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CHROMIUM TRIOXIDE-3,5-DIMETHYLPYRAZOLE COMPLEX AS A REAGENT FOR OXIDATION OF ALCOHOLS TO CARBONYL COMPOUNDS

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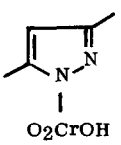
A wide range of alcohols can be oxidized efficiently and conveniently by a complex of chromium trioxide and 3,5-dimethylpyrazole. Addition of one equivalent of 3,5-dimethylpyrazole to a suspension o chromium trioxide in methylene chloride at room temperature forms a dark red solution; almost all the chromium trioxide dissolves within ten minutes. This complex is readily soluble in dichloromethane but sparingly soluble in ether or pentane.

The experimental study of the 3,5-dimethylpyrazole complex as a reagent for the oxidation of alcohols was prompted by the consideration that such a complex, formulated by analogy as I,[1] might



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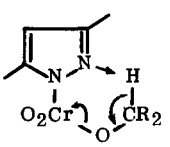

II

combine with an alcohol to form a chromate ester complex II from which oxidation could proceed by the cyclic, intramolecular course depicted. The outstanding utility of the chromium trioxide-pyridine complex[2] for the selective oxidation of alcohols provided an additional stimulus.

The chromium trioxide-dimethylpyrazole complex (ca. 5 mmole), prepared in situ, was treated with the alcohol (2 mmole) at room temperature; the reaction, followed either by thin layer

or vapor phase chromatography, was generally complete within 30 minutes. The reaction mixture was then evaporated and the residue was extracted with ether (or pentane) to separate the product from the bulk of the complex; alternatively, most of the complex could be removed by precipitation through the addition of five volumes of ether at the end of the reaction. The results of the oxidation are summarized in the table. The following experimental procedure is illustrative.

Acetophenone. 3,5-Dimethylpyrazole (580 mg, 6 mmole) was added to a suspension of chromium trioxide (600 mg, 6 mmole) in methylene chloride (20 ml) and the mixture was stirred at room temperature under argon for fifteen minutes. To the resulting dark red solution, α-phenylethanol (263 mg, 2.2 mmole) in dichloromethane (2 ml) was added in one portion and the reaction mixture was stirred at room temperature for 30 minutes (the reaction was monitored by vapor phase chromatography with a 6 ft, 5% Carbowax 20M column). The solvent was removed under reduced pressure, the brown residue was extracted with ether (50 ml) and the resulting mixture was filtered. The residue after concentration was dissolved in pentane and filtered through a short silica column. Evaporation of solvent gave acetophenone (260 mg, quantitative yield) identical with an authentic sample by ir and nmr spectra and pure by vapor phase chromatographic analysis.

The oxidation procedure has been used on amounts from 1 mmole to 0.1 mole of alcohol without difficulty. A molar solution of the oxidizing complex can be formed; both the initial and final complexes are soluble in methylene chloride but only sparingly soluble in ether. An alcohol can thus be oxidized on a 0.1 mole scale in a total reaction volume of 250 ml; on this scale, efficient stirring can be obtained using an external magnetic stirrer.

Table[a]

Alcohol	Product[b]	% Yield[c]
Geraniol	Geranial	96
Cyclohex-2-en-1-ol	Cyclohex-2-enone	83
Cinnamyl alcohol	Cinnamaldehyde	90
Oct-2-yn-1-ol[d]	Oct-2-ynal	75
Oct-1-yn-3-ol[d]	Oct-1-yn-3-one	78
Furfuryl alcohol[d]	Furfuraldehyde	47
Piperonyl alcohol	Piperonal	100
p-Nitrobenzyl alcohol	p-Nitrobenzaldehyde	98
Benzyl alcohol	Benzaldehyde	83
α-Phenylethanol	Acetophenone	100
Benzhydrol	Benzophenone	98
Octan-2-ol	Octan-2-one	93
Octan-1-ol	Octanal	84
β-Phenylethanol	Phenylacetaldehyde	70
4-t-Butylcyclohexanol	4-t-Butylcyclohexanone	98

Footnotes to Table

[a]The oxidations were performed on ca. 2 mmole of alcohol.

[b]Purity of product was established by comparison of products with authentic material (nmr and ir spectra, vapor phase chromatography) and where relevant melting point.

[c]The yield is based on isolated product.

[d]Oxidation at 0°; the other alcohols were oxidized at room temperature.

A typical example for an intermediate scale of oxidation is given.

4-t-Butylcyclohexanone. A mixture of cis- and trans-4-t-butylcyclohexanols (3.08 g, 20 mmole) in dichloromethane (10 ml) was added at room temperature over a period of 5 minutes to a stirred solution of the chromium trioxide-dimethylpyrazole complex (55 mmole) in methylene chloride (100 ml). The oxidation was complete after 40 minutes. Diethyl ether (500 ml) was then added to the reaction mixture, which was subsequently filtered, the precipitate washed with ether (50 ml) and the solvent then removed from the combined filtrate and washings. The residue was extracted with ether (75 ml); the ethereal extract was filtered, stirred over finely powdered sodium bisulphate, dried over magnesium sulphate and concentrated to give 4-t-butylcyclohexanone (2.95 g, 98%) of purity greater than 95%, mp 46-48°, having the same infrared and proton magnetic resonance spectra as authentic material.

The oxidative procedure described herein represents a promising addition to the existing methods.[2-7] The reagent is cheap and the experimental procedure is convenient over a wide range of both scale and structure.[8]

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