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REGIOSPECIFIC SYNTHESIS OF α-(PHENYLTHIO)KETONES VIA RHODIUM(II) ACETATE CATALYSED ADDITION OF THIOPHENOL TO α-DIAZOKETONES

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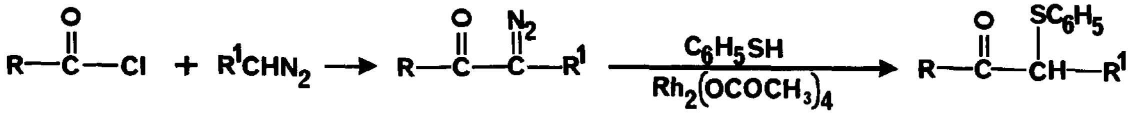
Summary αα-Addition of thiophenol to α-diazoketones is catalysed efficiently by rhodium(II) acetate in benzene solution at room temperature, offering a convenient regiospecific route to a variety of α-(phenylthio)ketones.

The versatility in synthesis of sulphur-containing substituents adjacent to the carbonyl group in aldehydes, ketones, carboxylic acids, esters, and lactones had led to the development of a number of useful transformations.[1] Most approaches to the introduction of sulphur-containing α-substituents involve either S_N2 displacement of a halogen atom from an α-halo carbonyl compound[2] or direct sulphenylation of a preformed enolate with a dialkyl or diaryl disulphide.[3] Since regiospecificity is frequently an important additional objective of the substitution process, the application of these methods requires access to regiodefined α-halo carbonyl compounds and enolates. We describe here a convenient alternative route which makes available a range of α-(phenylthio)ketones from non-ketonic precursors. The method is based on the insertion of α-diazocarbonyl compounds into acidic X-H bonds catalysed by transition metals. This reaction, which is formally an αα-addition with displacement of nitrogen, is well established with alcohols under copper,[5] palladium,[6] and rhodium[7] catalysis. We have found that thiophenol undergoes very efficient αα-addition to a variety of α-diazoketones in the presence of catalytic amounts of rhodium(II) acetate in benzene solution at room temperature. Since many acyclic α-diazoketones (3) can be prepared in excellent yield from acyl chlorides (1) and diazoalkanes (2), this route to α-(phenylthio)ketones (4) does not depend on the production of α-halo ketones or regiospecific enolates nor does it require the availability of the parent ketone. The following procedure is representative for the substrates summarised in the Table; the yields quoted refer to analytically pure products.



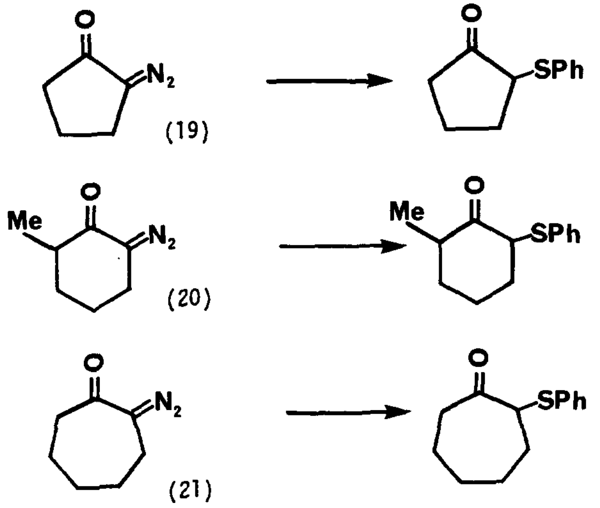
1 2 3 4

To a stirred solution of thiophenol (0.61g) in dry benzene (40 ml) containing rhodium(II) acetate (1 mg) was added a solution of diazoacetone (5) (0.42g) in dry benzene (10 ml) over 10 minutes at room temperature; nitrogen evolution was observed over the addition period. After an additional 25 minutes the solution was washed with 5% aqueous sodium hydroxide and water, then dried and concentrated to yield α-(phenylthio)acetone (0.79g,95%) of >95% purity by nmr. An analytically pure sample was obtained by distillation at 125-130°C/0.75 mm Hg. The product crystallised on standing, mp 31-32°C (lit.[8] 33-34°C).

Substrates (5)-(18) in the Table were prepared from the corresponding acyl chlorides and converted into the α-(phenylthio)ketones shown. Comparison of entries (5) and (11) shows that α-diazoketones derived from diazomethane and diazoethane produce adducts with comparable ease. Thus this route may be generally useful for

TABLE

α-Diazoketone		α-(Phenylthio)ketone	Yield
CH_3COCHN_2(5)	→	CH_3COCH_2SPh	84%
$PhCOCHN_2$(6)	→	$PhCOCH_2SPh$	72%
p-$CH_3C_6H_4COCHN_2$(7)	→	p-$CH_3C_6H_4COCH_2SPh$	79%
$PhCH_2COCHN_2$(8)	→	$PhCH_2COCH_2SPh$	76%
$PhCH_2CH_2COCHN_2$(9)	→	$PhCH_2CH_2COCH_2SPh$	73%
$PhCH_2CH_2CH_2COC(CH_3)N_2$(10)	→	$PhCH_2CH_2CH_2COCH(CH_3)SPh$	71%
$CH_3COC(CH_3)N_2$(11)	→	$CH_3COCH(CH_3)SPh$	83%
$N_2CHCO(CH_2)_4COCHN_2$(12)	→	$PhSCH_2CO(CH_2)_4COCH_2SPh$	81%
$N_2CHCO(CH_2)_5COCHN_2$(13)	→	$PhSCH_2CO(CH_2)_5COCH_2SPh$	86%
$N_2CHCO(CH_2)_6COCHN_2$(14)	→	$PhSCH_2CO(CH_2)_6COCH_2SPh$	85%
$N_2CHCO(CH_2)_7COCHN_2$(15)	→	$PhSCH_2CO(CH_2)_7COCH_2SPh$	88%
$N_2CHCO(CH_2)_8COCHN_2$(16)	→	$PhSCH_2CO(CH_2)_8COCH_2SPh$	86%
$N_2CHCO(CH_2)_{10}COCHN_2$(17)	→	$PhSCH_2CO(CH_2)_{10}COCH_2SPh$	88%
$N_2CHCO(CH_2)_{12}COCHN_2$(18)	→	$PhSCH_2CO(CH_2)_{12}COCH_2SPh$	92%



(19) 76%

(20) 72%

(21) 75%

$N_2CHCO_2CH_2CH_3$ (22) $\longrightarrow$ $PhSCH_2CO_2CH_2CH_3$ 75%

regiospecific α-activation of methyl and ethyl ketones in situations where conventional regiospecific enolate formation is difficult or impossible. Entry (10) provides an illustrative example of the regiospecific introduction of an α-(phenylthio) substituent at a position that would be very difficult to functionalise regiospecifically if one were to start with the parent ketone, $PhCH_2CH_2CH_2COCH_2CH_3$. The method works equally well with difunctional α-diazoketones as is demonstrated by entries (12)-(18), each of which produced the appropriate αω-bis-α-(phenylthio)ketone in excellent yield. Cyclic α-diazoketones (19), (20), and (21)[9] are also smoothly converted to α-(phenylthio)cycloalkanones[10] using this simple catalytic procedure and the final entry, ethyl diazoacetate (22) illustrates the application of the method to the production of α-(phenylthio) esters.

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10. Products were identified by their spectroscopic properties and all new compounds gave satisfactory analytical data on combustion.

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