, m.p. 247–250°, $[\alpha]_D$ +15° (*c*, 2.0); reported[14] m.p. 249–250°, $[\alpha]_D$ +22°.

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Pyridine 1-Oxides. X. pK_a Values for Some 4-Substituted Nicotinic Acid 1-Oxides

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During the course of recent investigations in pyridine 1-oxide chemistry,[1] a number of 4-substituted nicotinic acid 1-oxide derivatives were prepared and were thus available for study.[2] The pK_a values of these compounds have now been determined (see Table I, where pK_a refers to the dissociation of the neutral molecule relative to the monoanion). All the values were determined potentiometrically except for 4-nitronicotinic acid 1-oxide, which was done spectrophotometrically because of its high acidity. The pK_a values have been correlated with the appropriate sigma constants by means of the Hammett equation, and a satisfactory statistical fit in all respects (ρ = 2.347; r = 0.988; S = 0.207) has been found. This may be compared with a rho value of 1.89 for the equilibrium (a) below involving the dissociation of the conjugate acid of 4-substituted pyridine 1-oxides to the neutral molecule.[3,4] The statistical calculations were carried out according to the procedure suggested by Jaffé;[5] the sigma values were chosen from the same source. Since the substituent group in the 4-position is *ortho* to the carboxyl group in these compounds, it would seem that these compounds should exhibit an *ortho* or proximity effect[6] and therefore not be amenable to treatment by the Hammett equation. However, since excellent correlation has been found (see Fig. 1) it would appear that the determined pK_a value is not a measure of the equilibrium (b) but rather a measure of the ionization of the zwitterionic form of the nicotinic acid 1-oxide, as shown below in (c). Thus, the substituents affecting the group bearing the acidic proton are *para* (−*X*) and *meta* (—COO^-), and it is well known that substituents in these positions are

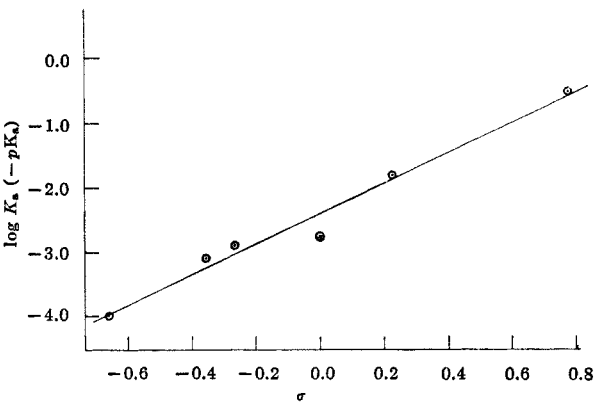
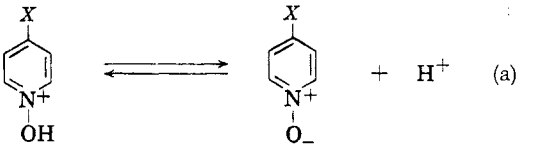


Figure 1

TABLE I

Compound	pK_a
4-Aminonicotinic acid 1-oxide	3.98 ± 0.03
4-Hydroxynicotinic acid 1-oxide	3.08 ± 0.02
4-Methoxynicotinic acid 1-oxide	2.88 ± 0.04
Nicotinic acid 1-oxide	2.74 ± 0.03
4-Chloronicotinic acid 1-oxide	1.80 ± 0.1
4-Nitronicotinic acid 1-oxide	0.50 ± 0.1



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