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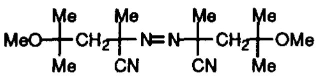
Additions of Malononitrile Radicals to Alkenes under Mild Conditions using 2,2'-Azobis-(2,4-dimethyl-4-methoxyvaleronitrile) (V-70) as an Initiator

Yasuyuki Kita*[a], Atsunori Sano[b], Takahiro Yamaguchi[b], Masahisa Oka[b], Kentoku Gotanda[a]
and Masato Matsugi[a]

[a]Faculty of Pharmaceutical Sciences, Osaka University, 1-6, Yamada-oka, Suita, Osaka 565, Japan
[b]Tokyo Research Laboratories, Wako Pure Chemical Industries, Ltd., 1633, Matoba, Kawagoe, Saitama 350-11, Japan

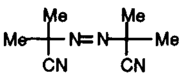
***Abstract*:** The attributes of 2,2'-azobis-(2,4-dimethyl-4-methoxyvaleronitrile) (V-70), which is an effective radical initiator at low temperature, in contrast to 2,2'-azobisisobutyronitrile (AIBN) are described. © 1997 Elsevier Science Ltd.

Although 2,2'-azobisisobutyronitrile (AIBN) is commonly used as the radical initiator in radical addition reactions, it requires an elevated temperature for the generation of the radicals. On the other hand, it was suggested that a similar azonitrile compound, 2,2'-azobis-(2,4-dimethyl-4-methoxyvaleronitrile) (V-70),[1] which is known as an effective initiator in the synthesis of polymers,[2] is expected to generate radical species at room temperature or below, because the half life data of this compound indicated a more unstable species than AIBN.[3] In spite of this half life data, there is no report on the use of V-70 as a radical initiator below room temperature. We wish to report some benefits when using V-70 as the radical initiator at low temperature in contrast to AIBN.



$$MeO{-}\overset{Me}{\underset{Me}{C}}{-}CH_2{-}\overset{Me}{\underset{CN}{C}}{-}N{=}N{-}\overset{Me}{\underset{CN}{C}}{-}CH_2{-}\overset{Me}{\underset{Me}{C}}{-}OMe$$

V-70

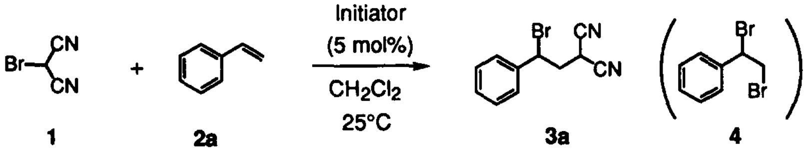


$$Me{-}\overset{Me}{\underset{CN}{C}}{-}N{=}N{-}\overset{Me}{\underset{CN}{C}}{-}Me$$

AIBN

Radical addition reactions of bromomalononitrile (**1**) to styrene (**2a**) were examined at room temperature in the presence of a radical initiator and the results are summarized in Table 1.[4] The reaction did not proceed at room temperature using AIBN and the typical peracid radical initiator benzoyl peroxide (BPO) (Entries 1 and 2). In the case of Et3B, which is known as a useful radical initiator at low temperature,[5] the yield of the desired adduct (**3a**) was low probably due to the decomposition of **1** (Entry 3). On the other hand, V-70 is quite effective for inducing the addition of **1** to **2a** at 25 °C to give **3a** in a satisfactory yield (Entry 5). The adduct **3a** was identical with an authentic sample which was obtained by the photo-irradiation method[6] (Entry 4). An important point in this reaction is that the dibromo derivative **4** is preferentially formed when the reaction mixture of **1** and **2a** is heated in refluxing benzene or toluene to generate the radical species in the presence of AIBN.

Table 1: Addition of bromomalononitrile **1** to styrene **2a** using various radical initiators



Entry	Initiator	Time(hr)	Yield(%) of **3a**
1	AIBN	24	no reaction[a]
2	BPO	24	no reaction
3	Et_3B	18	44
4	$h\nu$[b]	6	85
5	V-70	12	79

[a] If the reaction mixture was heated to generate the radical species, the dibromo adduct 4 was preferentially formed (33% yield).

[b] A 400W high-pressure mercury lamp was used through a Pyrex filter.

Next, we examined the effect of the temperature and the ability of chain propagation using V-70 as the initiator (Table 2). Although the relative reaction rate was somewhat low, a satisfactory yield of the adduct 3a was obtained at 0 °C (Entry 5). Furthermore, 3a was obtained in 80% yield even if a 1 mol% amount of V-70 was used (Table 3).

