SYNTHESES OF HETEROCYCLES STARTING FROM 1-BROMO-3-(ADAMANTYL-1)PROPANONE

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A series of new adamantyl imidazolin-2-ones-, imidazol-2-thiones and 2-aminothiazoles have been obtained by the reaction of 1-bromo-3-(adamantyl-1)propanone with urea and thiourea.

Cyclic derivatives of urea and thiourea can cause maturation of Friend erthyroleukemia nuclei [1]. Imidazolinones have herbicidal activity [2] and are also used to prepare plasticisers for the polymer industry. imidazol-2-thiones have a wide spectrum of biological activity and are also used as stabilizers in the resin industry and as synthons for the preparation of a large number of organic compounds [3].

We have previously studied the reactions of bromomethyl(adamantyl-1)ketone (I) with derivatives of urea and thiourea and we have synthesized the corresponding adamantyl substituted imidazolinones and imidazol-2-thiones in yields of less than 30% [4], we had suggested that the low yields were associated with steric hindrance caused by the adamantyl group which has been frequently noted in the literature [5-8]. A natural presumption is that separation of this bulky group from the keto group by a single CH_2 unit should result in increased yields of products containing the adamantane group.

In a continuation of our work on the synthesis of new heterocycles with adamantyl substituents [4, 9] and the study of the behavior of α-halogenoketones of the adamantane series we have investigated the reactions of 1-bromo-3-(adamantyl-1)propanone (II) with urea (IIIa), thiourea (IVa), and their phenyl (IIIb, IVb) and acetyl (IIIc, IVc) derivatives. Only a few similar reactions are reported in the literature [10, 11]. For example, F. N. Stepanov and co-workers used compounds I and II in reactions with thioformamide in the Bischler synthesis noted small yields of heterocycles based on ketone II. In our view these were by-products.

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Molecular formula	m.p., °C	R_f[*2]	IR spectrum, cm^{-1}	Yield, %
Va	$C_{14}H_{20}N_2O$	291...293	0,193	2890, 2840, 3350, 1680	23
Vb	$C_{20}H_{24}N_2O$	304...306	0,343	2890, 2840, 3400, 1680	59
Vc	$C_{16}H_{22}N_2O_2$	303...305	0,781	2900, 2850, 3400, 1700	49
VIa	$C_{14}H_{20}N_2S$	91...92	0,113	2900, 2850, 3400, 1510, 1180	19
VIb	$C_{20}H_{24}N_2S$	78...80	0,484	2890, 2840, 3400, 1510	25
VIc	$C_{16}H_{22}N_2OS$	141...143	0,322	2900, 2850, 3320, 1710, 1490	78
VIIa	$C_{14}H_{21}N_2SBr$	167...168	0,433	2890, 2840, 3390, 1580	84
VIIb	$C_{20}H_{25}N_2SBr$	224...225	0,157	2900, 2850, 3400, 1600	60
VIIc	$C_{16}H_{23}N_2OSBr$	178...179	0,174	2910, 2860, 3350, 1700, 1590	98

*Compounds IIIa-c and IVc were recrystallized from ethanol, compounds IVb and c from chloroform

*2Eluent 1:4 acetone–CCl_4, but ethanol for compound IIIc.

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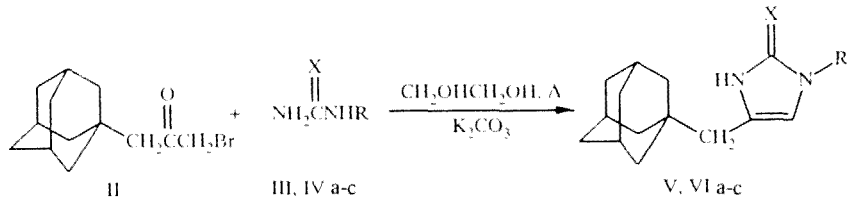
We have synthesized 4-(adamantyl-1-methylene)-N-R-imidazolin-2-ones (Va-c) and 4-(adamantyl-1-methylene)-N-R-imidazolin-2-thiones (VIa-c) in yields of 23-59% and 19-78% respectively (see Table 1).



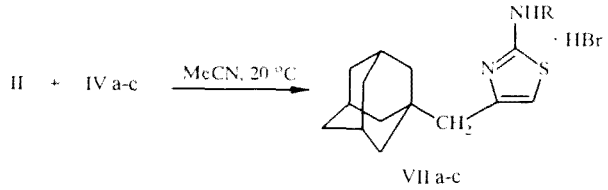
II III, IV a-c V, VI a-c

III, V X = O; IV, VI X = S; a R = H, b R = Ph, c R = Ac

The lower yields of compounds Va, Vc and VIa relative to the yields [4] of their homologs without the methylene bridge between adamantane and the heterocycle should be noted.

Use of the corresponding aminoketone in place of the halogenoketone in the reaction with urea is known to increase the yield of the imidazolin-2-one product [12]. However reaction of compound II with amines gave considerable tar formation and we were unable to obtain the desired aminoketones.

The reaction of ketone II with the thioureas IVa-c in acetonitrile at 20°C gave 2-(R-amino)-4-(adamantyl-1-methylene)thiazoles (VIIa-c) hydrobromides in 60-98% yield which is comparable with the yields of the analogous 2-(R-amino)-4-(adamantyl-1)thiazoles [5]:



VII a-c

VII a R=H, b R=Ph, c R=Ac

As a consequence of these results coupled with literature data we suggest that the yields at high temperatures of the products of the reactions discussed are determined by the presence of the methylene group in ketone II (which is associated with side reactions) and the nature of the substituents on urea and thiourea.

EXPERIMENTAL

The reactions were monitored and the purity of products were checked by TLC on Silufol UV-254 plates. IR spectra of thin films and KBr disks were recorded with Specord M-80 and IKS-22 spectrometers.

The principal characteristics of the products are cited in Table 1.

N-R-4-(Adamantyl-1-methylene)imidazolin-2-ones (Va-c) and N-R-4-(Adamantyl-1-methylene)imidazol-2-thiones (VIa-c). A mixture of ketone II (0.5 g, 1.8 mmol), urea III or thiourea IV (10.8 mol) and K_2CO_3 (0.14 g, 3.6 mmol) was heated in ethylene glycol (15 cm^3) for 3 h. The reaction mixture was cooled to room temperature an diluted with water, and the precipitated product was filtered off, washed with ether and recrystallized.

N-R-4-(Adamantyl-1-methylene)-2-aminothiazole Hydrobromides (VIIa-c). A solution of halogenoketone (II) (0.5 g, 1.8 mmol) in acetonitrile (5 cm^3) was added with stirring to a solution of a thiourea IV (2.7 mmol) in acetonitrile (5 cm^3). The product, which precipitated over 10-30 min, was filtered off and washed with ethyl acetate.

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