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SYNTHESIS OF 3,4-BIS(PIVALOYL)FUROXAN

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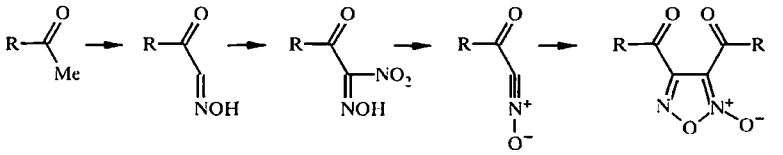
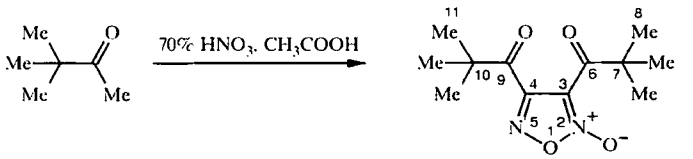
The interaction of alkylaryl (heteryl) methyl ketones with dilute nitric acid in acetic acid medium is one of the methods for preparing symmetrical furoxans [1,2].



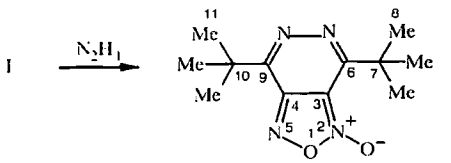
The reaction occurs *via* nitrosation of ketone, formation of nitrolic acid and its conversion to the corresponding nitrile oxide, dimerization of which gives the symmetrically substituted furoxan. The yield of furoxan depends on the structure of methyl ketone and on the concentration of the dilute nitric acid. For example 3,4-diaroylfuroxans were obtained in greater than 50% yield from aryl methyl ketones under action of 20-40% HNO_3. The reaction is much worse with aliphatic ketones: acetonylacetone was converted into the corresponding furoxan in a yield of 10%, ethyl acetoacetate gave 3% yield, while preparation of furoxan compound from pinacoline was completely unsuccessful. It was suggested that the principal cause of the low reactivity of aliphatic keto derivatives under these conditions was the difficulty of nitrosation [1].

We have observed that 3,4-di(2,2-dimethylpropanoyl)-1,2,5-oxadiazole-2-oxide (3,4-bis(pivaloyl)furoxan) (I) was formed in about 25% yield when 70% HNO_3 in acetic acid in the presence of nitrogen oxides (addition of sodium nitrite or nitric acid containing nitrogen oxides) was used.



I

The structure of 3,4-bis(pivaloyl)furoxan I was demonstrated by its conversion to the furoxanopyridazine–4,7-di(*tert*-butyl)[1,2,5]oxadiazolo-[3,4-*d*]pyridazine-1-oxide (II) on interaction with hydrazine hydrate analogously to [3].



II

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3,4-Di(2,2-dimethylpropanoyl)-1,2,5-oxadiazole-2-oxide (I). Mixture of pinacoline (60 g, 0.6 mol) and acetic acid (160 ml) was heated to 80-90°C, $NaNO_2$ (0.1 g) was added and then a mixture of acetic acid (120 ml) and 70% HNO_3 (102 ml) was added dropwise, keeping the temperature between 95 and 100°C (the reaction is exothermic and has an induction period). The reaction mixture was spontaneously cooled to room temperature and kept for two days after which it was poured onto ice. The precipitate was filtered off, washed with water and dissolved in pentane. The resultant solution was washed with 5% Na_2CO_3 solution (until gas evolution ceased), then with water, treated with activated charcoal and dried over anhydrous $CaCl_2$. Compound I (19 g, 25%) was obtained as colorless crystals; mp 30°C, after removing the solvent. IR spectrum: 2344, 1740, 1712, 1644, 1616, 1492, 1080 cm^{-1}. ^1H NMR spectrum (DMSO): 1.34 (CH_3, $C_{(9)}$–CH_3); 1.20 ppm (CH_3, $C_{(7)}$–CH_3). ^{13}C NMR spectrum (DMSO): 25.82 ($C_{(11)}$); 25.21 ($C_{(8)}$); 44.40 ($C_{(7)}$); 45.79 ($C_{(10)}$); 112.26 ($C_{(3)}$); 153.01 ($C_{(4)}$); 196.08 ($C_{(6)}$); 197.08 ppm ($C_{(9)}$). Found, %: C 56.3; H 7.2; N 10.8. $C_{12}H_{18}N_2O_4$. Calculated, %: C 56.6; H 7.1; N 11.0.

4,7-Di(*tert*-butyl)[1,2,5]oxadiazolo[3,4-*d*]pyridazine-1-oxide (II). 3,4-Bis(pivaloyl)furoxan I (3 g, 0.012 mol) was added with stirring at room temperature to solution of 98% hydrazine hydrate (3 g, 0.059 mol) in acetic acid (20-30 ml), the reaction mixture was kept at room temperature for 24 h, and was then poured into ice water. The precipitate was filtered off, washed with water, and dried in the air to give yellow glistening crystals of compound II (2.4 g, 81%); mp 95°C. IR spectrum: 2928, 1672, 1592, 1536, 1520, 1500, 1448, 1420, 1408, 1380, 1368, 1004, 984, 976 cm^{-1}. ^1H NMR spectrum (DMSO): 1.55 (CH_3, furazan); 1.4 ppm (CH_3, furoxan). ^{13}C NMR spectrum (DMSO): 28.29 ($C_{(11)}$); 27.18 ($C_{(8)}$); 37.76 ($C_{(7)}$); 38.19 ($C_{(10)}$); 108.68 ($C_{(3)}$); 145.50 ($C_{(4)}$); 155.96 ($C_{(6)}$); 160.28 ppm ($C_{(9)}$). Found, %: C 57.3; H 7.5; N 22.2. $C_{12}H_{18}N_4O_2$. Calculated, %: C 57.6; H 7.2; N 22.4.

REFERENCES

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