Table 2: Effects of the temperature on the radical addition reactions of bromomalononitrile **1a** to styrene **2a** using V-70 (5mol%)

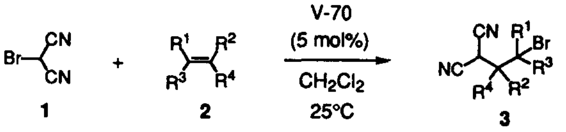
Entry	Temp.(°C)	Time(hr)	Yield(%) of **3a**
1	25	12	79
2	10	24	71
3	10	36	80
4	0	24	56
5	0	48	89

Table 3: Effects of the ratio of V-70 on the radical addition reactions of bromomalononitrile **1** to styrene **2a**

Entry	Ratio of V-70(mol%)	Time(hr)	Yield(%)
1	10.0	6	71
2	5.0	12	79
3	1.0	48	80
4	none	48	no reaction

The generality of the additions of **1** to other alkenes (**2b-j**) using V-70 was then examined (Table 4). The corresponding adducts (**3b-j**) were obtained in high yields under similar mild conditions. It is noteworthy that the malononitrile radical cleanly reacts with oxygen-substituted alkenes (**2f, g**) using V-70 at room temperature (Entries 6 and 7), although the addition of iodomalononitrile to oxygen-substituted alkenes using AIBN under the heated conditions was unsuccessful.[7]

Table 4: Additions of bromomalononitrile **1** to various alkenes **2** using V-70

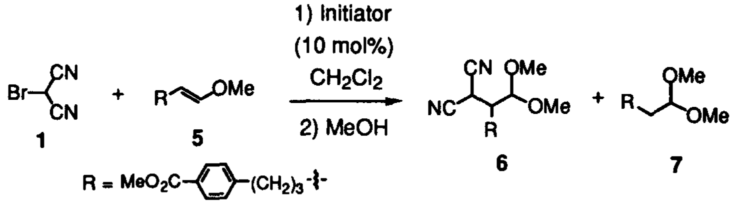


Entry	Alkene 2					Time(hr)	Yield of 3(%)
		R^1	R^2	R^3	R^4		
1	**a**	Ph	H	H	H	12	79
2	**b**	Ph	H	H	Me	72	68
3	**c**	Me	Me	Me	H	12	81
4	**d**	Me	Me	Me	Me	12	84
5	**e**	$I(CH_2)_8$	H	H	H	24	78
6	**f**	OAc	H	H	H	24	76
7	**g**	OEt	H	H	H	24	72
8	**h**	cyclopentene				24	88^a
9	**i**	cyclohexene				24	90^b
10	**j**	norbornene				24	89^c

The molar ratios of the *trans*- to *cis*-isomer were 2.82^a, 1.02^b, 0.18^c.

In addition, the advantage of V-70 over AIBN was observed in the reaction of **1** and an activated oxygen-substituted styrene derivative (**5**) followed by alcoholysis[8]. The use of V-70 predominantly gave the desired radical adduct (**6**) via a carbon-carbon bond forming reaction in good yield, although the use of AIBN predominantly gave the product (**7**) generated from the dibromo adduct (RCHBrCHBrOMe) (Table 5).

Table 5: Additions of bromomalononitrile **1** to **5**



Entry	Initiator	Time(hr)	Temp.(°C)	Combined yield of 6 and 7 (%)	ratio* 6	ratio* 7
1	V-70	2	25	80	55	45
2	AIBN	24	25	55	10	90

* Ratio was determined by ^1H NMR of crude products.

Although it is unclear why V-70 is so effective for the radical addition reactions, the use of V-70 causes radical addition reactions at room temperature or below and affords a high yield of the addition products. Other useful reactions using the excellent radical initiator, V-70, are now being developed.

References and Notes

1. 2,2'-Azobis-(2,4-dimethyl-4-methoxyvaleronitrile) is commercially available from Wako Pure Chemical Ind. Ltd., (Japan) and the abbreviation in parentheses is its trade name. This compound is a mixture of diastereomeric isomers whose melting point are 58 °C and 107 °C and should be stored below -10 °C to prevent any decomposition. V-70 is stable in a refrigerator for a few months and the pure V-70 can be easily obtained by the following procedure: V-70 (10.0 g, ca. 90% content) was added to dry acetone (20ml) at -10 °C under stirring. The heterogeneous solution was stirred for 30 min at -10 °C. Collecting the crystalline precipitates afforded 6.2g of pure V-70 (62%, >99% content).
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3. The temperature at which half of an initiator is decomposed in ten hours in toluene (first-order decomposition[2b]): AIBN, 65 °C; V-70, 30 °C.
4. Typical procedure: A mixture of **1** (10mmol), **2a** (10mmol) and V-70 (5mol%) in CH_2Cl_2 (10ml) was stirred at room temperature in the dark. After 12hr, the mixture was concentrated *in vacuo*. The residue was recrystallized from IPA (10ml) to give **3a** in 79% yield.
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